

14th International Symposium on Trace Elements in Man and Animals

Enshi, Hubei, China
September 19-24, 2011

Meeting in Se-Enriched Enshi, China
Exploring Trace Elements:
Science, Innovation, & Application





The 14th International Symposium on
Trace Elements in Man and Animals
第十四届国际人与动物微量元素大会

Dear Colleagues,

On behalf of the TEMA Parent Committee and the TEMA14 Organization Committee, we are pleased to welcome you to the 14th International Symposium on Trace Elements in Man and Animals, September 19-24, 2011, Enshi, Hubei, China.



The theme for the symposium is: Meeting in Se-Enriched Enshi, Exploring Trace Elements: Science, Innovation, & Application. We have received approximately 240 abstracts from active researchers around the world. The scientific program has been devised with a pre-Conference Se Forum, 3 Sunrise/Breakfast Lessons, 5 Plenary Sessions, 16 Symposia, and 2 Poster Sessions. The breadth and depth of the scientific program highlights current progress of trace element research and application. All delegates shall have ample opportunity to share their own new findings and to exchange ideas with colleagues in fields of their particular interest.

The social program includes a welcome reception, a full-day trip, a banquet, and a performance show of folk song and local dance. These activities are designed to create opportunities for maximal personal interaction and network with peers from different parts of the world.

We cordially invite you to read through this booklet to find out useful information on the scientific and social programs and other functions of TEMA14. After a warm summer, Enshi enters its best season of a year in September, with an average day-temperature of 24°C. We sincerely hope that you will enjoy not only the scientific venue of TEMA14, but also the nature beauty and splendid culture of Enshi. Our goal is to make your TEMA14 one of the most exciting, stimulating, and rewarding conferences.

Sincerely yours,

Xingen Lei, Ph.D.
Professor of Molecular Nutrition
Cornell University, Ithaca, NY, USA
Chair, TEMA14



14th International Symposium on Trace Elements in Man and Animals

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Exploring Trace Elements:
Science, Innovation, & Application



Local Hosts:

Enshi City Government, Hubei, China

Huazhong University of Science and Technology, Wuhan, China

Hubei Province Society of Selenium Resources Development and Utilization

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Chinese Nutrition Society

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TEMA14 Underwood Lecture Award

Raymond F. Burk



Dr. Burk is a Professor of Medicine and Pathology at Vanderbilt University, Nashville, Tennessee, USA. He received his B.A. degree from the University of Mississippi in 1963 and his M.D. from Vanderbilt University in 1968. After his intern and resident years, he served as a Research Internist in the U.S. Army Medical Research and Nutrition Laboratory in Denver, Colorado. From 1975 to 1987, Dr. Burk was Assistant, Associate, and Full Professor of Internal Medicine and Biochemistry at The University of Texas Southwestern Medical School at Dallas, Louisiana State University, and The University of Texas Health Science Center at San Antonio. From 1987 to the present, he has served as Professor of Medicine at Vanderbilt University as well as Director of the Division of Gastroenterology (1987-1998), Director of the Clinical Nutrition Research Unit (1995-2004), and founding Director of the Vanderbilt Center for Human Nutrition.

Dr. Burk began working on selenium in 1964 while he was a medical student. In his first research project he found that blood selenium was depressed in Guatemalan children with kwashiorkor. He followed up that observation with a series of clinical studies with Professor Y. Xia in Sichuan Province. Their findings have characterized selenium deficiency in populations of low-selenium areas and provided data to estimate the human selenium requirement. In complementary U.S. studies his group demonstrated that some patients with cirrhosis are selenium deficient. These clinical studies tie basic advances to the needs of the population and patients.

In the mid-1970s, Dr. Burk began to examine metabolic effects of selenium deficiency and found that hepatic heme metabolism was altered by selenium deficiency. Heme oxygenase activity was sharply up regulated in selenium-deficient rat liver. His group showed that glutathione S-transferase activity and glutathione synthesis were also up regulated and that this resulted in selenium deficiency protecting against liver injury caused by acetaminophen and by aflatoxin. In recent years, Dr. Burk's group has shown that selenium deficiency activates the Nrf2-ARE pathway by lowering thioredoxin reductase activity. This activation induces a number of protective enzymes and illustrates the relationship of selenium with oxidant defense enzymes.

In the 1970s and early 1980s, Dr. Burk and others reported the existence of plasma and liver proteins that bound selenium, suggesting that selenoproteins other than glutathione peroxidase existed. In the 1980s, Dr. Burk's group purified the major plasma selenoprotein, selenoprotein P (Sepp1), and characterized it. They subsequently cloned it and developed immunoassays to measure Sepp1 in rats, mice, and humans. Using knockout mice, they and the Berlin group showed that Sepp1 is responsible for supplying selenium to the brain and the testis. Dr. Burk's group then showed that the lipoprotein receptor apoER2 facilitates endocytosis of Sepp1 in the brain and testis while another related receptor, megalin, facilitates endocytosis of Sepp1 fragments by the proximal convoluted tubule cells of the kidney. Their finding that Sepp1 regulated whole-body selenium by competing with the production of urinary selenium metabolites in the liver shows how Sepp1 is central to selenium homeostasis.

For 47 years, Dr. Burk has made outstanding contributions to our understanding of human selenium metabolism and requirement. Dr. Burk has received the Lederle Award in Human Nutrition and the Osborne and Mendel Award from the American Institute of Nutrition, a MERIT Award from the NIH, and a Jinding Award from Sichuan Province, China. He has been happily married to Enikoe since 1967, and has had the good fortune to have Dr. K. E. Hill as a colleague for the last 31 years.



TEMA14 Distinguished International Collaboration Award

Yiming Xia

Professor Yiming Xia is the former Head of the Department of Trace Element Nutrition, Institute of Nutrition and Food Hygiene, Chinese Academy of Preventive Medicine, Beijing. After graduating from Fu Dan University, Shanghai, she served from 1964 to 1981 as a Research Assistant and Research Associate in the Institute of Health of the Chinese Academy of Medical Sciences, Beijing. Afterward, she became a Visiting Scientist at three active selenium laboratories in the US: first at Oregon State University, Corvallis (1981-1983); then twice at The University of Texas Health Science Center at San Antonio (1983-1984 and 1986-1987); and finally at the University of Missouri-Columbia (1998-1999). From 1984 to 2001, she served as Research Associate, Associate Professor, Professor, Head of the Maternal and Child Nutrition Department, and Head of Trace Element Nutrition, Institute of Nutrition and Food Hygiene of the Chinese Academy of Preventive Medicine, Beijing. From 2001 to 2005, Professor Xia was a Professor Emerita in the same Institute that had been renamed the Chinese Center for Disease Control and Prevention. From 2005 to 2010, Professor Xia was a Visiting Professor at the Sichuan Center for Disease Control and Prevention in Chengdu, China

Professor Xia began her selenium research in 1969 as a member of the Keshan Disease Research Group. In addition to studying this endemic cardiomyopathy, she has studied the biochemical characteristics of low-selenium populations and their response to selenium supplementation. Her work has provided data critical to determining the human selenium requirement. She has published a total of 130 articles on selenium and is the senior author of 70 of those publications. Due to its discovery of a close relationship between selenium deficiency and the incidence of Keshan Disease, the Keshan Disease Research Group, of which Professor Xia was a member, received team awards from the Chinese Ministry of Public Health in 1978, 1990 and 1998 and the Schwarz Medal from the International Association of Bioinorganic Scientists in 1984.

Professor Xia has been well known as an invaluable collaborator with the international community and for her key role in several NIH-funded studies on human selenium metabolism and requirement that were conducted in selenium-deficient areas of China. From 1986 to 1994, she served as a co-Principal Investigator for the project entitled, “Myocardial Oxidant injury: Keshan Disease as a Model”, in collaboration with Dr. R. F. Burk, through the University of Texas and Vanderbilt University. From 1987 to 1990 and 1994 to 1998, she collaborated with Dr. P. D. Whanger, Oregon State University, on the project entitled, “Effects of Selenium Intake on Human Blood and Urine Fraction”. From 2001 to 2010, she once again collaborated with Dr. R. F. Burk on the project entitled, “Human Selenium Nutritional Requirement and Biomarkers in Health and Disease”. Professor Xia was key to the success of all these studies. She has provided all her international colleagues with excellent knowledge of the human subjects in the testing area, strong leadership in supervising the local research teams, and an unselfish spirit toward recognitions derived from the success of the projects.

Over four decades, Professor Xia has made excellent contributions to international selenium nutrition research. She was awarded the Oldfield Prize by Oregon State University, USA in 1992. She has been highly regarded by her colleagues around the world, and has given many invited talks on selenium. She was the Secretary-General for the 6th International Symposium on Selenium in Biology and Medicine held in Beijing in 1996 and has served as an international committee member of subsequent ones.



TEMA14 Special Recognition Award
Donald Oberleas

Dr. Donald Oberleas is a Professor of Emeritus at Texas Tech University, Lubbock, Texas, USA. He was born on February 14, 1933 as the 7th child of a family of 8, and graduated from Sheridan High School, Indiana, in May 1951. He received a B.S. in Agriculture in 1955 from Purdue University, Indiana, and attended Graduate School at the same University, completing in January 1956. After he was drafted into the U.S. Army in February 1956 and finished his military service, he completed a M.S. in Agriculture at the University of Kentucky, Lexington where he studied sheep diets utilizing urea as the sole source of nitrogen and demonstrated that if much of the diet was provided by starch there was no ammonia toxicity. He then joined the Graduate Program in the Department of Agricultural Chemistry University of Missouri-Columbia to work with Dr. Boyd O'Dell, who was the first to demonstrate that phytate is an important compound in the genesis of zinc deficiency. Dr. Oberleas extended this concept to swine and the albino rat that became the species of choice.

After completing his Ph.D. degree in August 1964, he went to work at Wayne State University with Drs. Ananda Prasad and James Halstead, who were looking for someone to develop an animal colony and supervise laboratories with an interest in studying the metabolic effects of zinc deficiency. This was a successful match and in addition, they hosted two symposia in Detroit and a third written symposium for the American Journal of Clinical Nutrition. As Dr. Prasad was also a hematologist, Professor Oberleas had a chance to study some interesting hematological problems. He also collaborated with Drs. E.R. Miller and Richard Leucke of Michigan State University and Dr. George Brewer of University of Michigan. In 1976, Professor Oberleas took up the position of Chairman, Department of Food and Nutrition at The University of Kentucky, Lexington. After 7 further successful years, he took a 6 month sabbatical at the Agricultural Research Center, U.S. Department of Agricultural, Beltsville, MD to extend his existing research. He then became Chairman of Nutrition and Food Science Department, Texas Tech University, Lubbock. During this time he spent a sabbatical with Gerber Products Company, Fremont, Michigan. There he improved an HPLC analytical method for phytate and analyzed samples of all of the cereals and flour samples to be used in infant food manufacture. This information allowed accurate fortification of cereals which Gerber began in June 1997 and market share has increased from about 65% to over 90. To date, that would have affected 35-40 million babies, in the United States. Since 1969, Professor Oberleas has attended all 14 TEMA symposia held in different parts of the world. He is receiving this special recognition award not only for his faithful participation in this "TEMA family" but also for his long-term contribution to trace element research.

Winners of Graduate Student and Postdoctoral Paper Competition

Oral Presentation

First Place (US\$500)

Ewa Szymlek-Gay, Umeå University, Sweden

Second Place (US\$300)

Bianca Mergler, MRC Human Nutrition Research, UK

Third Place (US\$200)

Ethel H. Alcantara, Andong National University, Republic of Korea

Poster Presentation

First Place (US\$500)

Antonio Pinto, Heinrich-Heine-University, Germany

Second Place (US\$300)

Liyong Qiu, Sichuan University, Chengdu, China

Third Place (US\$200)

Ying Qi, Dalla Lana School of Public Health, Canada

Winners of Graduate Student and Postdoctoral Fellowship

<i>Name</i>	<i>Institute</i>
Ethel H. Alcantara	Andong National University, Republic of Korea
Dan Chen	Iowa State University, USA
Hongjie Chen	Huazhong University of Science and Technology, Wuhan
Xiaoman Dai	Medical School of Nanjing university, Nanjing
Shibin Ding	Huazhong University of Science Technology, Wuhan
Daoyin Dong	Sichuan University, Chengdu
Zhaoxin Fan	Sichuan University, Chengdu
Diego Gaitan	INTA - University of Chile, Chile
Yan Ge	Sichuan University, Chengdu
Yu Guo	China University of Geosciences, Wuhan
Jianglong Hou	Sichuan University, Chengdu
Xiaobo Hu	Nanchang University, Nanchang
Jiaqiang Huang	Sichuan Agricultural University, Chengdu
Rachel Hurst	Norwich Medical School, University of East Anglia, UK
Xuming Jia	Harvard School of Public Health, USA
Yi Jia	Huazhong University of Science and Technology, Wuhan
Shun Li	Sichuan University, Chengdu
Xiaoqi Lu	University of Science and Technology of China, Suzhou
Bianca Mergler	MRC Human Nutrition Research, UK
Agnes Michalczyk	Deakin Universty, Australia
Ou Ou	Rowett Institute of Nutrition & Health, University of Aberdeen, UK
Antonio Pinto	Heinrich-Heine-University, Germany
Danielle Pogge	Iowa State University, USA
Ying Qi	University of Toronto, Canada
Liyang Qiu	Sichuan University, Chengdu
Shelley Rhodes	Rowett Institute of Nutrition & Health, University of Aberdeen, UK
Chengkang Tang	Sichuan University, Chengdu
Abdulahadi Cihangir Uguz	Suleyman Demirel University, Turkey
Eva Katrin Wirth	Charité-Universitaetsmedizin Berlin, Germany
Min Hsuan Wu	Fu-Jen University, Taipei
Xi Yan	Cornell University, USA
Dan Yu	Institute of Nutrition and Food Safety, China CDC, Beijing
Ding Yuan	Sichuan University, Chengdu
Linxi Yuan	University of Science and Technology of China, Suzhou
Ningbo Zhang	Chinese Academy of Agricultural Sciences, Beijing
Zhuzhen Zhang	Institute for Nutritional Sciences, SIBS, CAS, Shanghai
Xiao Zuo	Sichuan University, Chengdu

CONTENTS

Conference Schedule	1
Scientific and Social Programs	2
Poster Presentation List and Schedule	31
Selenium Forum Abstracts	37
Plenary Session Abstracts	45
Symposium 1(A) Abstracts	62
Symposium 2(B) Abstracts	74
Symposium 3(C) Abstracts	86
Symposium 4(D) Abstracts	98
Symposium 5(E) Abstracts	105
Symposium 6(F) Abstracts.....	113
Symposium 7(G) Abstracts	124
Symposium 8(H) Abstracts	133
Symposium 9(I) Abstracts.....	145
Symposium 10(J) Abstracts	158
Symposium 11(K) Abstracts	169
Symposium 12(L) Abstracts	179
Symposium 13(M) Abstracts	190
Symposium 14(N) Abstracts.....	201
Symposium 15(O) Abstracts.....	212
Symposium 16(P) Abstracts.....	223
Poster Presentation Abstracts	233
Author Index	302
List of Participants	310
Schematic Drawing of the Meeting Hotel Location in Enshi.....	320
Schematic Drawing of the Meeting Rooms.....	321
Acknowledgements.....	324

TEMA14

14th International Symposium on Trace Elements in Man and Animals Enshi, Hubei, China, September 19-24, 2011

September 19	September 20	September 21	September 22	September 23	September 24
Registration: Reception Desk Open (8:30am-12:00noon)	Sunrise/Breakfast Lesson (7:10-7:45am)	Sunrise/Breakfast Lesson (7:10-7:45am)	Breakfast (7:00-8:00am) Tour of Enshi Sites (8:30am-5:30pm)	Sunrise/Breakfast Lesson (7:10-7:45am)	Breakfast (7:00-8:00am) Departure Have a safe trip home (8:00am-12:00noon)
	Plenary Session 1 (8:00-9:30am)	Plenary Session 3 (8:00-9:30am)		Symposia 12-16 (8:00am-12:30pm)	
	Poster Presentation/View and Coffe/Tea Break (9:30-10:30am)	Poster Presentation/View and Coffe/Tea Break (9:30-10:30am)		Coffe/Tea Break (10:00-10:30am)	
	Plenary Session 2 (10:30am-12:00noon)	Plenary Session 4 (10:30am-12:00noon)		Registration (8:00am-12:00noon)	
	Registration (8:00am-12:00noon)	Registration (8:00am-12:00noon)		Lunch (12:30 -1:45pm)	
	Poster Display (7:30am-7:00pm)	Poster Display (7:30am-7:00pm)		Plenary Session 5 (2:00-4:30pm)	
Lunch (12:00pm-14:00pm)	Lunch (12:00noon-1:20pm)	Lunch (12:00noon-1:20pm)	Registration: Reception Desk Open (1:00-7:00pm)	Closing Ceremony (4:40-5:20pm)	Welcome Reception (7:00-9:00pm)
Symposia 1-6 (1:30-6:30pm)	Symposia 7-11 (1:30-6:30pm)	Symposia 1-6 (1:30-6:30pm)			
Coffe/Tea Break (3:40-4:00pm)	Coffe/Tea Break (3:40-4:00pm)	Registration (1:00-6:00pm)			
Registration (1:00-6:00pm)	Dinner (7:00-8:30pm)	Dinner (7:00-8:30pm)	Dinner (7:00-8:30pm)	Farewell Banquet (6:00-7:30pm) Performance Show (Folk song and Dance) (8:00-9:30pm)	

Scientific and Social Programs of TEMA14

Monday, September 19, 2011

Morning Sessions

Registration (8:00am-12:00noon)

Lobby, Fuyuan Guobin Hotel

Pre-Conference Selenium Forum (8:20am –12.00 noon)

Title: Selenium in 21 Century: Science, Health, and Economy

Sponsor: TEMA-14 and Enshi City Government

Location: Large Auditorium, Fuyuan Guobin Hotel

8:20-8:40

Enshi City Leaders

Welcome and introduction

8:40– 8:50

X. G. Lei, TEMA14 Chair, Cornell University, USA

Welcome and introduction of invited speakers and chairs

Session I

Chairs: Dolph Hatfield, NCI, NIH, USA

Kaixun Huang, Huazhong University of Science and Technology, Wuhan

8:50-9:10

Roger A. Sunde

University of Wisconsin, USA

Chemistry, metabolism, requirements, and regulation of selenium (Se-F01)

9:10-9:30

Raymond F. Burk¹, Yiming Xia², Kristina E. Hill¹

¹Vanderbilt University School of Medicine, Nashville, TN, USA; ²Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention, Beijing

Biomarkers of selenium and determination of its requirement by humans (Se-F02)

9:30-9:50

Philip Taylor¹, Sanford Dawsey¹, Christian Abnet¹, Youlin Qiao²

¹Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, Bethesda, MD, USA; ²Cancer Institute, Chinese Academy of Medical Sciences, Beijing

Cancer prevention: the trials and tribulations of selenium (Se-F03)

9:50-10:10

Josef Köhrle

Charite Universitätsmedizin Berlin, Germany

Role of selenium in thyroid metabolism and chronic diseases (Se-F04)

10:10-10:30

Coffee/Tea Break

Session II

Chairs: Roger Sunde, University of Wisconsin, USA

Junquan Gao, Chinese Center for Disease Control and Prevention, Beijing

10:30-10:50

John Finley

USDA/ARS, USA

Pros and cons of selenium biofortification: Regulatory and legal considerations (Se-F05)

10:50-11:10

Zhengyu Bao

Faculty of Material Sciences and Chemistry, China University of Geosciences, and National Key Lab of Geological Process and Mineral Resources, Wuhan

Selenium resource in China and its potential impact on humankind (Se-F06)

11:10-11:30

Kunli Luo

Chinese Academy of Sciences, Beijing

Biosource of selenium in Enshi (Se-F07)

11:30-12:00

Mary L'Abbe

University of Toronto, Canada

Selenium capital ceremony

12:00 noon-2:00pm

Lunch, Ballroom, Fuyuan Guobin Hotel

Afternoon Session

Registration (1:00-7:00)

Lobby, Fuyuan Guobin Hotel

Evening Session

Welcome reception (7:00-9:00)

Ballroom, Fuyuan Guobin Hotel

Tuesday, September 20, 2011

Registration (8:00am-6:00pm)

Lobby, Fuyuan Guobin Hotel

Poster Display (7:30am-7:00pm)

Odd-numbered posters (e.g., PT1, 3, 5, 67) are displayed today (Tuesday, September 20, 2011)

Presentation time: 9:30-10:30am

Presenter: must stand before the poster during 9:30-10:30am for questions

Location: the corridor of Fuyuan Guobin Hotel

Morning Sessions

Sunrise/Breakfast Lesson (7:10-7:45)

Chair: Bo Lonnerdal, UC-Davis, USA

Speaker: John Beattie and Harry J. McArdle, Rowett Institute of Nutrition and Health, UK
Donald Oberleas, Texas Tech University, Lubbock, Texas, USA

Title: Why TEMA: past, present, and future?

Location: Ballroom, Fuyuan Guobin Hotel

Plenary Session 1 (8:00-9:30)

Location: Large Auditorium, Fuyuan Guobin Hotel

Chairs: Fengying Zhai, Chinese Society of Nutrition, Beijing
Emorn Wasantwisut, Mahidol University, Thailand

8:00-8:30

Robert J. Cousins

University of Florida, USA

Advances in zinc transporters and metabolism (PS-01)

8:30-9:00

Lothar Rink

Institute of Immunology, RWTH-Aachen University, Pauwelsstr, 30, D-52074 Aachen, Germany

Zinc homeostasis and signaling in the immune system (PS02)

9:00-9:30

M Leigh Ackland¹, Agnes A Michalczyk¹, Loveleen Kumar¹, Dianne Ford², Taiho Kambe³

¹Deakin University, School of Life and Environmental Sciences, Melbourne, Australia, ²Institute for Cell and Molecular Biosciences, Newcastle University, The Medical School, Newcastle upon Tyne, UK, ³Division of Integrated Life Science, Graduate School of Biostudies, Kyoto University, Kyoto, Japan

The role of zinc transporters in an inherited disorder of zinc deficiency (PS03)

Poster Presentation/View and Coffe/Tea Break (9:30-10:30)

Location: the corridor of Fuyuan Guobin Hotel

Plenary Session 2 (10:30-12:00)

Location: Large Auditorium, Fuyuan Guobin Hotel

Chairs: Gerald F. Combs, Jr., USDA/ARS, USA

Guoo-Shyng (Ivy) Wang Hsu, Fu-Jen University, Taipei

10:30-11:00

Joseph R Prohaska, Margaret Broderius, Elise Mostad, Melanie Jokinen

University of Minnesota Medical School Duluth, Duluth, MN 55812, USA

Holotransferrin dependent hepcidin expression is impacted by dietary copper deficiency in rodents (PS04)

11:00-11:30

Jerry W. Spears, Scott Fry

14th International Symposium on Trace Elements in Man and Animals

North Carolina State University, USA

Copper metabolism and oxidative stress in non-ruminants fed pharmacological concentrations of copper (PS06)

11:30-12:00

Magdalena Araya, Gerardo Weisstaub, Monica Andrews, Marcos Medina, Miriam Suazo
Institute of Nutrition and Food Technology (INTA), University of Chile
New biomarkers of body copper status in malnourished children and patients (PS05)

12:00 noon-1:20pm

Lunch, Ballroom, Fuyuan Guobin Hotel

Afternoon Session

Symposium 1-6 (1:30-6:30, all in Fuyuan Guobin Hotel)

Symposium 1(A)

Title: Fe and Zn Homeostasis across Pregnancy, Lactation and Early Childhood:
Translational Implications of Recent Research

Sponsor: Micronutrient Initiative, Canada and TEMA-14

Location: Conference Room 1

Chairs: Kimberly O'Brien, Cornell University, USA
Jianhong Zhu, Wenzhou Medical University, Zhejiang, China

1:30- 2:00

Namanjeet Ahluwalia

Faculty of Medicine, University of Paris 13, INSERM U557, France
Iron, inflammation, and infection (A01)

2:00-2:30

Nancy Krebs, Leland Miller, K. Michael Hambidge

University of Colorado Denver, School of Medicine, Aurora, CO 80045, USA
Challenges of zinc assessment in women and young children (A02)

2:30-3:00

Kimberly O'Brien

Cornell University, Ithaca, NY 14853, USA

Bioavailability of heme and non-heme iron: implications for maternal and child health (A03)

3:00-3:30

Bo Lonnerdal

University of California, Davis, CA 95616, USA

Absorption of Fe and Zn during infancy and childhood and their interactions (A04)

3:30-4:00

Coffee/Tea Break

Chairs: Jianhong Zhu, Wenzhou Medical University, Zhejiang, China
Stephane Durosoy, Animine, Sillingy, France

4:00-4:15

Amelie Casgrain, Rachel Collings, Linda J. Harvey, Lee Hooper, Susan J. Fairweather-Tait

Norwich Medical School, University of East Anglia, Norwich

Relationships between iron intake, status and health: The EURRECA systematic review approach (A05)

4:15-4:30

Manuel Ruz¹, Fernando Carrasco¹, Pamela Rojas¹, Attila Csendes², Karin Papapietro², Jorge Inostroza¹, Juana Codoceo¹, Karen Basfi-fer¹, Alejandra Valencia¹, Fernando Pizarro³, Manuel Olivares³, Nancy

Krebs⁴, Jamie Westcott⁴, K Michael Hambidge⁴

¹Department of Nutrition, Faculty of Medicine, ²Department of Surgery, Clinical Hospital, and ³Institute of Nutrition and Food Technology, University of Chile, Santiago, Chile; ⁴University of Colorado, Denver, USA

Heme and non-heme iron absorption and iron status after sleeve gastrectomy and Roux-en-Y gastric bypass (A06)

4:30-4:45

Manuel Ruz¹, Fernando Carrasco¹, Pamela Rojas¹, Attila Csendes², Karin Papapietro², Jorge Inostroza¹, Juana Codoceo¹, Karen Basfi-fer¹, Alejandra Valencia¹, Fernando Pizarro³, Manuel Olivares³, Nancy Krebs⁴, Jamie Westcott⁴, K Michael Hambidge⁴

¹Department of Nutrition, Faculty of Medicine, ²Department of Surgery, Clinical Hospital, and ³Institute of Nutrition and Food Technology, University of Chile, Santiago, Chile; ⁴University of Colorado, Denver, USA

Zinc and copper status after sleeve gastrectomy and Roux-en-Y gastric bypass (A07)

4:45-5:00

Stephane Durosoy¹, Wilfried Vahjen², Jürgen Zentek²

¹Animine, Sillingy, France; ²Free University of Berlin, Faculty of Veterinary Medicine, Institute of Animal Nutrition, Germany

Inhibitory action of analytical grade zinc oxide and of a new potentiated ZnO on the in vitro growth (A08)

5:00-5:15

Dora I. A. Pereira, B. Mergler, N. J. R. Faria, S. Bruggraber, J. J. Powell

MRC Human Nutrition Research, Elsie Widdowson Laboratory, Fulbourn Road, Cambridge, CB1 9NL, UK

Nanoparticulate iron: a quick-to-clinic strategy to address iron deficiency anemia (A09)

5:15-5:30

Sarojani Karakannavar (Absent), Anasuya Patil, Hemalatha Sreeramaiah, NirmalaYenagi

University of Agricultural Sciences, Dharwad 580 005, Karnataka, India

An intervention to improve the iron status of rural adolescent girls in Karnataka, India (A10)

5:30-5:45

Xiaobo Hu, Mingyong Xie, Shaoping Nie, Yi Gong, Yuanxing Wang

State Key Laboratory of Food Science and Technology, Nanchang University, Nanchang

Synthesis, structural characterization, safety and efficacy evaluation of zinc threoninate chelate (A11)

Symposium 2 (B)

Title: Trace Mineral Metabolism and Interactions: Implications for Animal and Human Health

Sponsor: Novus International, Inc., USA and TEMA-14

Location: Conference Room 2

Chairs: Xugang Luo, Chinese Academy of Agricultural Sciences, Beijing

James Richards, Novus International, Inc., USA

1:30-2:00

Mary L'Abbe¹, Kevin Cockell², Bruce Robertson², Karima Benkhedda², Alex Giroux²

¹Dept Nutritional Sciences, University of Toronto, Toronto ON M5S 3E2, Canada; ²Bureau of Nutritional Sciences, Health Canada, Ottawa ON K1A 0L2, Canada

As the sodium goes down -are we getting enough iodine? (B01)

2:00-2:30

Emily Ho

Oregon State University and Linus Pauling Institute, USA

Effects of zinc deficiency on oxidative stress and DNA integrity-from cells to humans (B02)

2:30-3:00

Xugang Luo^{1,2}, Lin Lu^{1,2}, Sufen Li^{1,2}, Feng Ji^{1,2}, Shiping Bai^{1,2}

¹Institute of Animal Science, and ²State Key Laboratory of Animal Nutrition, Chinese Academy of Agricultural Sciences, Beijing

Chelation strengths of organic manganese and zinc on their absorptions and utilizations in broilers (B03)

3:00-3:30

Stephanie Hansen¹, Hsiao-Ching Liu², Jerry Spears²

¹Iowa State University, USA; ²North Carolina State University, USA

Influence of dietary iron concentration on metabolism of other trace minerals in pigs and cattle (B04)

3:30-4:00

Coffer/Tea Break

Chairs: Stephanie Hansen, Iowa State University, USA
Chunxiang Ai, Xiamen University, Xiamen, China

4:00-4:30

Kehe Huang, Xianshi Wu, Linwu Ran, Xingxiang Chen

College of Veterinary Medicine, Nanjing Agricultural University, Nanjing 210095

Effects of selenium form on productivity of dairy cows and their mechanism of action (B05)

4:30-4:50

Chunxiang Ai¹, Hua Xu¹, Yunxia Jiang²

¹College of Oceanography and Environmental Science, Xiamen University, Xiamen; ²School of Public Health and Tropical Medicine, Southern Medical University, Guangzhou

Effect of sub-lethal waterborne cadmium on several enzyme activities in gills of mud crab *Scylla Paramamosain* (B06)

4:50-5:10

Karen Wedekind

Novus International, Inc., USA

Effect of varying selenium and iodine intake on feline thyroid function (B07)

5:10-5:30

James Richards¹, Ei Lin Ooi², Nguyen Thi Kieu Tuyen³, Bui Chau Truc Dan², Nguyen Huu Thinh³, Geoffrey I. Zanton¹, Junmei Zhao¹, Robert J. Harrell¹, and Craig Browdy¹

¹Novus International, Inc., 20 Research Park Dr., St. Charles, MO, 63304, USA; ²Novus Aqua Research Center, Linh Trung Ward, Thu Duc District, Ho Chi Minh City, Vietnam; ³Nong Lam University, Faculty of Fisheries, Linh Trung Ward, Thu Duc District, Ho Chi Minh, Vietnam

Impact of chelated trace minerals on immune function in production animals (B08)

5:30-5:45

Agnes Michalczyk, David Freestone, Leigh Ackland

Deakin University, School of Life and Environmental Sciences, Centre for Cellular and Molecular Biology

The effect of copper and ATP7A overexpression on CTR1, ATOX1, ATP7B and ceruloplasmin in PMC42-LA human breast cells (B09)

5:45-6:00

Yan Ge¹, Xueqing Ding¹, Tao Wang¹, Meirong Fan¹, Huiqi Xie¹, Y. James Kang^{1,2}

¹Regenerative Medicine Research Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041; ²Department of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Kentucky 40202

Copper chelation reduces HIF-1 α accumulation induced by dimethyloxallyl glycine in human umbilical vein endothelial cells (B10)

6:00-6:15

A. K. Garg¹(absent), R. S. Dass¹, P. K. Malik²

¹Indian Veterinary Research Institute, Izatnagar-243 122, India; ²Navsari Agricultural University, Navsari, Gujrat, India

Organic selenium supplementation improved growth performance of buffalo (*Bubalus bubalis*) calves (B11)

Symposium 3 (C)

Title: Trace Elements on Cell Death, Tumor, and Cancer

Sponsor: TEMA-14

14th International Symposium on Trace Elements in Man and Animals

Location: Conference Room 3
Chairs: Regina Brigelius-Flohe, German Institute of Human Nutrition, Germany
Huawei Zeng, USDA/ARS, USA

1:30-2:00

Regina Brigelius-Flohe

German Institute of Human Nutrition Potsdam-Rehbruecke, Germany
Selenium, selenoproteins, sulforaphane and colon cancer (C01)

2:00-2:30

An-Sik Chung

Korea Advanced Institute of Science and Technology, South Korea
Selenium induces apoptosis and blocks tumor invasion (C02)

2:30-3:00

Yongping Bao, Lawrence Barrera, Dan Li, Wei Wang

Department of Nutrition, Norwich Medical School, University of East Anglia, Norwich NR4 7TJ, UK
Synergistic interactions between isothiocyanates and selenium in the up-regulation of TR-1 and GI-GPX and protection against free radical mediated cell death (C03)

3:00-3:30

Petra A. Tsuji^{1,2,3}, Bradley A. Carlson², Salvador Naranjo-Suarez², Min-Hyuk Yoo², Xue-Ming Xu², Dmitri E. Fomenko⁴, Vadim N. Gladyshev⁵, Dolph L. Hatfield², Cindy D. Davis³

¹Cancer Prevention Fellowship Program, ²Molecular Biology of Selenium Section, Laboratory of Cancer Prevention, and ³Nutritional Science Research Group, Division of Cancer Prevention, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892; ⁴Department of Biochemistry, University of Nebraska, Lincoln, NE 68588; ⁵Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115

Deficiency of the 15-kDa selenoprotein inhibits colon cancer risk (C04)

3:30-4:00

Coffer/Tea Break

Chairs: Cindy Davis, NCI, NIH, USA
Wen-Hsing Cheng, University of Maryland, USA

4:00-4:20

Zhaoming Xu, Markus Purtzki

Food, Nutrition & Health Program, University of British Columbia, Canada
Zinc depletion, intracellular calcium disturbance, and apoptosis (C05)

4:20-4:40

Wen-Hsing Cheng

University of Maryland at College Park, USA
Selenium-induced senescence as an early barrier of tumorigenesis (C06)

4:40-5:00

Young R. Seo (Absent)

Department of Life Science, Dongguk University-Seoul, Seoul, South Korea
A novel molecular mechanism of cancer chemoprevention by selenium: p53-mediated DNA repair (C07)

5:00-5:20

Huawei Zeng
USDA/ARS, USA

Methylselenol, a selenium metabolite, plays a critical role in inhibiting colon cancer cell growth (C08)

5:20-5:35

Shih-Wen Lin^{1,2}, Neal D Freedman², Youlin Qiao³, Ti Ding⁴, Nan Hu², Kai Yu², Sanford M Dawsey², Jinhua Fan³, Zezheng Tang⁴, Philip R. Taylor², Christian C. Abnet²

¹Cancer Prevention Fellowship Program, NCI, Bethesda, MD, USA; ²Division of Cancer Epidemiology & Genetics, NCI, Bethesda, MD, USA; ³Cancer Institute, Chinese Academy of Medical Sciences, Beijing; ⁴Shanxi Cancer Hospital & Institute,

Taiyuan, Shanxi

Selenoprotein gene variants and risk of esophageal and gastric cancer in a Chinese population (C09)

5:35-5:50

Rachel Hurst¹, Lee Hooper¹, Teresa Norat², Rosa Lau², Dagfinn Aune², Darren Greenwood³, Rachel Collings¹, Linda Harvey¹, Susan J. Fairweather-Tait¹

¹Norwich Medical School, University of East Anglia, Norwich, Norfolk, NR4 7TJ, UK; ²Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, St. Mary's Campus, Norfolk Place, Paddington, London W2 1PG, UK; ³Centre for Epidemiology and Biostatistics, University of Leeds, Leeds, LS2 9LN, UK

Selenium status and advanced/aggressive prostate cancer risk reduction: results from dose-response meta-analysis (C10)

5:50-6:15

Wenjie Yang, Deqian Mao, Weidong Li, Yiming Xia

Institute of Nutrition and Food Safety, Chinese Center for Disease Control & Prevention 29 Nan Wei Road, Beijing 10050
Efficacy and safety of different phyto-selenocompounds in the prevention and control of stomach cancer (C11)

Symposium 4 (D)

Title: Link between Trace Elements in Soils and Their Deficiencies in Animals/Humans

Sponsor: HavestPlus, Washington DC, USA and TEMA-14

Location: Conference Room 4

Chairs: Ross M. Welch, Cornell University, USA
Robin Graham, Flinders University of South Australia

1:30-1:55

Ross M. Welch

Department of Crop and Soil Sciences, Cornell University, USA

The role of soils in trace element deficiencies in animals and humans: an overview (D01)

1:55-2:20

Robin Graham

Flinders University of South Australia, Adelaide, Australia

How much iron deficiency anemia in people is the result of zinc deficiency in soils? (D02)

2:20-2:45

Lianghuan Wu

Zhejiang University, Hangzhou

Efficiency of different iron fertilizers on iron accumulation and bioavailability in rice grain (D03)

2:45-3:10

Xuebin Yin, Ying Liu, Fei Li, Zhiqing Lin

Advanced Lab for Selenium and Human Health, Suzhou Institute of University of Science and Technology of China, Suzhou
Plant-based biofortification from phytoremediation to selenium-enriched agricultural products (D04)

3:10-3:25

Linxi Yuan, Xuebin Yin

Suzhou Key Lab for Selenium and Human Health & Jiangsu Bio-Engineering Research Centre of Selenium, Suzhou
Adenocaulon himalaicum, a novel selenium-hyperaccumulating plant in Enshi, Hubei, China (D05)

3:25-3:40

Tao Zeng¹, Yu Qiao¹, Qin Shuai², Minghou Xu¹

¹State Key Laboratory of Coal Combustion, Huazhong University of Science and Technology, Wuhan 430074; ²Faculty of Materials Science & Chemistry, China University of Geosciences, Wuhan 430074

Leaching characteristics and co-combustion characteristics of a Chinese high-selenium stone coal (D06)

(Note: Please keep the presentations on schedule as the same room will be used for the following Symposium at 4.00pm)

Symposium 5 (E)

Title: Trace Elements on Cardiovascular Function and Disease

Sponsor: TEMA-14

Location: Conference Room 4

Chairs: John H. Beattie, Rowett Institute of Nutrition and Health, University of Aberdeen, UK

In-Sook Kwun, Andong National University, South Korea

4:00-4:30

Y. James Kang^{1,2}

¹Regenerative Medicine Research Center, Sichuan University West China Hospital, Chengdu, Sichuan 610041; ²Department of Pharmacology and Toxicology, University of Louisville, Louisville, Kentucky 40202, USA

Copper in cardiovascular pathogenesis and regeneration (E01)

4:30-5:00

Markus Brielmeier

Helmholtz Zentrum München, Research Unit Comparative Medicine, Germany

Modeling human pancreatic disease in thioredoxin reductase knockout mice (E02)

5:00-5:30

John H. Beattie

Rowett Institute of Nutrition and Health, University of Aberdeen, Aberdeen AB21 9SB, UK

Zinc status related to vascular function, inflammation and atherosclerosis (E03)

5:30-6:00

In-Sook Kwun, Ethel Alcantara, Mee-Young Shin

Andong National University, South Korea

Role of zinc in osteogenic and vascular calcification (E04)

Chairs: Y. James Kang, Sichuan University, China and Louisville University, USA

Markus Brielmeier, German Research Center for Environmental Health, Germany

6:00-6:20

Hongmei Liu, Fei Qin, Weixia Bian, Kaixun Huang

Hubei Key Laboratory of Bioinorganic Chemistry & Material Medicine, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan

Selenium suppressed oxidative stress-induced vascular smooth muscle cells calcification via regulation of ERK signaling pathway (E05)

6:20-6:35

Ethel Alcantara, Mee-Young Shin, In-Sook Kwun

Department of Food Science and Nutrition, Andong National University, South Korea

Zinc deficiency promotes calcification in rat vascular smooth muscle cells independent of alkaline phosphatase (E06)

6:35-6:50

Ou Ou¹, Keith Allen-Redpath², Graeme F. Nixon², Henian Yang³, Margaret-Jane Gordon¹, In-Sook Kwun⁴, Gillian Campbell¹, and John H. Beattie¹

¹Rowett Institute of Nutrition & Health, and ²Department of Medicine and Therapeutics, University of Aberdeen, Aberdeen, UK; ³Luton Institute of Research in Applied Natural Sciences, University of Bedfordshire, UK; ⁴Department of Food Science and Nutrition, Andong National University, Andong, South Korea

Vascular smooth muscle protein responses and gene expression in zinc deficiency (E07)

Symposium 6 (F)

Title: Trace Elements Brain Function and Neural Disease

Sponsor: TEMA-14

Location: Conference Room 5

14th International Symposium on Trace Elements in Man and Animals

Chairs: Ulrich Schweizer, Charite Universitätsmedizin Berlin, Germany
Mustafa Naziroglu, Suleyman Demirel University, Turkey

1:30-2:00

Katalin Toth

Centre de recherche Université Laval Robert Giffard, Canada

The role of zinc in neurotransmission (F01)

2:00-2:30

Peng Lei (for Ashley Bush)

Mental Health Research Institute, University of Melbourne, Parkville, Australia

Cu, Zn and Fe in Alzheimer's disease: from bench to clinic (F02)

2:30-3:00

Ulrich Schweizer

Charité-Universitätsmedizin Berlin, Augustenburger Platz 1, 13353 Berlin, Germany

Role of the trace element selenium in brain development and function (F03)

3:00-3:30

Qiong Liu, Jiazuan Ni, Chao Wang, Ping Chen, Xifeng Qiao

College of Life Sciences, Shenzhen University, Shenzhen 518060

Selenoprotein-protein interactions in human brain indicate their possible roles in Alzheimer's disease (F04)

3:30-4:00

Coffer/Tea Break

Chairs: Peng Lei (for Ashley Bush), Mental Health Research Institute, Australia
Qiong Liu, Shenzhen University, Shenzhen

4:00-4:30

Zhanyou Wang

Key Laboratory of Medical Cell Biology of Ministry of Education, China Medical University, Shenyang 110001

Involvement of metal transporters, ZnTs and DMT1, in Alzheimer's disease (F05)

4:30-5:00

Mustafa Naziroglu

Department of Biophysics, Medical Faculty, Suleyman Demirel University, Isparta, Turkey

Role of selenium on molecular pathways of TRPM2 cation channels and Ca²⁺ signaling in neuron cells (F06)

5:00-5:30

Kuanyu Li^{1,2}, Xiaoman Dai¹, Tracey Rouault²

¹Medical School of Nanjing University, Nanjing; ²Molecular Medicine Program, NICHD/NIH, USA

Putative pathological mechanism of neurodegenerative disease Friedreich ataxia, caused by frataxin deficiency (F07)

5:30-5:45

Dan Chen¹, Manju Reddy¹, Anumantha Kanthasamy²

¹Department of Food Science and Human Nutrition, and ²Department of Biomedical Sciences, Iowa State University, IA, USA

EGCG protects against 6-OHDA induced neurotoxicity in a cell culture model (F08)

5:45-6:00

Wei Pang¹, Yugang Jiang¹ (Absent), Hao Lu^{1,2}, Yandan Hu^{1,2}, Hongpeng Yang¹, Xue Leng¹

¹Department of Nutrition, Institute of Health & Environmental Medicine, Academy of Military Medical Sciences, Tianjin;

²Department of Nutrition and Food Hygiene, West China School of Public Health, Sichuan University, Chengdu

Depletion of intracellular zinc induced apoptosis in cultured hippocampal neurons through

RAF/MEK/ERK pathways (F09)

14th International Symposium on Trace Elements in Man and Animals

6:00-6:15

Andrey Skalny² (Absent), Anatoly Fesyun¹, Igor Ivashkiv¹

¹Military Medical Directorate of Internal Forces at Ministry of the Interior of Russia, Moscow, Russia; ²Federal State Scientific Institution "Institute of toxicology", Federal Medico-Biological Agency of Russia, St. Petersburg, Russia

Zinc and adaptation of army conscripts to intensive military service (F10)

7:00-8.300

Dinner, Ballroom, Fuyuan Guobin Hotel

Wednesday, September 21, 2011

Registration (8:00am-6:00pm)

Lobby, Fuyuan Guobin Hotel

Poster Display (7:30am-7:00pm)

Even-numbered posters (e.g., PT2, 4, 6, ... 68) are displayed today (Wednesday, September 21, 2011)

Presentation time: 9:30-10:30am

Presenter: must stand before the poster during 9:30-10:30am for questions

Location: the corridor of Fuyuan Guobin Hotel

Morning Sessions

Sunrise/Breakfast Lesson (7:10-7:45)

Chair: Robert J. Cousins, University of Florida, USA

Speaker: Joseph R. Prohaska, University of Minnesota-Duluth, USA

Title: Write to win: Guidelines and tips for writing papers and grants on trace elements

Location: Ballroom, Fuyuan Guobin Hotel

Plenary Session 3 (8:00-9:30)

Location: Large Auditorium, Fuyuan Guobin Hotel

Chairs: Dennis D. Miller, Cornell University, USA

Xu Lin, Institute for Nutritional Sciences, Chinese Academy of Sciences, Shanghai

8:00-8:30

Greg Anderson

Queensland Institute of Medical Research, Australia

Systemic control of body iron intake (PS07)

8:30-9:00

Harry J. McArdle, Christine Lang, Alison Richmond, Lorraine Gambling

Rowett Institute of Nutrition and Health, University of Aberdeen, Aberdeen AB21 9SB UK

The effect of maternal iron deficiency on growth and development in the rat (PS08)

9:00-9:30

Mary L'Abbe¹, Ying Qi², Wendy Lou²

¹Department of Nutritional Sciences, and ²Dalla Lana School of Public Health, University of Toronto, Canada

Modeling of the iron bioavailability of the Canadian diet (tentative) (PS09)

Poster Presentation/View and Coffee/Tea Break (9:30-10:30)

Location: the corridor of Fuyuan Guobin Hotel

Plenary Session 4 (10:30-12:00)

Location: Large Auditorium, Fuyuan Guobin Hotel

Chairs: Mary R. L'Abbe, University of Toronto, Canada

Xingen Lei, Cornell University, USA

10:30-11:15

Underwood Lecture

Raymond F. Burk, Gary E. Olson, Kristina E. Hill, Virginia P. Winfrey, Amy K. Motley

Vanderbilt University School of Medicine, Nashville, TN, USA

The central role of selenoprotein P (Sepp1) in selenium transport and homeostasis (PS10)

11:15-11:45

International Collaboration Award Lecture

Yiming Xia

Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention, Beijing

Review on selenium research relating to human health in China (PS11)

11:45-12:00

Presentation of Awards

12:00 noon-1:20pm

Lunch, Ballroom, Fuyuan Guobin Hotel

Afternoon Session

Symposium 7-11 (1:30-6:30, all in Fuyuan Guobin Hotel)

Symposium 7 (G)

Title: Zinc intakes world wide – are we making any progress towards reducing the prevalence of zinc undernutrition?

Sponsor: TEMA-14 and IZiNCG

Location: Conference Room 1

Chairs: Emorn Wasantwisut, Mahidol University, Thailand
Sonja Hess, UC-Davis, USA

1:30-1:40

Chairs' introduction

1:40-2:10

Kenneth H. Brown, Sonja Y Hess

Department of Nutrition and Program in International and Community Nutrition, University of California, Davis, CA 95616 USA

Plasma zinc concentration as a biomarker of zinc status (G01)

2:10-2:40

Christine Hotz

Nutridentics and IZiNCG, Toronto, Canada

Dietary assessment of zinc intakes (G02)

2:40-3:10

Baseer Achakzai, Shujaat H. Zaidi, Sajid B. Soofi, Atif Habib; Imtiaz Hussain, Didar Alam, Zulfiqar A. Bhutta

Department of Paediatrics & Child Health, Aga Khan University, Pakistan Nutrition Cell, National Institute of Health, Pakistan

Evaluation of zinc status and community perceptions in Pakistan: the National Nutrition Survey 2011 (G03)

3:10-3:40

Rosalind S. Gibson¹, Karl B. Bailey¹, Winsome R. Parnell¹, Noela Wilson², and Elaine L. Ferguson¹

¹Department of Human Nutrition, and ²LINZ Activity and Health Research Unit, University of Otago, Dunedin, New Zealand

Higher risk of zinc deficiency in New Zealand Pacific school children compared to their Māori and European counterparts: a New Zealand national survey (G04)

3:40-4:00

Coffee/Tea Break

4:00-4:30

Reina Engle-Stone¹, Alex Ongla Ndjebayi², Martin Nankap², Grant Aaron¹, Kenneth Brown^{1,2}

¹Program in International and Community Nutrition, Department of Nutrition, University of California, Davis, USA; ²Helen Keller International, USA

Assessment of zinc status in the national survey in Cameroon (G05)

4:30-4:50

Emorn Wasantwisut, Panel Coordinator

Panel discussion

Chairs: Emily Ho, Oregon State University, USA
Christine Hotz, Nutridemics and IZiNCG, Toronto, Canada

5:00-5:15

Amanda Amorim¹ (Absent), Rafael Brandao¹, Waldemar Barchewsky Jr.², Marcelo Ribeiro², Adail Castro¹, Dilina Marreiro³, Nadir Nogueira³, Semiramis Monte¹

¹Immunogenetics and Molecular Biology Laboratory-LIB, UFPI, Teresina, Piaui, Brazil; ²USF, Bragança Paulista, Sao Paulo, Brazil; ³Federal University of Piaui-UFPI, Brazil

Expression of genes that encode zinc transport proteins suggest that zinc deficiency is not real in hemodialysis patients (G06)

5:15-5:30

Sidooun Bun¹ (Absent), Yuming Guo¹, Fengjie Ji², Fucun Guo¹, Hong Cao²

¹State Key lab of Animal Nutrition, College of Animal Science and Technology, China Agricultural University, Beijing;

²Novus International, Inc., USA

MINTREX-Zn improves tibia zinc deposition and antioxidant status of broilers under stress with coccidiosis infection (G07)

5:30-5:45

Shelley Rhodes¹, Grainne O'Donoghue¹, Graham Horgan¹, Nancy Krebs², Jamie Westcott², John Draper³, Manfred Beckmann³, Amanda J. Lloyd³, Sylvia Stephen¹, Louise J. Valentine¹, John H. Beattie¹

¹The Rowett Institute of Nutrition and Health, Aberdeen University, Greenburn Road, Bucksburn, Aberdeen, AB21 9SB, Scotland. ²University of Colorado Denver, Research Complex 2, Room 5025, 12700 East 19th Ave, Box C225, Aurora, CO 80045, United States. ³Edward Llwyd Building, B1.05, IBERS, Penglais, Aberystwyth University, Ceredigion, SY23 3DA, U.K.

Evaluation of metallothionein as a biomarker of zinc status in a human dietary intervention study (G08)

Symposium 8 (H)

Title: Trace Element Biomarkers of Body Status and Responses

Sponsor: TEMA-14

Location: Conference Room 2

Chairs: Bo Lonnerdal, UC-Davis, USA
Yongping Bao, Norwich Medical School University of East Anglia, UK

1:30-2:00

Berislav Momcilovic

Institute for Research and Development of the Sustainable Eco Systems, Ivana Lučića 5, 10000 Zagreb, Croatia

Body trace element responses to human depression and strenuous soccer training (H01)

2:00-2:30

Junquan Gao

National Institute for Nutrition and Food Safety, Chinese Center for Disease Control and Prevention, Beijing

Dietary exposure assessments of heavy metals and trace elements in China (H02)

2:30-3:00

Gerald Combs, Matthew Jackson

Grand Forks Human Nutrition Research Center, USDA-ARS, Grand Forks, ND 58202-9034, USA

Determinants of selenium status in healthy adults (H03)

3:00-3:30

Margaret Rayman, Sarah Bath

Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK

Deficient iodine status and its correlates in a developed European country: the UK (H04)

3:30-4:00

Coffer/Tea Break

Chairs: Wanqi Zhang, Medical University of Tianjin, Tianjin
Terry Ward, Zinpro Corporation, USA

4:00-4:30

Zhongna Sang¹, Peizhong Peter Wang², Zhaixiao Yao¹, Jun Shen¹, Beth Halfyard², Long Tan¹, Na Zhao¹, Yuntang Wu¹, Shuo Gao³, Jian Tan³, Jiayu Liu⁴, Zupei Chen⁴, and Wanqi Zhang¹

¹Department of Nutrition and Food Hygiene, School of Public Health, Tianjin Medical University, Tianjin; ²Division of Community Health & Humanities, Faculty of Medicine Memorial University of Newfoundland, Canada; ³Tianjin Medical University General Hospital, Tianjin; ⁴Institute of Endocrinology, Tianjin Medical University, Tianjin

Research into the safe intake levels of iodine in adults (H05)

4:30-4:50

Mary L'Abbe¹, Ying Qi², Wendy Lou²

¹Department of Nutritional Sciences, and ²Dalla Lana School of Public Health, University of Toronto, Canada

Iodine status of the Canadian population (H06)

4:50-5:05

Reina Engle-Stone¹, Alex Ongla Ndjebayi², Martin Nankap², Kenneth H. Brown^{1,2}

¹Program in International and Community Nutrition, Department of Nutrition, University of California, Davis, USA, ²Helen Keller International, USA

The estimated prevalence of iron deficiency in Cameroon differs greatly depending on the iron status indicator used (H07)

5:05-5:20

Dan Yu, Junsheng Huo, Jing Sun, Wenxian Li, Ling Lin

Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention, Beijing

Is serum ferritin < 15µg/l appropriate for identifying iron deficiency among marginal anemia populations in China (H08)

5:20-5:35

Yu-Te Yeh, Jon-Hang Jiang, Yih-Fong Liew

Department of Nutritional Science, Fu Jen Catholic University, Taiwan

The effect of inflammation and iron overload on the expression of iron-sulfur protein and thio-modification of tRNAs in microglial BV2 cell (H09)

5:35-5:50

Diego Gaitán^{1,2}, Manuel Olivares¹, Bo Lonnerdal³, Daniel López de Romaña¹, Fernando Pizarro¹

¹INTA - University of Chile, Chile; ²GIANH - University of Antioquia, Colombia; ³University of California – Davis, USA

Non-heme iron does not interact with heme iron absorption in humans (H10)

5:50-6:05

Melissa Miranda-Durán, Diego Gaitán, Alex Brito, Manuel Olivares, Daniel López de Romaña, Fernando Pizarro.

Food Technology and Nutrition Institute, University of Chile, Chile

A randomized controlled trial investigating the effect of calcium supplementation on iron status in Chile (H11)

Symposium 9 (I)

Title: Trace Elements on Metabolic or Chronic disease

Sponsor: TEMA-14

Location: Conference Room 3

Chairs: Roger Sunde, University of Wisconsin, USA

Fong-Fong Chu, Beckman Research Institute of City of Hope, USA

1:30-2:00

Josef Köhrle

Institut für Experimentelle Endokrinologie, Charité University Medicine Berlin

The role of selenium in metabolism and chronic diseases (I01)

2:00-2:30

Xin Gen Lei

Department of Animal Sciences, Cornell University, Ithaca, NY 14853, USA

Roles of Se, GPX1, and SOD1 in insulin resistance, diabetes, and obesity (I02)

2:30-3:00

Holger Steinbrenner

Institute for Biochemistry and Molecular Biology I, Heinrich-Heine-University Duesseldorf, Germany

The current debate on selenium as risk factor for type 2 diabetes: evidence for interplay of selenium and carbohydrate metabolism (I03)

3:00-3:30

Kaixun Huang

Huazhong University of Science and Technology, Wuhan

Selenoprotein R and cataract (I04)

3.30-4.00

Coffer/Tea Break

Chairs:

Zhaoming Xu, University of British Columbia, Canada

Holger Steinbrenner, Heinrich-Heine-University Duesseldorf, Germany

4:00-4:30

Fong-Fong Chu¹, Ye-Shih Ho², Byung-Wook Kim¹, Robert Steven Esworthy¹

¹Beckman Research Institute of The City of Hope, USA; ²Institute of Environmental Health Sciences, Wayne State University, USA

Mice deficient in Se-dependent glutathione peroxidase-1 and -2 have inflammatory bowel disease (I05)

4:30-5:00

Zhiwu Zhu

Zhengzhou University, Henan

The essential role for Cu/Zn superoxide dismutase-dependent Ca²⁺ homeostasis in cellular thermo-tolerance (I06)

5:00-5:15

Xi Yan, Lvhui Sun, Xin Gen Lei

Department of Animal Science, Cornell University, USA

A novel correlation of hepatic p53 protein with Se- and glutathione peroxidase-1-mediated murine lipid metabolic disorders (I07)

5:15-5:30

Jazmin Chiu-Ugalde, Eva K. Wirth, Marc O. Klein¹, Remy Sapin², Lutz Schomburg, Josef Köhrle, Ulrich Schweizer

Institut für Experimentelle Endokrinologie, Charité-Universitätsmedizin Berlin, 13353 Berlin, Germany, ¹Service D'Endocrinologie, Centre Hospitalier et Universitaire de Nancy, France ²FRE 3289, Université de Strasbourg, Centre National de la Recherche Scientifique, Strasbourg, France

Subclinical hypothyroidism and increased lipid peroxidation in mice lacking selenoprotein biosynthesis (I08)

5:30-5:45

Xiuju Xu (Absent), Bo Gong, Yan Guo

Baotou Medical College, Inner Mongolia, Baotou 14060

Study of Se-added Ginkgo tea effect on mouse enzyme of stomach in alcoholic (I09)

5:45-6:00

Daoyin Dong¹, Xinhua Xu¹, Biao Wang¹, Huiqi Xie¹, Y. James Kang^{1,2}

¹Regenerative Medicine Research Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041; ²Department of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Kentucky 40202, USA

Copper-homocysteine complex formation manipulates copper chaperone proteins (I10)

6:00-6:15

Zhuzhen Zhang, Fan Zhang, Peng An, Xin Guo, Fudi Wang

Key Laboratory of Nutrition and Metabolism, Institute for Nutritional Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Graduate School of the Chinese Academy of Sciences, Shanghai

Ferroportin1 deficiency in mouse macrophages impairs iron homeostasis and inflammatory responses (I11)

6:15-6:30

Irina Ivanova¹ (Absent), Alexey Trefilov², Vladimir Rodionov³

¹The Postgraduating Doctors' Training Institute" of the HealthCare and Social Development Ministry of the Chuvash Republic; ²City children's hospital №3 Cheboksary; ³City children's hospital №1 Cheboksary

Features of hair and urine elemental composition of children with kidney malformations (I12)

Symposium 10 (J)

Title: Global Iron and Zinc Biofortification: Potential, Success, and Challenge

Sponsor: HarvestPlus, Washington DC, USA and TEMA-14

Location: Conference Room 4

Chairs: Erick Boy, HarvestPlus, Washington DC, USA
Chengyu Huang, Sichuan University, Chengdu

1:30-2:00

Erick Boy

HarvestPlus, Washington DC, USA

Zinc and iron biofortification: HarvestPlus crop development update (J01)

2:00-2:30

Jere Haas

Cornell University, Ithaca, NY 14853, USA

Efficacy of iron biofortification: Results from two human feeding trials of rice and beans (J02)

2:30-3:00

Chengyu Huang¹, Yong Zhang², Chuanxiao Xie², Guangtang Pang³, Kangning Wang³, Ji Lei¹, Qing Jia¹, Ming Li¹, Zhongfu He², Shihuang Zhang², Junrong Hong¹, Mingqiu Zhang¹, Xiangfeng Yue¹, Jian Zhang¹, Lin Bai¹

¹West China School of Public Health, Sichuan University, China; ²Institute of Crop Science, Chinese Academy of Agricultural Sciences, China; ³Sichuan Agriculture University, Yaan

Assessment of iron and zinc bioavailability of biofortified wheat and maize in China (J03)

3:00-3:30

Sam Newton¹, Yassir Islam², K. Michael Hambidge², Erick Boy²

¹Kintampo Health Research Centre, Ghana; ²HarvestPlus, Washington DC, USA

Importance and future of iron and zinc biofortification in Africa (J04)

3:30-4:00

Coffer/Tea Break

Chairs: John Finley, USDA/ARS, USA
Manju Reddy, Iowa State University, USA

4:00-4:30

John Finley

United States Department of Agriculture, Agricultural Research Service, USA

The importance of food composition data for a clear understanding of mineral nutrients in the food supply (J05)

4:30-4:45

Qin Shuai¹, Shengrui Xu¹, Ruicheng Huang¹, Sen Yan²

¹Faculty of Material Science & Chemistry Engineering, and ²Faculty of Earth Sciences, China University of Geosciences, Wuhan

Comprehensive utilization of selenium resources in black shales of Enshi (J06)

4:45-5:00

Manju Reddy¹, Steve Rodermel², Maneesha Aluru²

¹Food Science & Human Nutrition, and ²Department of Genetics, Development & Cell Biology, Iowa State University, IA, USA

Improving iron bioavailability with ferritin overexpression in low phytate maize (J07)

5:00-5:15

Yang Huang^{1,2}, Quanxin Wang^{1,2}, Xuebin Yin^{1,2}

¹Advanced Lab for Selenium and Human Health, Suzhou Institute for Advanced Study, University of Science and Technology of China, Suzhou 215123; ²School of Earth and Space Science, University of Science and Technology of China, Hefei 230026

Daily selenium intake in high selenium area of Enshi, China (J08)

5:15-5:45

Emorn Wasantwisut

Institute of Nutrition, Mahidol University, Thailand

Key issues and challenges of iron and zinc biofortification in Asia (J09)

5:45-6:15

Kenneth H. Brown

University of California, Davis, CA 95616, USA

Zinc biofortification of rice in Bangladesh (J10)

Symposium 11 (K)

Title: Transporter, Systemic Control of Body Intake, and Homeostasis

Sponsor: TEMA-14

Location: Conference Room

Chairs: Fudi Wang, Institute for Nutritional Sciences, CAS, Shanghai

Mitchell Knutson, University of Florida, USA

1:30-2:00

Xiaobin We, Heejeong Kim, Jaekwon Lee

Department of Biochemistry and Redox Biology Center, University of Nebraska, Lincoln, NE 68588-0664, USA

Potassium in Metabolism of Copper and Iron (K01)

2:00-2:30

Fudi Wang

Key Laboratory of Nutrition and Metabolism, Institute for Nutritional Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Graduate School of the Chinese Academy of Sciences, Shanghai

New insights into mammalian iron homeostasis (K02)

2:30-3:00

Lukas C. Kühn, Liviu Vanoaica, Deepak Darshan, Larry Richman

Ecole Polytechnique Fédérale de Lausanne (EPFL), ISREC - Swiss Institute for Experimental Cancer Research, Lausanne, Switzerland

Consequences of conditional ferritin H gene deletion on cellular iron homeostasis and iron absorption in mice (K03)

3:00-3:30

Yanzhong Chang¹, Shumin Wang¹, Linhao You¹, Lijuan Fu¹, Ning Zhao¹, Tracey Rouault², Benjamin Dehay³, Erwan Bezard³

¹Hebei Normal University, Shijiazhuang 050016, Hebei Province, China, ²National Institute of Child Health and Human Development, Bethesda, MD, 20892, USA, ³Neurodegenerative Diseases Institute, UMR 5293, F-33000 Bordeaux, France
Hepcidin regulating brain iron metabolism (K04)

3:30-4:00

14th International Symposium on Trace Elements in Man and Animals

Coffer/Tea Break

Chairs: James F. Collins, University of Florida, USA
Bing Zhu, Tsinghua University, Beijing

4:00-4:30

Mitchell Knutson, Chia-Yu Wang, Hyeyoung Nam
University of Florida, Food Science and Human Nutrition Department, PO Box 110370, Gainesville, FL, USA
Roles of DMT1 and ZIP14 in iron uptake by the liver (K05)

4:30-5:00

James Collins
University of Florida, USA
Copper and the compensatory response to iron deficiency (K06)

5:00-5:30

Bing Zhou, Xiaoxi Wang
School of Life Sciences, Tsinghua University, Beijing 100084
Study metal homeostasis in the *Drosophila* model (K07)

5:30-5:45

Xuming Jia, Jong-Han Kim, Sihao Liu, Peter Buckett, Marianne Wessling-Resnick
Harvard School of Public Health, USA
Lipoprotein lipase: a new target of iron regulation (K08)

5:45-6:00

Yu Yu, Fudi Wang
Key Laboratory of Nutrition and Metabolism, Institute for Nutritional Sciences, Chinese Academy of Sciences, Shanghai
A novel mammalian zinc transporter, Zip11 regulated by zinc through transcription and mRNA stability (K09)

7:00-8.300

Dinner, Ballroom, Fuyuan Guobin Hotel

Thursday, September 22, 2011

7:00am-8:00am

Breakfast, Ballroom, Fuyuan Guobin Hotel

8:30am-5:30pm

Tour of Enshi Sites (please gather in front of Fuyuan Guobin Hotel before 8:20am and depart at 8:30am sharp!)

7:00pm-8.300pm

Dinner, Ballroom, Fuyuan Guobin Hotel

Friday, September 23, 2011

Registration and pick up of certification document of attending TEMA14

(8:00am-12:00noon)

Lobby, Fuyuan Guobin Hotel

Morning Sessions

Sunrise/Breakfast Lesson (7:10-7:45)

Chair: Magdalena Araya, University of Chile, Chile

Speaker: Mary R. L'Abbe, University of Toronto, Canada

Title: Bridge science to real world: challenge and opportunity for translational research

Location: Ballroom, Fuyuan Guobin Hotel

Symposium 12-16 (8:00-12:30, all in Fuyuan Guobin Hotel)

Symposium 12 (L)

Title: New Frontiers of Trace Elements in Animal Nutrition

Sponsor: Kemin AgriFoods, Herentals, Belgium and TEMA-14

Location: Conference Room 1

Chairs: Jerry W. Spears, North Carolina State University, USA

Bruce Duan, Kemin AgriFoods China

8:00-8:30

Jerry W. Spears

North Carolina State University, Raleigh, NC 27695, USA

Recent advances in chromium nutrition of animals (L01)

8:30-9:00

Xin Gen Lei

Department of Animal Science, Cornell University, Ithaca, NY 14853, USA

Functional genomics of selenoproteins in pigs and chickens (L02)

9:00-9:30

Darren Juniper¹, Gérard Bertin²

¹School of Agriculture, Policy and Development, University of Reading, Reading, Berks, UK; ²Erawan Consulting, Asnières Affaires, 25 Rue de Bas, Asnières sur Seine, France

Distribution of total selenium species within the tissues and products of food producing animals offered different sources of selenium (L03)

9:30-10:00

Joel Caton, K. A. Vonnahme, D. A. Redmer, L. P. Reynolds

Center for Nutrition and Pregnancy, Department of Animal Sciences, North Dakota State University, Fargo, ND, USA

Impacts of supranutritional selenium on growth and vascularity of key nutrient transferring tissues (L04)

10:00-10:30

Coffee/Tea Break

Chairs: Darren T. Juniper, University of Reading, UK

Kehe Huang, Nanjing Agricultural University, Nanjing

10:30-11:00

John Finley

United States Department of Agriculture, Agricultural Research Service, USA

Variation in mineral content of the food supply: lessons learned from studies of selenium (L05)

11:00-11:30

Y. E. Ting, Kexiong Tian, Rejun Fang, Zhiyong Fan, Jianhua He (Absent)
College of Animal Science and Technology, Hunan Agricultural University, Changsha
Study on the effect of threonine chelated iron in piglets (L06)

11:30-11:45

Yunxia Jiang¹ (Absent), Hua Xu², Chunxiang Ai²
¹School of Public Health and Tropical Medicine, Southern Medical University, Guangzhou; ²College of Oceanography & Environmental Sciences, Xiamen University, Xiamen
Effects of Cr⁶⁺ stress on the non-specific immunity of *Scylla paramamosain* (L07)

11:45-12:00

Danielle Pogge, Erin Richter, Mary Drewnoski, Stephanie Hansen
Iowa State University, IA, USA
Mineral clearance from plasma and liver following injection with a trace mineral complex is affected by cattle breed (L08)

12:00-12:15

Nicole Spiegel¹, Se Zhu², Nick Costa¹, Halina Kobryn¹, Geoffrey Judson¹, Nyima Tashi², Peter Thomson³, Lin Lu⁴, Su Qi⁴, Yu Shunxiang⁴ and Xugang Luo⁴
¹Murdoch University, Murdoch WA, Australia; ²Tibetan Livestock Research Institute, Lhasa TAR; ³The University of Sydney, NSW, Australia; ⁴Institute of Animal Science, Chinese Academy of Agricultural Sciences, Beijing
Selenium status of livestock in the Tibetan Autonomous Region of China (L09)

12:15-12:30

Jiangyong Zeng¹, Wujin Cuomu¹, Nicole Spiegel², Se Zhu¹, Nick Costa², Halina Kobryn², Geoffrey Judson², Nyima Tashi¹, Peter Thomson³, Yu Shunxiang⁴ and Xugang Luo⁴
¹Tibetan Livestock Research Institute, Lhasa TAR China; ²Murdoch University, Murdoch WA, Australia; ³The University of Sydney, NSW, Australia; ⁴Institute of Animal Science, Chinese Academy of Agricultural Sciences, Beijing
Copper status of livestock in the Tibetan Autonomous Region of China (L10)

Symposium 13 (M)

Title: Genomics of Selenocysteine and Selenoproteins

Sponsor: TEMA-14

Location: Conference Room 2

Chairs: Josef Köhrle, Charite Universitätsmedizin Berlin, Germany
An-Sik Chung, Korea Advanced Institute of Science and Technology, South Korea

8:00-8:30

Anton A. Turanov¹, Ryuta Tobe², Bradley A. Carlson², Xue-Ming Xu², Min-Hyuk Yoo², Vadim N. Gladyshev¹, Dolph L. Hatfield²
¹Division of Genetics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston MA 02115 USA; ²Molecular Biology of Selenium Section, Laboratory of Cancer Prevention, Center for Cancer Research, NCI, NIH, Bethesda, MD 20892 USA
Cysteine/selenocysteine replacement in selenoproteins: a novel pathway for cysteine biosynthesis and its consequences on selenoprotein function (M01)

8:30-9:00

Laurence Wurth¹, Akiko Takeuchi¹, Olga Kossinova^{1,2}, Galina Karpova², Christine Allmang¹, Alain Krol¹
¹Architecture and Reactivity of RNA, University of Strasbourg – National Center for Scientific Research, Institute for Molecular and Cellular Biology 15, Rue René Descartes, 67084 Strasbourg Cedex, France; ²Institute of Chemical Biology and Fundamental Medicine, Russian Academy of Sciences, Novosibirsk, Russia
Biogenesis and translation of selenoprotein mRNAs (M02)

9:00-9:30

John E. Hesketh, Catherine Méplan
Newcastle University, UK
Functional genomic studies of selenoprotein function (M03)

9:30-10:00

Jiangyun Wang¹ (Absent), Tianyuan Wang²

¹Institute of Biophysics, Chinese Academy of Sciences, Beijing; ²University of Science and Technology of China, Hefei
Selenoprotein engineering (M04)

10:00-10:30

Coffer/Tea Break

Chairs: K. Sandeep Prabhu, Pennsylvania State University, USA

Qiong Liu, Shenzhen University, Shenzhen

10:30-11:00

P. D. Whanger

Oregon State University, Corvallis, OR 97330, USA

Selenoprotein W, a selenoprotein in search of a function (M05)

11:00-11:30

K. Sandeep Prabhu, Shakira Nelson, Ujjawal Gandhi, Shailaja Hegde, Naveen Kaushal, Vivek Narayan, Robert F. Paulson

Pennsylvania State University, USA

Selenium-dependent skewing of macrophage phenotypes and its consequences in a cancer model (M06)

11:30-11:45

Bradley A. Carlson¹, Jin Young Kim², Xue-Ming Xu¹, Yu Zeng³, Shawn Chen³, Vadim N. Gladyshev⁴,

Byeong Jae Lee², Dolph L. Hatfield¹

¹Laboratory of Cancer Prevention, Center for Cancer Research, NCI, NIH, Bethesda, MD 20892, USA; ²Laboratory of Molecular Genetics and Genomics, School of Biological Sciences, Institute of Molecular Biology and Genetics, Seoul National University, Seoul 151-742, Korea; ³Department of Biological Sciences, Ohio University, Athens, OH 45701, USA

Inhibition of selenocysteine tRNA^{[Ser]Sec} aminoacylation provides evidence that aminoacylation is required for regulatory methylation of this tRNA (M07)

11:45-12:00

Yih-Fong Liew¹ (Absent), Yun-Hsin Hsu¹, Yi-Shen Hsu¹, Yu-Shun Lin², Ning-Sing Shaw²

¹Department of Nutritional Science, Fu Jen Catholic University, New Taipei City 24205 Taiwan; ²Department of Biochemical Science and Technology, National Taiwan University, Taipei, 10617 Taiwan

Iron status modulate the tRNA thiouridine biosynthesis and its modification in rat skeletal muscle and L6 myotube cell (M08)

12:00-12:15

Henian Yang¹ (Absent), Fergus Nicol², Martin D. Reid², Ou Ou², Margaret-Jane Gordon², Tiantian Zhang¹, Shaobo Zhou¹, John H. Beattie²

¹Luton Institute of Research in Applied Natural Sciences, University of Bedfordshire, UK; ²Aberdeen University Rowett Institute of Nutrition and Health, Aberdeen, UK

Application of proteomic techniques for the discovery of zinc status biomarkers (M09)

12:15-12:30

Jichang Zhou^{1,2}, Hua Zhao², Jiayong Tang², Jungang Li², Xinjie Xia², Xiaoli Liu¹, Yumei Zhu¹, and Xin Gen Lei³

¹Molecular Biology Lab, Shenzhen Center for Chronic Disease Control, Shenzhen Guangdong, 518020; ²Animal Nutrition Institute, Sichuan Agricultural University, Ya'an Sichuan, 625014; ³Department of Animal Science, Cornell University, Ithaca, NY 14853, USA

Molecular cloning, chromosomal localization and expression profiling of porcine selenoprotein M gene (M10)

Symposium 14 (N)

Title: Trace Element Toxicology and Geochemistry

Sponsor: TEMA-14

14th International Symposium on Trace Elements in Man and Animals

Location: Conference Room 3
Chairs: Xuebin Yin, Suzhou Institute of University of Science and Technology of China, Suzhou
Shunsuke D. Meshitsuka, Tottori University, Japan

8:00-8:30

Xinbin Feng

State key Laboratory of Environmental Geochemistry, Institute of Geochemistry, Chinese Academy of Sciences, Beijing
MeHg exposure pathway to inhabitants in Guizhou, China (N01)

8:30-9:00

Shunsuke Meshitsuka

Tottori University Graduate School of Medicine, Institute of Regenerative Medicine and Biofunction, Yonago, 683-8503, Japan

Influence of aluminum on the transcriptional regulation of gene expression (N02)

9:00-9:30

Yanxin Wang (Absent)

China University of Geosciences, Wuhan

Environmental biogeochemistry of high arsenic groundwater (N03)

9:30-10:00

Jan-Ying Yeh¹, Chao-Hsiang Lin¹, Bor-Rung Ou²

¹Department of Biotechnology, Asia University, Taichung, Taiwan; ²Department of Animal Science and Biotechnology, Taichung, Taiwan

Effect of selenium-enriched broccoli extract and various selenocompounds on arsenic-induced toxicity (N04)

10:00-10:30

Coffer/Tea Break

Chairs: Jan-Ying Yeh, Asia University, Taichung
Wenjie Yang, Chinese Center for Disease Control and Prevention, Beijing

10.30-11.00

Hyo-Taek Chon

Department of Energy Resources Engineering, Seoul National University, Seoul 151-744, Korea

Heavy metals contamination and human risk assessment in the vicinity of abandoned gold mine sites in Korea (N05)

11:00-11:15

Yufeng Li¹, Jing Lin¹, Chunying Chen^{1,2}, Yuxi Gao¹, Zhifang Chai¹

¹CAS Key Laboratory of Nuclear Analytical Techniques and CAS Key Laboratory for Bio-environmental Effects of Nanomaterials and Nanosafety, Institute of High Energy Physics, Chinese Academy of Sciences, Beijing 100049; ²National Center for Nanoscience and Technology, Beijing 100190

Potential health risk of multielemental exposure through foodstuffs from Wanshan mercury mining area, China and effect of selenium supplementation in local residents (N06)

11:15-11:30

Peter Winship, Sylvaine Bruggraber, Jonathan Powell

MRC Human Nutrition Research, 120 Fulbourn Road, Cambridge, CB1 9NL, UK

Aluminium contamination in parenteral iron therapies: is patient exposure a problem? (N07)

11:30-11:45

Min-Hsuan Wu, Wen-Mein Wu, Guoo-Shyng Wang Hsu

Department of Nutritional Science, Fu-Jen University, Taipei, Taiwan

High aluminum intake affects the immune response toward Th2 in neonatal SD rats (N08)

11:45-12:00

Marta López-Alonso¹, Marta Miranda², José Luis Benedito¹, Richard F. Shore³, Isabel Blanco-Penedo⁴

14th International Symposium on Trace Elements in Man and Animals

¹Departamento de Patología Animal, and ²Departamento de Ciencias Clínicas Veterinarias, Facultad de Veterinaria, Universidade de Santiago de Compostela, 27002, Lugo, Spain; ³Centre for Ecology & Hydrology, Lancaster Environment Centre, UK; ⁴KV, Unit for Epidemiology, Swedish University of Agricultural Sciences, Uppsala, Sweden
Characterization on beef-cattle farm systems according to toxic and trace metal levels (N09)

12:00-12:15

Shibin Ding, Dan Liao, Chong Tian, Chenjiang Ying

Department of Nutrition and Food Hygiene and MOE Key Lab of Environment and Health, School of Public Health, Tongji Medical College, Huazhong University of Science Technology, Wuhan

The effect of zinc on lead expelling, copper and iron in lead toxicity mice (N10)

Symposium 15 (O)

Title: Trace Element Food Fortification and Bioavailability

Sponsor: TEMA-14

Location: Conference Room 4

Chairs: Junsheng Huo, Chinese Center for Disease Control and Prevention, Beijing
Okhee Han, Penn State University, USA

8:00-8:30

Junsheng Huo, Jing Sun, Jian Huang

Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention, Beijing

Development of food fortification in China (O01)

8:30-9:00

Okhee Han

Pennsylvania State University, University Park, PA 16802, USA

Effects of bioactive polyphenolic compounds on iron and zinc absorption (O02)

9:00-9:30

Xiaoguang Yang¹, Jianhua Piao¹, Lichen Yang¹, Jun Wang²

¹Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention; ²National Research Center for Certified Reference Materials, Beijing

Study on iron bioavailability from a representative diet in Chinese urban women of childbearing age (O03)

9:30-10:00

Dennis Miller¹, Chi Kong Yeung², Le Zhu³

¹Department of Food Science, Cornell University, Ithaca, New York, USA; ²Food Science and Technology Program BNU-HKBU United International College Zhuhai, Guangdong; ³Department of Human Biology, University of Wisconsin-Green Bay, Green Bay, Wisconsin, USA

NaFeEDTA as a food fortificant: implications for iron homeostasis and tissue iron distribution (O04)

10:00-10:30

Coffee/Tea Break

Chairs: Dennis D. Miller, Cornell University, USA

Yiming Xia, Chinese Center for Disease Control and Prevention, Beijing

10:30-11:00

Jianhua Piao¹, Yuan Tian¹, Lichen Yang¹, Jun Wang², Xiaoguang Yang¹

¹Institute of Nutrition and Food Safety, Chinese Center for Disease Control and Prevention, Beijing; ²National Research Center for Certified Reference Materials, Beijing

Assessment of zinc bioavailability in Chinese representative diet (O05)

11:00-11:30

G. A. Ravishankar

Plant Cell Biotechnology Department, Central Food Technological Research Institute, Mysore 570020, India

Biotechnological approaches for micronutrient enrichment for food applications (O06)

11:30-11:45

Bianca Mergler, Nuno Faria, Sylvaine Bruggraber, Jonathan Powell, Dora Pereira
MRC Human Nutrition Research, Elsie Widdowson Laboratory, Cambridge, CB1 9NL, UK
Investigating the uptake of nanoparticulate dietary iron (O07)

11:45-12:00

Ewa A Szymlek-Gay¹, Sheila A Skeaff², Ying Zhao², Andrew R Gray³, Elaine L Ferguson⁴, Anne-Louise M Heath²

¹Department of Clinical Sciences, Pediatrics, Umea University, SE-901 85 Umea, Sweden; ²Department of Human Nutrition, University of Otago, PO Box 56, Dunedin 9054, New Zealand; ³Department of Preventive and Social Medicine, University of Otago, PO Box 913, Dunedin 9054, New Zealand; ⁴Department of Nutrition and Public Health Intervention Research, London School of Hygiene and Tropical Medicine, London, WC1E 7HT, UK
Iodine-fortified milk improves iodine status in toddlers (O08)

12:00-12:15

Edwin Habeych, Marie-Caroline Augueres, Martin Michel
Natural Products Group, Food Science and Technology Department, Nestlé Research Center, Vers-Chez-Les-Blanc CH-1000 Lausanne 26, Switzerland
Simple Strategies to Assess Fe Fortificants in Commercial Product Formulations (O09)

12:15-12:30

Madhu Patted (Absent), Pushpa Bharati, Hemalatha S, Bharati Chimmad
University of Agricultural Sciences, Dharwad-580 005, Karnataka State, India
Bioaccessibility of iron and zinc from green leafy vegetable based foods (O10)

Symposium 16 (P)

Title: State-of-the-Art Instruments and Methodology
Sponsor: TEMA-14
Location: Conference Room 5

Chairs: Zijian Guo, Nanjing University, Nanjing
Anatoly Skalny, Orenburg State University, Russia

8:00-8:30am

David Paterson¹, Martin D. de Jonge¹, Daryl L. Howard¹, Chris G. Ryan², Barbara E. Etschmann³
¹Australian Synchrotron, Clayton VIC 3168, Australia; ²CSIRO, Clayton 3168 VIC, Australia; ³Department of Geology, University of Adelaide SA, Australia
X-ray fluorescence microscopy: a new and versatile view of trace metals in biological systems (P01)

8:30-9:00

Zijian Guo
State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing
Fluorescent imaging of biological zinc at in vitro and in vivo conditions (P02)

9:00-9:30

Zoltan Mester
Institute for National Measurement Standard, National Research Council Canada, Ottawa, Ontario K1A 0R6, Canada
From selenols to selenium nanoparticles: mapping Se metabolic pathway in yeast using mass and X-ray spectroscopy (P03)

9:30-10:00

Sheng Zhang¹, Shikui Wang², Jeremy Weaver¹, Xin Gen Lei¹
¹Cornell University, USA; ²Institute of Animal Science, Guangdong Academy of Agricultural Sciences, Beijing
Quantitative LC-MS/MS techniques for characterizing selenocysteine abundance change in the hepatic GPX1 protein of SOD1 knockout mice (P04)

10:00-10:30

Coffer/Tea Break

Chairs: Zoltan Mester, National Research Council, Canada
Tejo Prakash, Thapar University, India

10:30-11:00

H. Yang¹, O. Ou², M. Beckmann³, D. Zheng⁴, J. Draper³, C. Hogstrand⁴, P.W. Emery⁴, T. Zhang¹, J. H. Beattie², Shaobo Zhou¹

¹Luton Institute of Research in Applied Natural Sciences, University of Bedfordshire, UK; ²Aberdeen University Rowett Institute of Nutrition and Health, Aberdeen, UK; ³Institute of Biological Environmental and Rural Sciences, Aberystwyth University, Penglais Campus, Aberystwyth, UK; ⁴Nutritional Sciences Division, King's College London, UK
Application of omic techniques for the discovery of zinc status biomarkers (P05)

11:00-11:30

Anatoly Skalny

Russian Society of Trace Elements in Medicine, Russia

Bioelementology as integrative approach in trace element research (P06)

11:30-11:50

Xiaoqi Lu^{1,2,3}, Xuebin Yin^{1,2,3}, Yuanyuan Zhu^{1,3}, Zisen He^{1,2,3}

¹Key Lab for Selenium and Human Health Suzhou institute for Advanced Study, USTC, Suzhou; ²School of Earth and Space Science, University of Science and Technology of China, Hefei; ³Suzhou Selenium Valley Technology Co., Ltd, Suzhou;
Speciation of selenium in selenium-enriched cereal from higher selenium area by LC-UV-HG-AFS (P07)

11:50-12:10

Tejo Prakash¹, Sumit Kumar Jaiswal¹, Ranjana Prakash², Raghunath Acharya³, Venkata Ramana Reddy Annareddy⁴

¹Department of Biotechnology and Environmental Sciences, and ²School of Chemistry and Biochemistry, Thapar University, Patiala, India; ³Radiochemistry Division, Bhabha Atomic Research Centre, Mumbai, India; ⁴Analytical Chemistry Division, Bhabha Atomic Research Centre, Mumbai, India

Selenium content in raw, cooked and in vitro bioaccessible fractions of Se-enriched rice (P08)

12:10-12:30

Juraj Prejac¹, Vjerman Visnjevic², Sandra Morovic³, Ninoslav Mimica⁴, Anatoly V.Skalny⁵, Berislav Momčilović²

¹University Hospital Center Zagreb, Zagreb, Croatia; ²Institute for Research and Development of the Sustainable Eco Systems, Zagreb, Croatia; ³"Sisters of Mercy" Clinical Hospital, Zagreb, Croatia; ⁴Psychiatric Hospital Vrapce, Zagreb, Croatia; ⁵Center for Biotic Medicine, Moscow, Russia

Comparative analysis of gallium in human hair and blood (P09)

12:30 -1:45

Lunch, Ballroom, Fuyuan Guobin Hotel

Afternoon Sessions

Plenary Session 5 (2:00-4:30)

Location: Large Auditorium, Fuyuan Guobin Hotel

Chairs: Kaixun Huang, Huazhong University of Science and Technology, Wuhan
John E. Hesketh, Newcastle University, UK

2:00-2:30

Vadim N. Gladyshev

Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Selenocysteine genomics (PS12)

2:30-3:00

Roger A. Sunde, Anna M. Raines

University of Wisconsin, Madison WI 53706, USA

Selenium regulation of Se-dependent and Se-independent genes (PS13)

3:00-3:30

Philip Taylor¹, Sanford Dawsey¹, Christian Abnet¹, Youlin Qiao²

¹Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, Bethesda, MD, USA; ²Cancer Institute, Chinese Academy of Medical Sciences, Beijing

Cancer prevention: the trials and tribulations of selenium (PS14)

3:30-4:00

Margaret Rayman¹, Gabrielle Blundell-Pound¹, Saverio Stranges², Roberto Pastor-Barriuso³, Eliseo Guallar^{4,5}

¹Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK; ²University of Warwick Medical School, Coventry, UK; ³National Center for Epidemiology, Carlos III Institute of Health and Consortium for Biomedical Research in Epidemiology and Public Health, Madrid, Spain; ⁴Johns Hopkins University Bloomberg School of Public Health, Baltimore, USA; ⁵National Center for Cardiovascular Research (CNIC), Madrid, Spain

Selenium and type-2 diabetes: rationale for, and results of, a randomised trial of selenium on type-2 diabetes risk, as assessed by plasma adiponectin (PS15)

4:00-4:30

Huibi Xu, Xiangliang Yang, Kaixun Huang (Qiong Liu presented the paper for Huibi Xu)

School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan

Progress in chemical mimics of glutathione peroxidase-GPx (PS16)

4:40-5:20

Closing Ceremony

Large Auditorium, Fuyuan Guobin Hotel

6:00-7:30

Farewell Banquet

Ballroom, Fuyuan Guobin Hotel

8:00-9:30

Performance Show (Folk song and dance)

Large Auditorium, Fuyuan Guobin Hotel

Saturday, September 24, 2011

7:00am-8:00am

Breakfast, Ballroom, Fuyuan Guobin Hotel

8:30am-

Departure

Have a safe trip home!

Poster Presentation List and Schedule

Note:	<p>Odd-numbered posters (e.g., PT1, 3, 5, 67) will be displayed on Tuesday, September 20, 2011</p> <p>Even-numbered posters (e.g., PT2, 4, 6,68) will be displayed on Wednesday, September 21, 2011</p> <p>Poster board size: 3.9' wide and 5.4' high. Prepare your poster to fit in a 3.6' x 5.2' (110 cm x 160 cm) area</p> <p>Detailed instructions for preparing effective poster presentation refer to the TEMA14 web</p> <p>Poster view time: 9.30-10.30am</p> <p>Poster display/view place: the corridor of Fuyuan Guobin Hotel</p> <p>Instructions for the poster preparation are referred to TEMA14 web</p>		
NO.	Author	Institute	Title
PT01	<u>Chengkang Tang</u> ¹ , Weihong He ¹ , Qifeng Li ¹ , Bo Su ¹ , Huiqi Xie ¹ and Y. James Kang ^{1,2}	¹ Regenerative Medicine Research Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China; ² Department of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Kentucky 40202, USA	A Novel Nanobiomaterial for Time-controlled Tissue Delivery of Copper Enhances Vascular Responses in a Mouse Model of Limb Ischemia
PT02	<u>Hemalatha Sreeramaiah</u> ¹ (Absent), Suman Kapila ² , Manju Reddy ³	¹ University of Agricultural Sciences, Dharwad 580005, India; ² National Dairy Research Institute, Karnal, 132001, Haryana, India; ³ Iowa State University, Ames, Iowa, 50011, USA	Bioavailability of Iron from Malted Finger Millet (<i>Eleusine coracana</i>)-based Supplementary Food
PT03	Anatoly Fesyun ¹ , <u>Anatoly Skalny</u> ² , Sevil Grabeklis ³ , Andrei Grabeklis ²	¹ Military Medical Directorate of Internal Forces at Ministry of the Interior of Russia, Moscow, Russia; ² Russian Society of Trace Elements in Medicine, Moscow, Russia; ³ A.N.Belozersky Research Institute of Physico-Chemical Biology, M.Yu. Lomonosov Moscow State University, Moscow, Russia	Changes in Mineral Status of Internal Forces Conscripts Induced by Use of an Arginine Preparation
PT04	<u>Yan Zhang</u> ¹ , Vadim Gladyshev ²	¹ Key Laboratory of Systems Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031 China; ² Division of Genetics, Department of Medicine, Brigham & Women's Hospital and Harvard Medical School, Boston, MA 02115, USA	Comparative Genomics Analyses Reveal Complexity of Trace Element Dependence in Biology
PT05	<u>Zhaoxin Fan</u> ¹ , Shun Li ¹ , Zhen Zhang ¹ , Huiqi Xie ¹ , Y. James Kang ^{1,2}	¹ Regenerative Medicine Research Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China; ² Department of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Kentucky 40202, USA	Copper Chelator Tetraethylenepentamine Reduces Deferoximine-induced Hypoxia-inducible Factor-1 Accumulation and Vascular Endothelial Growth Factor Expression
PT06	<u>Liyang Qiu</u> ¹ , Xueqing Ding ¹ , Zhen Zhang ¹ , Huiqi Xie ¹ , Y. James Kang ^{1,2}	¹ Regenerative Medicine Research Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China; ² Department of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Kentucky 40202, USA	Copper is Required for Cobalt-induced Transcriptional Activity of Hypoxia-inducible Factor-1
PT07	<u>Elena Sizova</u> ¹ (Absent), Sergey Miroshnikov ¹ , Valentina Polyakova ² , Natalya Gluschenko ³ , Anatoliy Skalny ¹	¹ Orenburg State University, Orenburg, Russia; ² Orenburg State Medical Academy of Federal Agency in Public Health and Social Development, Orenburg, Russia; ³ Institute of Energy Problems in Chemical Physics RAS, Moscow, Russia	Copper Nanoparticles as Modulators of Apoptosis and Structural Changes in Tissues
PT08	<u>Shun Li</u> ¹ , Huiqi Xie ¹ , Shengfu Li ¹ , Y. James Kang ^{1,2}	¹ Regenerative Medicine Research Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China; ² Department of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Kentucky 40202, USA	Copper Stimulates Proliferation of Human Umbilical Vein Endothelial Cells in a Vascular Endothelial Growth Factor-independent Pathway
PT09	<u>Antonio Pinto</u> , Bodo Speckmann, Helmut Sies and Holger Steinbrenner	Institute for Biochemistry and Molecular Biology I, Heinrich-Heine-University, Düsseldorf, Germany	Delaying of Insulin Signal Transduction in Skeletal Muscle Cells by Selenium Compounds
PT10	<u>Jiahua Zhang</u>	Nutritional health institute of Panzhihua city, Panzhihua, Sichuan, China	Development and Utilization of Mineral Elements to Enhance the Quality of Distinctive Agriculture

14th International Symposium on Trace Elements in Man and Animals

PT11	<u>Jing Lin</u> ^{1,2} , Yufeng Li ¹ , Jinting Yan ³ , Xu Ma ³ , Bai Li ¹ , Chunying Chen ⁴ , Bin Qiu ²	¹ CAS Key Laboratory for Nuclear Analytical Techniques, Institute of High Energy Physics, Chinese Academy of Sciences, Beijing, 100049, China; ² Ministry of Education Key Laboratory of Analysis and Detection for Food Safety, Department of Chemistry, Fuzhou University, Fuzhou, 350002, China; ³ National Research Institute for Family Planning, Beijing, 100081, China; ⁴ CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, National Center for Nanoscience and Technology of China, Beijing, 100190, China	Distribution and Speciation of Arsenic in Mice after Subchronic Exposure to Sodium Arsenite
PT12	Valeria Candia, <u>Diego Gaitán</u> , Manueal Olivares, Daniel Lòpez de Romaña, Fernando Pizarro	Institute of Nutrition and Food Technology, University of Chile, Santiago, Chile.	Effect of Calcium Salts on the Bioavailability of Non-heme Iron in Humans
PT13	<u>Yugang Jiang</u> ¹ , (Absent) Jing Li ^{1,2} , Hao Lu ^{1,3} , Wei Pang ¹ , Hongpeng Yang ¹ , Shijun Lu ¹ , Wenjie Li ²	¹ Department of Nutrition, Institute of Health & Environmental Medicine, Academy of Military Medical Sciences, Tianjin, China; ² Department of Nutrition and Food Hygiene, College of Public Health, Zhengzhou University, Zhengzhou, China; ³ Department of Nutrition and Food Hygiene, West China School of Public Health, Sichuan University, Chengdu, China	Effects of Sub-chronic Aluminium Exposure on Learning and Memory Functions and Antioxidative Capacity in Rats
PT14	<u>Lin Lu</u> ^{1,2} , Zehui Liu ^{1,3} , Sufen Li ^{1,2} , Xugang Luo ^{1,2} , Lin Xi ⁴	¹ Mineral Nutrition Research Division, Institute of Animal Science, Chinese Academy of Agricultural Sciences, Beijing 100193, China; ² State Key Laboratory of Animal Nutrition, Beijing 100193, China; ³ Animal Nutrition Institute, Sichuan Agricultural University, and Key Laboratory of Education Ministry, Yaan 625014, China; ⁴ Department of Animal Science, NC State University, Raleigh NC 27695-7621, USA	Effects of Supplemental Zinc in Broiler Diets on Carcass Traits and Meat Quality
PT15	<u>Nianhua Zhu</u> ^{1,2} (Absent), Yanghua Liao ² , Fuqing Deng ² , Weijun Zhang ² , Yiqiang Huang ²	¹ College of Animal Science and Technology, Jiangxi Agricultural University, Nanchang, 330045, China; ² Xinjia Bio-engineering Co., Ltd, Changsha, 410011, China	Efficacy of Dietary Selenium Sources and Vitamin E on Growth and Carcass Characteristics of Finishing Pigs
PT16	Yandan Hu ^{1,2} , Wei Pang ¹ , Hao Lu ^{1,2} , Jing Li ¹ , <u>Yugang Jiang</u> ¹ (Absent), Chengyu Huang ²	¹ Institute of Hygiene and Environmental Medicine, Academy of Military Medical Sciences, Tianjin, China; ² Department of Nutrition and Food Hygiene, West China School of Public Health, Sichuan University, Chengdu, China	Epigenetic Effects of Zinc Deficiency on Learning and Memory Ability in Rats Aged 0~2 Years'old
PT17	Christopher J. Boehler, Anna M. Raines, <u>Roger A. Sunde</u>	Department of Nutritional Sciences, University of Wisconsin, 1415 Linden Dr., Madison, Wisconsin 53706 USA	Essentiality of Selenium and Thioredoxin Reductase in <i>C. elegans</i>
PT18	<u>Yu Hsin Chen</u> , Mei Po Lu, Yi Ting Shih, Feili LoYang	Department of Nutritional Science, Fu Jen Catholic University, Taipei, Taiwan	Estimation of Dietary Selenium Intakes of Taiwanese by a Self-constructed Food Selenium Content Data
PT19	<u>Ying Qi</u> ¹ , W. Y. Wendy Lou ¹ , Marcia Cooper ³ , Mary R. L'Abbe ²	¹ Dalla Lana School of Public Health, and ² Department of Nutritional Sciences, University of Toronto, Toronto ON M5S 3E2, Canada; ³ Bureau of Nutritional Sciences, Health Canada, Ottawa ON K1A 0L2, Canada	Food Iron Bioavailability of the Mixed Canadian Diets
PT20	<u>Juraj Prejac</u> ¹ , Sasa Badzek ¹ , Vjeran Visnjevic ² , Ninoslav Mimica ³ , Andrei ASkalny ⁴ , Berislav Momčilović ²	¹ University Hospital Center Zagreb, Zagreb, Croatia; ² Institute for Research and Development of the Sustainable Eco Systems, Zagreb, Croatia; ³ Psychiatric Hospital Vrapce, Zagreb, Croatia; ⁴ Center for Biotic Medicine, Moscow, Russia	Hair Tungsten (Wolfram) is Increased in Human Depression
PT21	<u>Marta López-Alonso</u> , Jose Luis Benedito, Cristina Castillo, Betiana Gutiérrez, Marco García-Vaquero	Universidade de Santiago de Compostela, Departamento de Patoloxía Animal, Facultad de Veterinaria, 27002, Lugo, Spain	Hepatic Oxidative Damage Induced by Moderate Cu Supplementation in Cattle

14th International Symposium on Trace Elements in Man and Animals

PT22	<u>Liang Jiang</u> , Hua Chen, Qiong Liu, Jiazuan Ni	College of Life Sciences, Shenzhen University, Shenzhen, China	Identification of Selenoproteins from Amphioxus Genomes via Bioinformatics Method
PT23	<u>Margarita Skalnaya</u> ^{1,2} , Vasily Yurasov ¹	¹ Institute of Bioelementology, Orenburg State University, Pobedy ave. 13, Orenburg, 460352, Russia; ² ANO Centre for Biotic Medicine, Zemlyanoy Val str., 46, Moscow 105064, Russia	Impact of Macro- and Trace Elements in Reproductive Health: Data of Multielement Ejaculate Investigation in Subfertile Males
PT24	<u>Abdulhadi Cihangir Uguz</u> , Mustafa Naziroglu	Department of Biophysics, Faculty of Medicine, Suleyman Demirel University, Isparta, Turkey	Investigation of Effects of Selenium on Ca ²⁺ Signaling and Apoptotic Cell Death in Oxidative Stress-Induced Dorsal Root Ganglion Neurons
PT25	<u>Kevin A. Cockell</u> ¹ (Absent), André Robichaud ² , Pascal Lapointe ²	¹ Nutrition Research Division, Food Directorate, Health Canada, Ottawa, Ontario, Canada K1A 0K9; ² Quebec Region Food Laboratory, Health Canada, Longueuil, Quebec, Canada J4K 1C7	Iodine Content of Breads in Canada is Highly Variable by Product Type, Region and Time
PT26	<u>Barbara Stoecker</u> ² , Tafere G Egziabher ^{1,2} , Afework Mulugeta ³ , Alemtsehay Bogale ^{1,2} , K Michael Hambidge ⁴	¹ Hawassa University; ² Oklahoma State University; ³ Mekelle University; ⁴ University of Colorado Denver	Iodine Status of Women from Selected Rural Areas of Sidama Zone, Southern Ethiopia
PT27	<u>Bharati Chimmad</u> (Absent), Kavita Kotagi, Rama Naik	University of Agricultural Sciences, Dharwad-580005, Karnataka, India	<i>Lepidium sativum</i> L. for Iron Enrichment of RTE Flakes of <i>Panicum Miliare</i>
PT28	Seden Demirci ¹ , Mustafa Naziroglu ² , Suleyman Kutluhan ¹ , <u>A. Cihangir Uguz</u> ² , Vedat Ali Yurekli ¹	¹ Department of Neurology, and ² Department of Biophysics, Faculty of Medicine, Suleyman Demirel University, Isparta, Turkey	Selenium and Antiepileptic Drug Topiramate modulate Ca ²⁺ Signaling, Oxidative Stress and Cell Viability in PC 12 Cells
PT29	<u>Antonio Pinto</u> ¹ , Mert Sanil ² , Margaret Rayman ² , Linda Morgan ² , Helmut Sies ¹ , Darren Juniper ³ , Lynne Clark ³ , Holger Steinbrenner ¹	¹ Institute for Biochemistry and Molecular Biology I, Heinrich-Heine-University, Düsseldorf, Germany; ² Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK; ³ School of Agriculture, Policy and Development University of Reading, Reading, UK	Male Pigs Fed a Supranutritional Selenium Diet may Develop a Predisposition to Type 2 Diabetes
PT30	<u>Shunsuke Meshitsuka</u> ¹ , Ojeiru FEzomo ¹ , Hitoshi Kawamoto ² , Yasunari Miki ² , Takayuki Kimura ²	¹ Tottori University Graduate School of Medicine, Institute of Regenerative Medicine and Biofunction, Yonago, Tottori 683-8503 Japan; ² Marine Products Kimuraya, 3307 Watari, Sakaiminato, Tottori 684-0072 Japan	Metabolism of Platinum after Anti-tumor Agent Oxaliplatin Treatment was Altered by the Ingestion of Fucoidan
PT31	<u>James Richards</u> , Karen Wedekind	Novus International, Inc., 20 Research Park Dr., St. Charles, MO, 63304, USA	Methods to Estimate Trace Mineral Bioavailability
PT32	<u>Fakira Borkovec</u> ¹ (Absent), Pushparajah Thavarajah ² , Kevin McPhee ³ , Gerald Combs Jr ⁴ , Dil Thavarajah ¹	¹ School of Food Systems, Department of Cereal and Food Sciences, ² Department of Plant Sciences, and ³ Department of Plant Sciences, North Dakota State University, Fargo, ND 58105, USA; ⁴ Grand Forks Human Nutrition Research Center, ARS/USDA, Grand Forks, ND 58202, USA	Will Selenium Increase Lentil Grain Yield and Nutritional Quality?
PT33	<u>Veronique Dermauw</u> ¹ , Kechero Yisehak ² , Ellen S.Dierenfeld ³ , Gijs Du Laing ⁴ , Johan Buyse ⁵ , B. Wuyts ⁶ , G. P. J. Janssens ¹	¹ Laboratory of Animal Nutrition, Faculty of Veterinary Medicine, Ghent University, Heidestraat 19, B-9820 Merelbeke, Belgium; ² Department of Animal Science, Jimma University College of Agriculture and Veterinary Medicine, PO Box 307, Jimma, Ethiopia; ³ Novus International, 20 Research Park Drive, St. Charles, MO, 63304 USA; ⁴ Department of Applied Analytical and Physical Chemistry, Ghent University, Coupure Links 653, B-9000 Ghent, Belgium; ⁵ Department of Biosystems, Laboratory of Livestock Physiology, Immunology and Genetics, K.U. Leuven, Kasteelpark Arenberg 30, B-3001 Leuven, Belgium; ⁶ Department of Clinical Chemistry, Laboratory of Metabolic Disorders, University Hospital Ghent, De Pintelaan 185, B-9000 Ghent, Belgium	Micromineral Status and Nutrient Utilisation in Zebu Cattle

14th International Symposium on Trace Elements in Man and Animals

PT34	<u>Ningbo Zhang</u> ¹ , Wenqian Jing ^{1,2}	¹ Institute of Animal Science, Chinese Academy of Agricultural Sciences, Beijing, China; ² Linyi Normal University, Linyi, Shandong, China	Molecular Characterization and NF-κB-regulated Transcription of Selenoprotein S from the Bama Mini-pig
PT35	Zairong Lei ¹ , <u>Jie Liu</u> ¹ , Jiahua Zhang ²	¹ Eastern Microelement Science and Technology Co. Ltd, Panzhihua, Sichuan, China; ² Institute of Nutritional Health Protection for Panzhihua CDC, Sichuan, China	Distribution of V, Zn, Cr, Cu and Se in Panzhihua Sichuan
PT36	<u>Youssef Aboussaleh</u> (Absent)	Ibn Tofail University, Kenitra, Morocco	Prevalence of Anemia among Schoolchildren in Morocco
PT37	Hao Lu ^{1,2} , <u>Yugang Jiang</u> ¹ (Absent), Jing Li ^{1,3} , Wei Pang ¹ , Yandan Hu ^{1,2} , Hongpeng Yang ¹ , Wenjie Li ³ , Chengyu Huang ²	¹ Department of Nutrition, Institute of Health & Environmental Medicine, Academy of Military Medical Sciences, Tianjin, China; ² Department of Nutrition and Food Hygiene, West China School of Public Health, Sichuan University, Chengdu, China; ³ Department of Nutrition and Food Hygiene, College of Public Health, Zhengzhou University, Zhengzhou, China	Protective Effect of Zinc Supplementation against Aluminium Neurotoxicity: Possible Behavioral, Biochemical and Histopathological Alterations in Male Rats
PT38	<u>Ding Yuan</u> ¹ , Xiaorong Sun ¹ , Xiaorong Wen ¹ , Huiqi Xie ¹ , Y. James Kang ^{1,2}	¹ Regenerative Medicine Research Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China; ² Department of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Kentucky 40202, USA	Regression of Abdominal Aortic Aneurysms by a Novel Nanobiomaterial for Time-controlled Delivery of Copper in a Rabbit Model
PT39	<u>Jiaqiang Huang</u> ¹ , Dai-Lin Li ¹ , Hua Zhao ¹ , Lv-Hui Sun ¹ , Xin-Jie Xia ^{1,2} , Kang-Ning Wang ¹ , Xu-Gang Luo ³ , and Xin Gen Lei ^{1,3,4}	¹ International Center of Future Agriculture for Human Health, Sichuan Agricultural University, Chengdu, Sichuan 611134, China; ² Department of Animal Science, Cornell University, Ithaca, New York 14853, USA	Selenium-deficiency Diseases in Chicks are Associated with Down-regulation of Seven Common Selenoprotein Genes in Liver and Muscle
PT40	<u>Colin Cercamondi</u> , Ines Egli, Christophe Zeder, Richard Hurrell	Laboratory of Human Nutrition, Institute of Food, Nutrition and Health, ETH Zurich, Zurich, Switzerland	Sodium Iron EDTA Can Partly Overcome the Strong Inhibitory Effect of Polyphenols from Brown Sorghum on Iron Absorption in Young Women and Causes Less Colour Changes in Sorghum Porridges than Ferrous Sulfate
PT41	<u>Hongjie Chen</u> , Kaixun Huang	Hubei Key Laboratory of Bioinorganic Chemistry & Materia Medica, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan 430074, China	Effect of the Antioxidant Ability on Formation of Selenite Cataract in Different Development Stage of Rat Lens
PT42	Zhuqing Zhao(Absent)	Huazhong Agriculture University	The strategies of regulation of plant selenium content
PT43	<u>Xiao Zuo</u> ¹ , Rui Li ¹ , Huiqi Xie ¹ , Y. James Kang ^{1,2}	¹ Regenerative Medicine Research Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China; ² Department of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Kentucky 40202, USA	Suppression of Cytochrome C Oxidase and Copper Chaperones by Phenylephrine in Primary Cultures of Neonatal Rat Cardiomyocytes: the Effects of Vascular Endothelial Growth Factor
PT44	<u>Hwa-Young Kim</u> ¹ , Moon-Jung Kim ¹ , Byung Cheon Lee ^{2,3} , Jaeho Jeong ⁴ , Kong-Joo Lee ⁴ , Kwang Yeon Hwang ⁵ , Vadim N. Gladyshev ³	¹ Department of Biochemistry and Molecular Biology, Yeungnam University College of Medicine, Daegu 705-717, Republic of Korea; ² Department of Biochemistry, University of Nebraska, Lincoln, NE 68588, USA; ³ Division of Genetics, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, USA; ⁴ The Center for Cell Signaling & Drug Discovery Research, College of Pharmacy and Division of Life & Pharmaceutical Sciences, Ewha Womans University, Seoul 120-750, Republic of Korea; ⁵ Division of Biotechnology, College of Life Sciences & Biotechnology, Korea University, Seoul 136-701, Republic of Korea	Tandem Use of Selenocysteine: Adaptation of a Selenoprotein Glutaredoxin for Reduction of Selenoprotein Methionine Sulfoxide Reductase
PT45	<u>Mohsen Rasti</u> (Absent), Ahmad Reza Ranjbari, Vahid Noaman	Isfahan Centre of Agriculture & Natural Resources Research, P.O. Box: 81785-199.Isfahan-Iran	The Iron and Selenium Status of Grazing Ewe in Semirom Rangelands (Isfahan-Iran)
PT46	<u>Yijing Zhou</u> (Absent), Yunqing Cai, Shiping Zhang, Changwei Liu	Department of Nutrition and Food Hygiene, Nanjing Medical University, China	The Protective Effects of Selenium against Cadmium-induced Apoptosis of LLC-PK ₁ Cells: Involvement of Reactive Oxygen Species and Mitochondria

14th International Symposium on Trace Elements in Man and Animals

PT47	<u>Yo Ying Chang</u> (Absent), Yu Sheng Yang, Yih Fong Liew	Department of Nutritional Science, Fu Jen Catholic University, No. 510 ZhongZheng Rd., Xinzhuang Dist., New Taipei City 24205, Taiwan	The Regulation of Initiation of mRNA Translation by Dietary Iron Intake in Skeletal Muscle of Rats
PT48	<u>Isabel Blanco-Penedo</u> ¹ (Absent), Nils Fall ¹ , Thomas Lundh ² , Marta López-Alonso ³ , Ulf Emanuelson ¹	¹ Swedish University of Agricultural Sciences, Department of Clinical Sciences, Uppsala, Sweden; ² Lund University Hospital, Department of Occupational and Environmental Medicine, Lund, Sweden; ³ University of Santiago de Compostela, Animal Pathology Department, Spain	Trace Element Status and Disease Occurrence in Swedish Organic Dairy Herds
PT49	<u>Marta Miranda</u> ¹ , José Luis Benedito ² , Isabel Blanco-Penedo ³ , Joaquín Hernández ² , Marco García-Vaquero ²	¹ Departamento de Ciencias Clínicas Veterinarias, and ² Departamento de Patología Animal, Universidade de Santiago de Compostela, Facultad de Veterinaria, 27002, Lugo, Spain; ³ Swedish University of Agricultural Sciences, Department of Clinical Sciences, Uppsala, Sweden	Trace Elements and Meat: Does What You Eat Matter?
PT50	<u>Jianglong Hou</u> ¹ , Pengfei Han ¹ , Huiqi Xie ¹ , Xiang Zhou ¹ , Y. James Kang ^{1,2}	¹ Regenerative Medicine Research Center, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China; ² Department of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Kentucky 40202, USA	Ultrasound Contrast Microbubble Targeted Copper Therapy for Ischemic Myocardial Infarction in New Zealand Rabbits
PT51	<u>Karen Wedekind</u> , Joseph Evans, Jenea Lunneman, Cindy Atwell	Novus International, Inc. 20 Research Park Dr., St. Charles, MO, 63304, USA	Use of Chelated Trace Minerals to Improve Efficacy of Osteoarthritis (OA) Joint Supplements
PT52	<u>Ethel Alcantara</u> , Mee-Young Shin, In-Sook Kwun	Department of Food Science and Nutrition, Andong National University, 388 Songchundong, Andong, Kyungpook 760-749, South Korea	Zinc Deficiency Increases Ca and P Deposition in Rat Aortic Primary Vascular Smooth Muscle Cells
PT53	<u>In-Sook Kwun</u> ¹ , Young-Eun Cho ¹ , Ria-Ann R. Lomeda ¹ , Hong-In Shin ² , Je-Yong Choi ³ , Young-Hee Kang ⁴ , and John H. Beattie ⁵	¹ Department of Food Science and Nutrition, Andong National University, 388 Songchundong, Andong, Kyungpook 760-749, South Korea; ² Department of Oral Pathology, School of Dentistry, Institute for Hard Tissue and Bio-Tooth Regeneration (IHBR), Kyungpook National University, Daegu 700-412, South Korea; ³ Department of Biochemistry and Cell Biology, School of Medicine, Kyungpook National University, Daegu 700-422, South Korea; ⁴ Department of Food and Nutrition, Hallym University, Chuncheon 200-702, South Korea; ⁵ Division of Vascular Health, Rowett Institute of Nutrition and Health, University of Aberdeen, Aberdeen, AB21 9SB, UK	Zinc Deficiency Suppresses Matrix Mineralization and Retards Osteogenesis Transiently with Catch-up Possibly through Runx2 Modulation
PT54	<u>Yanqing Wang</u> ¹ , Caixia Zhang ¹ , Zhixia Ji ² , Shouwen Chen ²	¹ College of Animal Science and Technology, Huazhong Agricultural University; ² State Key Laboratory of Agricultural Microbiology, Huazhong Agricultural University, Wuhan, China	γ -Poly-glutamic Acid Improves Iron Bioavailability in Rats
PT55	<u>Yun Wu</u> ^{1,2} , Li Ding ^{1,2} , Hui Li ²	¹ Key Laboratory of Biologic Resources Protection and Utilization of Hubei province, Enshi 445000, China; ² Hubei Institute for Nationalities, Enshi 445000, China	Study on the Contents of Selenoprotein and Se-polysaccharide in Selenium-enriched <i>Lentinan Edodes</i>
PT56	<u>James Richards</u> , Julia Dibner	Novus International, Inc. 20 Research Park Dr., St. Charles, MO, 63304, USA	Use of Chelated Trace Minerals to Improve Bone Health in Poultry
PT57	<u>Xiaoman Dai</u> , Kuanyu Li	Medical School of Nanjing University, 22 Hankou Rd, Nanjing, 210093 China	Putative Expression Mechanism of the Novel Transcripts of Human Frataxin, Causing Neurodegenerative Disease
PT58	Melissa Miranda-Duran, <u>Diego Gaitán</u> , Alex Brito, Manuel Olivares, Daniel López de Romaña, Fernando Pizarro.	Institute of Nutrition and Food Technology, University of Chile, Santiago, Chile	A Randomized Controlled Trial Investigating the Effect of Calcium Supplementation on Iron Status in Chile
PT59	<u>Vekoslava Stibilj</u> ¹ (Absent), Larisa Pograjc ² , Ingrid Falnoga ¹	¹ “Jožef Stefan” Institute, Jamova 39, Ljubljana, Slovenija; ² Ministry of Defence, Vojkova 59, Ljubljana, Slovenija	Correlations between Se–status Biomarkers during Military Training

14th International Symposium on Trace Elements in Man and Animals

PT60	<u>Xugang Luo</u> ^{1,2} , <u>Shiping Bai</u> ^{1,2} , <u>Lin Lu</u> ^{1,2} , <u>Runlian Wang</u> ³ , <u>Lin Xi</u> ⁴ , and <u>Liyang Zhang</u> ^{1,2}	¹ Mineral Nutrition Research Division, Institute of Animal Science, Chinese Academy of Agricultural Sciences, Beijing 100193, China; ² State Key Laboratory of Animal Nutrition, Beijing 100193, China; ³ Department of Animal Science, Guangdong Ocean University, Zhanjiang 524088, China; ⁴ Department of Animal Science, NC State University, Raleigh NC 27695-7621, USA	Manganese Source Affects Manganese Transport and Divalent Metal Transporter One Expression in the Small Intestine of Broilers
PT61	<u>Yi Jia</u> , <u>Yi Li</u> , <u>Kaixun Huang</u>	Hubei Key Laboratory of Bioinorganic Chemistry & Materia Medica, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan 430074, China	Influence of SeIR Gene Silence on Peroxynitrite Induced Cell Apoptosis in Human Lens Cells
PT62	<u>Chi Zhang</u> ^{1,2} , <u>Qibin Huang</u> ^{1,2}	¹ Key Laboratory of Biologic Resources Protection and Utilization of Hubei Province; ² Hubei Institute for Nationalities, Enshi, Hubei, 445000, China	A Preliminary Study on the Antioxidant Activity of Selenoprotein in <i>Cordyceps Militaris</i> Rich in Selenium
PT63	<u>Li Ding</u> ^{1,2} , <u>Hui Li</u> ² , <u>Yun Wu</u> ^{1,2}	¹ Key Laboratory of Biologic Resources Protection and Utilization of Hubei Province, Enshi 445000, China; ² Hubei Institute for Nationalities, Enshi 445000, China	Studies on Photosynthetic Characteristics of <i>Cardamine</i> Growing in Different Site Conditions in the High Selenium Area in Yutangba
PT64	<u>Xinping Liu</u>	Department Of Chemistry and Key Laboratory of Biologic Resources Protection and Utilization of Hubei Province, and Hubei Institute for Nationalities, Hubei 445000, China	Antioxidant Activity in vitro of Selenium Polysaccharide of <i>Thlaspi Caerulescens</i> L. Rich in Selenium
PT65	<u>Mauricio Latorre</u> ¹ , <u>Jung Rho</u> ^{2,3} , <u>Barbara E. Murray</u> ^{2,3} , <u>Alejandro Maass</u> ^{4,5} , <u>Mauricio Gonzalez</u> ^{1,4}	¹ Laboratorio de Bioinformática y Expresión Génica, INTA-Universidad de Chile. Santiago, Chile., ² Department of Internal Medicine, Division of Infectious Diseases, Center for the Study of Emerging and Reemerging Pathogens, Houston, TX, USA., ³ Department of Microbiology and Molecular Genetics, University of Texas Medical School at Houston, Houston, TX, USA., ⁴ Center of Genome Regulation. Santiago, Chile., ⁵ Laboratorio de Bioinformática y Matemática del Genoma, CMM-Universidad de Chile. Santiago, Chile.	Identification and verification of transcriptional networks involved in iron homeostasis and oxidative stress damage activated by copper in <i>Enterococcus faecalis</i> .
PT66	<u>Yu Guo</u> ¹ , <u>Zhengyu Bao</u> ^{1,2} , <u>Sen Yan</u> ¹ , <u>Hui Li</u> ³ , <u>Zhenzhen Ma</u> ¹	¹ Faculty of Earth Science, China University of Geosciences, Wuhan 430074, PR China, ² State Key Laboratory of Geological Processes and Mineral Resources; China University of Geosciences, Wuhan, 430074, PR China, ³ Faculty of Materials Science and Chemical Engineering; China University of Geosciences, Wuhan, 430074, P. R China	Speciation and bioavailability of selenium in soil from Enshi, China
PT67	<u>Ping Li</u> ¹ (Absent), <u>Dingyou Zhou</u> ¹ , <u>Lili Zhang</u> ¹ , <u>Xiaofang Chen</u> ¹ , <u>Lan Zhu</u> ¹ , <u>Chaoke Liang</u> ²	¹ Sichuan Center for Disease Control and Prevention, 6# Zhiongxue Road, Chengdu 610041, Sichuan, China, ² Institute for Environmental Health and Related Product Safety, China CDC, Beijing 100050, China	Study on the Correlation between Selenium Levels and APOE Gene Polymorphism in Aged People in Rural Areas of Sichuan Province
PT68	<u>Kun Zhang</u> (Absent)	Sichuan Center for Disease Control and Prevention, 6# Zhiongxue Road, Chengdu 610041, Sichuan, China	Determination of selenium in food by atomic fluorescence spectrometry

Pre-Conference Selenium Forum

Se-F01---Se-F07

Sponsor: TEMA-14 and Enshi City Government

Location: Large Auditorium, Fuyuan Guobin Hotel

Chemistry, metabolism, requirements, and regulation of selenium

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Selenium (Se) deficiency dramatically down-regulates selenoenzyme activity, protein and mRNA levels for glutathione peroxidase-1 and several additional selenoproteins. These levels increase sigmoidally with increasing dietary Se and reach defined plateaus at the Se requirement, making them sensitive biomarkers for Se deficiency. These levels, however, do not further increase with super-nutritional Se status, making them ineffective for detection of high Se status. To characterize Se regulation of the transcriptome, we conducted studies in weanling mice and rats fed Se-deficient diets supplemented with up to 5 µg Se/g as Na₂SeO₃. There was no effect of Se status on growth of mice fed 0 to 0.2 µg Se/g or rats fed 0 to 2 µg Se/g, but rats fed 5 µg Se/g showed a 23% decrease in growth. Rats fed Se-deficient diets or supplemented with 5 µg Se/g had elevated plasma alanine and aspartate aminotransferase activity, indicating increased reactive oxygen species (ROS) under both conditions. Se deficiency only significantly down-regulated selenoprotein genes, and the few genes up-regulated by Se deficiency were targets of the stress response transcription factor, Nrf2. Rats fed 5 µg Se/g had significantly altered expression of 1193 liver transcripts, whereas mice or rats fed ≤2 µg Se/g had <10 transcripts significantly altered relative to Se-adequate animals within an experiment. Filtering to remove genes regulated by calorie restriction or general drug toxicity resulted in 437 genes that were regulated by 5 µg Se/g, including 49 known Nrf2 targets, indicating increased ROS is associated with Se toxicity as well deficiency, but also indicating that a number of these changes are mediated by Nrf2-independent processes. Transcripts significantly altered by 2 µg Se/g and Se-deficient diets were an 11-transcript biomarker panel that accounted for 99% of the variation in liver Se over the full range from 0 to 5 µg Se/g. This study shows that Se toxicity in rats vastly alters the liver transcriptome whereas Se-deficiency or high but non-toxic Se intake elicits relatively few changes. This is the first evidence that a vastly expanded number of transcriptional changes itself can be a biomarker of Se toxicity, and that these transcripts include both Nrf2-specific and non-Nrf2-regulated genes. (Supported in part by NIH DK74184 and DK07665 and by UW Se Nutrition Research Fund) (*This abstract is the same as PS13)

Keywords: Se, Transcriptome, Toxicity

Biomarkers of selenium and determination of its requirement by humans

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Selenium biomarkers in plasma are often used to determine “selenium status.” Our group has carried out three clinical studies to characterize plasma selenium biomarkers and to determine the human selenium requirement. Selenium-deficient Chinese subjects were supplemented with selenomethionine or selenite for 20 weeks in one study and with selenomethionine for 40 weeks in another. Selenium-replete subjects in the U.S. were given moderate or high doses of selenium in the form of selenomethionine, high-selenium yeast, or selenite for 16 weeks. Plasma biomarkers measured were selenoprotein P (SEPP1, a selenium transport protein), glutathione peroxidase activity (GPX, due largely to the enzyme GPX3), and selenium. Plasma selenium includes both selenoproteins and selenomethionine incorporated non-specifically into plasma proteins. Our major findings were: (1) Once selenoprotein levels had been optimized, higher selenium intake had no effect on them. (2) Optimization of SEPP1 required a higher selenium intake than GPX. (3) Plasma selenium increased in proportion to the intake of selenomethionine without physiological regulation. (4) Selenium intake of 49 µg/day optimized SEPP1 in Chinese subjects who weighed an average of 58 kg. (5) Bioavailability of selenite is ~55% that of selenomethionine. We conclude that SEPP1 is the best plasma biomarker of selenium nutritional status, that selenium in the form of selenomethionine has almost twice the bioavailability of selenium in the form of selenite, that ~60 µg of selenium as selenomethionine would optimize selenoproteins in a 70 kg person, and that plasma selenium concentration can be used to monitor intake of selenomethionine.

Supported by NIH DK58763.

Keywords: Selenium, Biomarkers, Requirements, Supplements

Cancer prevention: the trials and tribulations of selenium

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Selenium (Se) inhibits tumorigenesis in a variety of experimental models and is considered a promising cancer chemopreventive agent for humans. A systematic review from 2007 which assessed the effect of antioxidant supplements on mortality in randomized primary and secondary prevention trials identified 21 trials in which selenium was given either singly (N=3) or in combination (N=18) with other antioxidants. Results for cancer endpoints from the largest five of these 21 trials (each with over 1000 subjects) and the more recent SELECT trial are reviewed here. Overall, three of the six trials showed significant effects for Se or Se-containing supplements on cancer incidence or mortality. The General Population component of the Nutrition Intervention Trials in Linxian, China showed significant reductions in all cancer mortality and gastric cancer mortality for Se given in combination with vitamin E and beta-carotene, while supplementation with Se plus 25 other vitamins/minerals in the Dysplasia component of the Nutrition Intervention Trials in Linxian found no significant effects on cancer. The Nutritional Prevention of Cancer Trial in the U.S. observed reduced total and incident prostate cancers among Se recipients, but increased rates of non-melanoma skin cancer. The SU.VI.MAX trial in France determined that all incident cancers were reduced in men supplemented with a combination of vitamins C and E, beta-carotene, Se, and zinc, while the supplement increased skin cancer in women. Supplementation with vitamins C and E plus Se in Shandong, China did not affect the development of gastric cancer in persons with precancerous gastric lesions. Finally, Se supplementation in SELECT did not affect the incidence of prostate, lung, colorectal, or other cancers. Se remains a promising cancer chemopreventive agent with demonstrated efficacy against some cancer sites in selected populations. Intervention dose, form, and duration, as well as subgroup susceptibility should be considered in interpreting results of completed trials and in planning future efforts. (*This abstract is the same as PS14)

Keywords: Cancer, Prevention, Trials

Role of selenium in thyroid metabolism and chronic diseases

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Adequate supply of selenium (Se) is relevant for normal human development and health. Most of Se actions are mediated by selenoproteins, which contain selenocysteine as a catalytic component of their active site if they act as enzymes or as critical residue for their function as structural proteins. Two genetic defects have been reported which lead to impaired or complete loss of function of the corresponding selenoproteins. Several mutations in Selenoprotein N result in early onset, developmental severe myopathy (rigid spine disease, minicore disease). Selenoprotein N is expressed in myocytes and its cellular functions are involved in protections against oxidative stress and redox reactions relevant for calcium homeostasis. Several mutations were also reported for SECIS-binding protein 2, which initially manifest by impaired thyroid function due to decreased deiodinase and in severe cases several other (metabolic) impairments (delayed bone maturation, myopathy, mental and motor coordination, altered immune function, enhanced insulin sensitivity) were identified. Enhanced Se supply may only be partially effective as treatment. Inadequate Se status has also been associated with alterations in the thyroid hormone axis. Severe Se deficiency in combination with iodine deficiency is involved in development of myxedematous cretinism or Kashin-Beck disease. Iodine deficiency must be treated first before Se is supplemented in order to prevent further deterioration. Beneficial effects of Se supplementation occur in goiter prevention and two autoimmune diseases of the thyroid gland. 100 to 200 µg of Se compounds (selenite, selenmethionine or Se-yeast) for 3 or more months decreases thyroperoxidase (TPO) antibodies and improves health status in patients with M. Hashimoto, an autoimmune thyroid disease prevalent in adult females and similar results were also described for Graves`disease (M. Basedow). The underlying mechanism (Se deficiency?) or molecular targets (thyrocytes or the immune system) have not been identified. Molecular and cellular details of Se action on the immune system or its cellular components require more research. (*This abstract is the same as I01)

Keywords: Selenoprotein, Thyroid, Metabolism

Pros and cons of selenium biofortification: Regulatory and legal considerations.

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Nutrition and health, especially in relation to chronic disease, is a major driver of food product selection for many consumers. The reported health benefits of selenium have resulted in many groups attempting to develop and market selenium-enriched products, but entering the food stream with such a product requires successful negotiation of a number of scientific, regulatory and marketing hurdles. In the U.S. a product may be targeted as a dietary supplement, food additive or food, all subject to different regulations. Regulatory approval also requires complete physical, chemical and toxicological characterization, and label claims regarding health benefits requires evidence from human studies. The cancer prevention properties of selenium resulted in a qualified health claim by the U.S. FDA. This claim was recently modified to reflect a lower level of evidence, but was subsequently overturned by a successful legal appeal. Parties interested in developing selenium-enriched products should be aware that the SELECT trial results have resulted in highly visible negative publicity and this has resulted in a substantial drop in sales of selenium-enriched products for human consumption.

Keywords: Regulatory Approval, Selenium, Enrichment

Selenium resource in China and its potential impact to humankind

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Selenium (Se) is an element which can be either beneficial to the health of humankind when a proper amount is taken up, or causes serious problems when too much or too low content of it is accessed, which results symptoms of selenosis or selenium-deficiency. Se concentration in rocks and soils vary greatly in China. Many recent projects of eco-geochemical survey, or multi-targets survey, conducted by Geological Survey of China in many parts of the country, had revealed that there are many areas in the vast territory where Se-rich soils are potentially suitable to develop Se-rich agriculture enterprises, and products, including Se-rich tea, rice, eggs, and many others, have been on the market with very high prices. This paper summarizes the main results of the eco-geochemical survey in the country. Most of the Se-rich rocks are found to be related to black-shales and, in a less extent, to metamorphic rocks, while Se in the soils weathered from such rocks is ready to dissolve into surface waters and ground waters and be absorbed by and accumulated in crops and other plantations. The presentation also analyzes the many aspects which will limit the development of Se-rich agriculture.

Keywords: Selenium Resource, Se-rich Agriculture, China

Characters and source of selenium resources in Enshi, Hubei, China

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In 2004-9, in Enshi, about 400 samples of coal gangue, bedrock, soil, water, and crops samples were collected from different strata outcrop areas to determine the Se, F, As, Hg, Mo, Ni, and Zn contents. The outcrop area of carbonate of Ordovician-Permian covers over 70 % of the Enshi area. Se content ranged from 0.027-0.59mg/kg, with the majority between 0.05-2.90 mg/kg in bedrock. Purple fine sandstone and sandy shale of Triassic and Jurassic (10 % the area) have Se content ranging from 0.01 to 0.045 mg/kg, with the majority between 0.016-0.26 mg/kg. The Se content of soil in this lower Se strata distribution area is from 0.25-0.95 mg/kg; beans from 0.21-0.64 mg/kg (0.406) mg/kg; rice from 0.41-1.34mg/kg (0.954); corn from 0.11-0.523 (0.354)mg/kg. Only the coals, which are burnable black shale situated in or near the sequence of strata of specific geological times, e.g. rock bed of Late Permian, Late Precambrian and Early Cambrian (not considered a part of Chinese coal reserves), possessed unusually high Se content (>50 mg/kg). The bedrock in the highest Se concentration area is one bed of black shale of Late Permian, its Se content is from 50 -7150 mg/kg, (majority between 100-200mg/kg). This Se-rich Late Permian black shale (coal gangue) is about 14 m thick and covers nearly 5 % of the Enshi district. The Se content of soil in this Se-rich strata distribution area is from 2.25-55.60 mg/kg (majority about 15 mg/kg). The Se content of beans in this area is from 3.21-50.427 mg/kg (majority 5-10 mg/kg); rice from 1.20-3.93 mg/kg (majority 0.05-0.20 mg/kg); corn from 0.67-6.37 mg/kg (majority 1.0 -2.20 mg/kg) and water from 12-230 µg/kg (majority 20 -40 µg/kg). Selenium content in bedrock in Enshi is closely related to the geological age of rock. Se is mainly in the rock bed which deposited in the Late Permian. The big outcrop of this Se-rich bedrock bed is the main reason for high Se Enshi. Thus concentration of selenium in the strata and bedrock influences regional geochemical abundance and regional differences in soil, grain and water Se.

Keywords: Se-rich Area, Source of Selenium, Enshi, Potential Exploration

Plenary Session

PS01-PS16

Location: Large Auditorium, Fuyuan Guobin Hotel

Advances in zinc transporters and metabolism

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There are 24 proteins from two families that are believed to transport zinc. ZnT transporters are responsible for lowering the cytoplasmic Zn²⁺ concentration by cell efflux or uptake into organelles. ZIP transporters facilitate cellular entry and efflux from vesicles/organelles to elevate cytoplasmic Zn²⁺ levels. A number of the ZnT/ZIP transporter genes respond to dietary zinc intake while others respond to cytokines/hormones and exhibit marked differences in expression among differing cell types. A global analysis of zinc transporter expression in humans during a 10 day acute zinc depletion revealed that ZnT1, ZnT4, ZnT5 and Zip3 were differentially expressed in blood cells and may serve as biomarkers. Microarray analysis identified genes of two functional networks (cell cycle and organization and cellular growth and proliferation) that were differentially expressed during the zinc depletion. In addition, the depletion reduced the abundance of specific microRNAs in serum. In studies with mice, we have focused Zip10 and Zip14. Zip10 is markedly up regulated during dietary zinc restriction. Zip10 expression is high in the liver, but Zip10 mRNA levels are 30-fold greater in the basal ganglia region of the brain than liver. Expression is regulated by unique placement of a MTF-1 binding site within Zip10 that restricts Pol II movement and Zip10 transcription when zinc levels are adequate. When cellular zinc is limited, nuclear translocation of MTF1 does not occur and Pol II movement is not restricted and hence Zip10 transcription is high. In contrast, Zip14 expression responds to immune mediators such as IL-6 and TNF α , but not to dietary zinc. During the early phase of liver regeneration in the mouse, Zip14 is up regulated by processes involving these mediators. Zip14 over expression in hepatocytes increases markers of cell proliferation as does supplemental dietary zinc in vivo in regenerating liver. Regeneration as indicated by proliferation markers is less in Zip14 knockout mice. This has been found to be caused by reduction in the c-Met signaling pathway through an inhibitory effect of zinc on PTP1B phosphatase activity. These results suggest zinc transporters have a major cellular signaling role via phosphatase activity inhibition. Supported by NIH Grant DK31127.

Keywords: Zinc, Transporter, Metabolism

Zinc homeostasis and signalling in the immune system

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Zinc is an essential trace element for the immune system and zinc deficiency compromises the immune function of all cells of the immune system. However, an excess of zinc can have negative effects on the immune system. Therefore zinc homeostasis must be delicately regulated for an effective immune response. Recent years have brought a paradigm shift for the role of zinc in immunity. Although zinc's function as a structural component of many enzymes is well known, current experimental evidence points to an additional function of the concentration of free or loosely bound zinc ions as an intracellular signal. The interaction of zinc with major signaling pathways that regulate immune cell activity, and the implications of zinc deficiency or supplementation on zinc signaling as the molecular basis for an effect of zinc on immune cell function will be discussed. Furthermore, the modulation of the TH1 vs. TH2 immune response by zinc will be described in detail focusing on the immune response in elderly and the mixed lymphocyte reaction as a transplantation model. This will include data from zinc in signal transduction up to the effect of zinc supplementation in vivo. The data should explain the molecular basis of the effects of zinc observed during zinc supplementation or zinc deficiency.

Keywords: Zinc, Immunity, Signaling

The role of zinc transporters in an inherited disorder of zinc deficiency

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Zinc deficiency results in a diminished immune response, reduced healing and neurological disorders, and can be fatal in newborn or growing animals. Zinc deficiency is commonly caused by dietary factors, however, several inherited defects of zinc deficiency have been identified. Acrodermatitis enteropathica, the most commonly described inherited condition found in humans, is associated with a wide variety of mutations in the hZIP4 gene, a member of the SLC39 family. A different inherited form of zinc deficiency occurs in the “lethal milk” mouse, where a mutation in ZnT4 gene, a member of the SLC30 family of transmembrane proteins. This defect impairs secretion of zinc from the mammary gland into milk. A similar disorder to the “lethal milk” mouse occurs in humans, causing neonates to develop severe zinc deficiency due to reduced zinc levels in the maternal milk. In several unrelated patients studied, we found no changes in the human ZnT4 orthologue, hZnT4, suggesting that the “lethal milk” mouse is not the corresponding model for the human zinc deficiency condition. Further analysis of the human zinc deficiency condition revealed reduced mRNA and protein expression of the zinc transporters hZnT5 and hZnT6. Sequence analysis showed no mutations in the coding region of these genes however. Significant decreases in alkaline phosphatase activity were found in patient cells compared to controls, suggesting impaired ZnT5/ZnT6 function. Analysis of the promoter region of the gene 4000 base pairs upstream from the start codons of hZnT5 and hZnT6 showed point changes including substitutions and a deletion, but no mutations were detected in the 5' regions that may affect transcription. At present, the etiology of this zinc deficiency disease is not clear. Further studies will provide insights into the underlying defect and the normal cellular roles of the ZnT5 and ZnT6 zinc transporters.

Keywords: Zinc, Zinc Transporter, Zinc Deficiency

Holotransferrin dependent hepcidin expression is impacted by dietary copper deficiency in rodents

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Recognition that anemia in humans can be caused by copper deficiency has been known since the 19th century. Many believe this is due to impairment in iron efflux from intestine and storage sites in liver and spleen because copper is necessary for catalytic function of ferroxidases, which are multicopper oxidases (MCO) such as hephaestin in intestine and plasma ceruloplasmin (sCp). Recent work has reported widespread expression of an additional splice variant of Cp anchored by glycosylphosphatidylinositol (GPI-Cp) and a MCO enriched in placenta called zyklopen. MCO work in tandem with ferroportin (FPN) the only known iron efflux transporter. Thus, iron efflux might be impacted by either limitation of MCO or FPN. FPN expression is regulated partially by cellular iron via iron regulatory elements and binding proteins (IRE and IRE-BP) but also by the liver hormone hepcidin. Hepcidin binds to FPN and results in degradation. Thus, high hepcidin blunts iron efflux and conversely low hepcidin favors iron efflux. Studies were conducted in Sprague Dawley rats and Swiss Webster mice to investigate regulation of hepcidin following copper deficiency. Dietary copper-deficient (CuD) rat pups exhibit a profound reduction in hepcidin expression but their anemic dams do not. Examination of several putative regulators (plasma Fe, transferrin (Tf), and GDF15; liver TfR1, TfR2, BMP6) suggest that a threshold value for holotransferrin is the primary determinant in explaining the difference between pups and dams. Further, differential dietary manipulation allowed us to characterize anemic CuD Swiss Webster mice with hypoferremia and with normal plasma Fe. Attenuation in hepcidin was detected only when mice were hypoferremic. Adequate copper is necessary to achieve normal plasma Tf saturation. When holo-Tf levels fall below a critical level, approximately 40 μ M, hepcidin transcription is attenuated. However, additional research is needed to determine the mechanism for copper deficiency induced anemia because reduced MCO function, by diet or genetics, cannot explain anemia. Limitation in sCp, GPI-Cp, nor hephaestin do not appear to be main factors in this pathology.

Keywords: Copper, Hepcidin, Anemia

New biomarkers of body copper status in malnourished children and patients

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Although human genetic conditions represent good models to assess intense copper deficiency and copper excess, earlier effects are not clear mainly because available indicators of copper status are not sensitive enough. However, chaperone of superoxide dismutase (CCS) in different tissues has yielded reproducible results in animal (mice and rats) models of copper deficiency, increasing with deficiency. We reported high frequency of copper deficiency in malnourished children. Also, in Santiago we found that in 23% of men and 30% of women older than 65 years serum copper concentration was below the cut off. We report here a study in children 3mo-3y receiving medical care and nutritional rehabilitation at Hospital Patio, Cochabamba, Bolivia. G1 was formed by children admitted with severe acute malnutrition (n=12); G2 moderate acute malnutrition (n=17) and G3 (controls, n=17) by well nourished children that attended a routine medical outpatient check up. After clinical stabilization (WHO Guidelines, 1999), blood samples were collected on Day 1 and Day 15 for blood biochemistry and isolation of peripheral mononuclear cells (PMNCs). In these latter, mRNA abundance of CCS and MT2 transcripts were measured. Sample size was 12 per group. Analysis of results included T test for unpaired samples and multivariate analysis for repeated measures (Two-way ANOVA). Results showed that on admission, general demographic and blood biochemical indicators were not different between groups. On admission and also in both study groups, CCS transcripts abundance in PMNCs was greater than in controls (one way Anova, $p < 0.05$). After 15 days of nutritional recovery receiving copper supplementation, transcripts expression decreased in both study groups (two way Anova, $p < 0.001$). On admission, MTA2 transcripts expression in severely but not in moderately malnourished children were decreased in comparison to controls. After 15 days of nutritional recovery and copper supplementation MTA2 transcripts increased in both study groups. mRNA CCS transcripts expression changed consistently in all cases, supporting the hypothesis that changes of this protein may be an indicator of copper status in copper deficient states. *This project was supported by Fondecyt grants 1070595 and 1110099*

Keywords: Copper, CCS, Malnutrition Children

Copper metabolism and oxidative stress in nonruminants fed pharmacological concentrations of copper

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The nutritional requirement for copper (Cu) in swine and poultry is 5 to 8 mg/kg of diet. Feeding poultry and weanling pigs pharmacological levels of Cu (100 to 250 mg/kg diet) often increases growth and feed intake. However, it is unclear how pharmacological concentrations of Cu are regulated to prevent toxicity. Weanling pigs were used to study the effects of dietary Cu level and source on Cu metabolism. Pigs were fed a control diet (6.7 mg Cu/kg) or the control diet supplemented with 225 mg Cu/kg, from either CuSO₄ or Cu hydroxyl chloride (CHC; Cu₂OH₃Cl). Copper sulfate is water soluble while CHC is relatively insoluble in water but soluble under acidic conditions in the stomach. Pigs were harvested after receiving diets for 35 days. Soluble and mucosal Cu concentrations in the duodenum, proximal jejunum, and ileum were much lower in controls than pigs fed 225 mg Cu/kg diet. Liver and bile Cu concentrations were also much lower in controls. Expression of Ctr1, the major transporter involved in uptake of Cu by enterocytes, was down-regulated by CHC in the duodenum and reduced by both Cu sources in the proximal jejunum. Antioxidant 1 (Atox1), a Cu chaperone protein was up-regulated in the jejunum and liver by pharmacological levels of both Cu sources. Dietary level and source of Cu did not affect mRNA for the Cu exporters, Atp7a or Atp7b. Mucosal Cu concentration and metallothionein mRNA in the duodenum were higher in CuSO₄ than in CHC fed pigs. However, in the proximal jejunum mucosal and bile, Cu concentrations were higher in pigs supplemented with CHC. Duodenal malondialdehyde concentrations were higher in pigs fed CuSO₄ than controls but did not differ among CHC and control pigs. The increased malondialdehyde concentrations in CuSO₄ pigs were associated with reduced villus height in the duodenum and proximal jejunum. Pharmacological concentrations of CHC did not affect villus height. These results suggest that CuSO₄ promotes lipid peroxidation and oxidative stress in the small intestine to a greater extent than pharmacological levels of CHC. Down-regulation of Ctr1 in the jejunum appears to be involved in regulating Cu absorption in pigs fed high Cu.

Keywords: Copper, Pigs, Transporters

Systemic control of body iron intake

Greg Anderson

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Iron is absolutely required for a wide range of biological processes but it is also toxic in excess due to catalysis of the formation of reactive oxygen species. Thus both iron deficiency and iron excess can have profound clinical consequences. Iron traffic into and around the body is controlled by the peptide hepcidin, and its expression in turn reflects body iron requirements. Hepcidin controls iron entry into the plasma by binding to the iron export protein ferroportin and facilitating its internalisation and degradation. For Fpn to function efficiently, it requires an iron oxidase. In the small intestine the copper-dependent oxidase hephaestin is the main oxidase, but systemically ceruloplasmin and other oxidases are more important. We have been particularly interested in the hepcidin-ferroportin-oxidase axis as it relates to intestinal iron absorption and macrophage iron turnover and are addressing this using a range of knockout mouse models in different physiological settings. Deletion of hephaestin specifically in the small intestine leads to reduced iron absorption and iron deficiency, and combined deletion of both hephaestin and ceruloplasmin leads to an even more severe phenotype. However, even the double knockout is not lethal suggesting further redundancy in the system. Mice lacking ferroportin are much more severely affected, indicating that ferroportin is the sole or predominant iron exporter from most tissues, including the intestinal epithelium. In certain situations, such as during suckling when iron requirements and iron absorption are very high, or in some chronic haemolytic anaemias, iron export is uncoupled from changes in hepcidin expression. During suckling this appears to reflect developmental changes in the nature of the ferroportin protein which render it insensitive to hepcidin action. In the case of certain haemolytic anaemias, constitutive recycling of iron through reticuloendothelial macrophages appears to provide sufficient iron for new haemoglobin production. Only when iron demands increase do changes in hepcidin expression facilitate enhanced macrophage iron recycling. Disturbances in hepcidin expression or its action underlie a range of iron metabolism defects in humans, attesting to the physiological importance of this pathway.

Keywords: Iron, Hepcidin, Ferroportin

The effect of maternal iron deficiency on growth and development in the rat

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During pregnancy, the developing fetus is dependent on its mother for its nutrition. It follows that unless the placenta can correct any shortfall, a sub-optimal diet in the mother will result in problems for the fetus. Iron deficiency during pregnancy is a common problem throughout the world. The consequences are serious, and can result in changes in psychological and physical development. To understand how and why iron deficiency exerts its effects, we have developed a rat model. We have shown that maternal iron deficiency results in alterations in fat metabolism, in obesity and hypertension, which persists even into old age in the offspring, despite being on a normal diet for its entire postnatal life (1). However, our data do not explain the mechanisms underpinning the changes. We have used DNA array and proteomics technologies to probe deeper into placental and fetal tissue function and changes in response to iron deficiency. Using high throughput analytical techniques, we showed that, as expected, there were significant changes in genes involved in iron metabolism. GO process analysis showed changes in proteins in protein catabolism, changes in DNA repair proteins and in regulation of apoptosis. These results all suggested mechanisms of iron deficiency inducing a pathological phenotype, but we also demonstrated changes in expression of genes involved in the cell cycle, which fitted with other data we obtained with our collaborators, who showed that iron deficiency resulted in a decrease in glomerular number. Thus, we could hypothesise that iron deficiency during pregnancy slows the cell cycle, resulting in fewer glomeruli and increasing the risk of hypertension in the offspring. Of course, the data do not necessarily explain why lipid metabolism is disturbed or why there should be an increased risk of obesity. However, parallel experiments showed that phosphorylation of Akt1, a key regulator of nutritional pathway, was altered in some tissues, but not others, in iron deficiency. This may be another mechanism whereby iron deficiency alters fetal growth development and wellbeing as an adult. Gambling, L., Dunford, S., Wallace, D. I., Zuur, G., Solanky, N., Srai, S. K. S., and McArdle, H. J. (2003) *J. Physiol.* **552**, 603-610

Keywords: Iron Deficiency, Rat, Hypertension, Offspring, Glomerulus

Modelling the iron bioavailability of the Canadian diet

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Although total iron intake is the primary determinant of iron intake adequacy, the proportion of ingested iron available for absorption can vary from <1 to >50% , depending on the form of iron ingested, the quantity of inhibitors or enhancers present in the meal, and the iron status of the individual. Since dietary factors have such a large effect on iron absorption, estimates of iron requirement include an allowance for bioavailability. The latest iron EARs were derived by the factorial method, summing the amount of absorbed iron needed to replace basal losses and the amount needed for tissue accretion during growth and pregnancy and then multiplying the required 'absorbed iron' by '1/iron bioavailability', which was estimated at 18% for the North American diet. Stable isotope tracer techniques are the ideal method of determining iron bioavailability from mixed diets; however, they are costly and time-consuming and rarely involve complex food mixtures which are seen in normal mixed diets. We have applied the Mosen algorithm of food iron bioavailability to Canadian national dietary intake survey data to calculate iron adequacy at the population level. Results from these analyses indicate that the bioavailability of North American mixed diets is well below the 18% estimate that was used to derive the DRIs for iron. *Funding – Beef Information Centre*

Keywords: Iron, Bioavailability, Mosen algorithm, Canadian National Survey

The central role of selenoprotein P (Sepp1) in selenium transport and homeostasis

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Nutritional selenium deficiency causes redistribution of selenium in the body so that some tissues, especially brain and testis, maintain selenium better than others. Deficiency also decreases urinary excretion of the element, lessening selenium loss from the body. Mice with knockout of Sepp1, a plasma protein that contains 10 selenocysteine residues and that originates in the liver, were found to have depressed whole-body selenium and dysfunction of the brain and the testis. Those findings suggested that Sepp1 plays a role in selenium transport and homeostasis. More recent studies identified endocytosis of Sepp1 by the Sertoli cells of the testis and by the capillary endothelial cells of the brain. In both cases endocytosis was dependent on the presence of apoER2, a member of the low-density lipoprotein receptor (LDLR) family. Knockout of this receptor lowered selenium levels in these tissues and caused their dysfunction when low-selenium diet was fed. The proximal convoluted tubule cells in the kidney have a high selenium requirement because they synthesize and secrete Gpx3, the plasma glutathione peroxidase. Megalin, another member of the LDLR family, was identified as the mediator of endocytosis of Sepp1 fragments that had been filtered by the glomerulus. Knockout of megalin sharply reduced plasma Gpx3. It is likely that other members of the LDLR family are involved in Sepp1 endocytosis in other tissues. Deletion of Sepp1 in hepatocytes lowers the plasma concentration of Sepp1 to about 5% of control and increases urinary excretion of selenium. We have suggested that synthesis of Sepp1 and of urinary selenium metabolites compete for selenium in the liver. Deletion of Sepp1 would reduce the competition and allow more selenium to be excreted, lowering whole-body selenium. Thus, Sepp1 is central to selenium disposition in the body and to its homeostasis.

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Keywords: Selenoprotein P, Selenium Homeostasis, Selenium Transport

Review on selenium research relating to human health in China

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Selenium research in China was started in middle of the 1960s. In that period two unknown human endemic diseases broke out and finally it was recognized that both were linked with selenium. One is human selenosis characterized by hair and nail loss that occurred in Enshi County, Hubei Province of China. The other is Keshan disease related selenium deficiency, an endemic cardiomyopathy with high mortality, that occurred in certain regions of China. The main causes for both endemic diseases are unsuitable selenium intakes, either excessive or low. Then the studies on human dietary requirements and safe range of dietary intakes of selenium in China were carried out in 1982-1992. Later on, the data of adequate selenium intake were adapted for setting DRIs in many countries. Thereafter the research has moved to clinical studies on selenium supplements for prevention of some chronic diseases, such as cancer. In recent years the research has involved in looking for the function of new selenoproteins and selenoenzyme mimics etc.

Keywords: Selenium, Human, China

Selenocysteine genomics

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Selenoproteins contain a rare amino acid, selenocysteine, which occurs in all three domains of life and functions as the catalytic redox group in several classes of oxidoreductases. Full sets of selenoproteins have recently been identified in a variety of organisms, including humans, which have 25 selenoprotein genes. These proteins explain the role dietary selenium plays in biology and human health and point to new biological processes that are dependent on this trace element. Comparative genomic analyses of selenoproteins revealed unusual features of the use of selenium in nature. We will report the examples of both expanded and decreased use of selenocysteine. Selenoproteins are members of diverse protein families. Thioredoxin-like proteins are particularly prone to conversion into selenoprotein forms. Because dietary selenium is required for selenoprotein expression, diets differing in selenium levels provide means of regulating selenoprotein function and redox homeostasis in mammals. Selenoproteins may also be used as tools to identify proteins that contain catalytic redox-active cysteine residues and determine the location of these residues in protein sequences. In addition, studies on selenoproteins provide new information about the genetic code. Being redox catalysts, selenoproteins are involved in the repair of oxidatively damaged proteins, activation and inactivation of thyroid hormone, regulation of the redox state of thioredoxin, removal of hydrogen peroxide, and other functions. In turn, these functions implicate selenoproteins in cancer prevention, regulation of the aging process, and male reproduction.

Keywords: Selenocysteine, Selenoprotein, Genomics

Selenium regulation of Se-dependent and Se-independent genes

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Selenium (Se) deficiency dramatically down-regulates selenoenzyme activity, protein and mRNA levels for glutathione peroxidase-1 and several additional selenoproteins. These levels increase sigmoidally with increasing dietary Se and reach defined plateaus at the Se requirement, making them sensitive biomarkers for Se deficiency. These levels, however, do not further increase with super-nutritional Se status, making them ineffective for detection of high Se status. To characterize Se regulation of the transcriptome, we conducted studies in weanling mice and rats fed Se-deficient diets supplemented with up to 5 µg Se/g as Na₂SeO₃. There was no effect of Se status on growth of mice fed 0 to 0.2 µg Se/g or rats fed 0 to 2 µg Se/g, but rats fed 5 µg Se/g showed a 23% decrease in growth. Rats fed Se-deficient diets or supplemented with 5 µg Se/g had elevated plasma alanine and aspartate aminotransferase activity, indicating increased reactive oxygen species (ROS) under both conditions. Se deficiency only significantly down-regulated selenoprotein genes, and the few genes up-regulated by Se deficiency were targets of the stress response transcription factor, Nrf2. Rats fed 5 µg Se/g had significantly altered expression of 1193 liver transcripts, whereas mice or rats fed ≤2 µg Se/g had <10 transcripts significantly altered relative to Se-adequate animals within an experiment. Filtering to remove genes regulated by calorie restriction or general drug toxicity resulted in 437 genes that were regulated by 5 µg Se/g, including 49 known Nrf2 targets, indicating increased ROS is associated with Se toxicity as well deficiency, but also indicating that a number of these changes are mediated by Nrf2-independent processes. Transcripts significantly altered by 2 µg Se/g and Se-deficient diets were an 11-transcript biomarker panel that accounted for 99% of the variation in liver Se over the full range from 0 to 5 µg Se/g. This study shows that Se toxicity in rats vastly alters the liver transcriptome whereas Se-deficiency or high but non-toxic Se intake elicits relatively few changes. This is the first evidence that a vastly expanded number of transcriptional changes itself can be a biomarker of Se toxicity, and that these transcripts include both Nrf2-specific and non-Nrf2-regulated genes. (Supported in part by NIH DK74184 and DK07665 and by UW Se Nutrition Research Fund)

Keywords: Se, Transcriptome, Toxicity

Cancer prevention: the trials and tribulations of selenium

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Selenium (Se) inhibits tumorigenesis in a variety of experimental models and is considered a promising cancer chemopreventive agent for humans. A systematic review from 2007 which assessed the effect of antioxidant supplements on mortality in randomized primary and secondary prevention trials identified 21 trials in which selenium was given either singly (N=3) or in combination (N=18) with other antioxidants. Results for cancer endpoints from the largest five of these 21 trials (each with over 1000 subjects) and the more recent SELECT trial are reviewed here. Overall, three of the six trials showed significant effects for Se or Se-containing supplements on cancer incidence or mortality. The General Population component of the Nutrition Intervention Trials in Linxian, China showed significant reductions in all cancer mortality and gastric cancer mortality for Se given in combination with vitamin E and beta-carotene, while supplementation with Se plus 25 other vitamins/minerals in the Dysplasia component of the Nutrition Intervention Trials in Linxian found no significant effects on cancer. The Nutritional Prevention of Cancer Trial in the U.S. observed reduced total and incident prostate cancers among Se recipients, but increased rates of non-melanoma skin cancer. The SU.VI.MAX trial in France determined that all incident cancers were reduced in men supplemented with a combination of vitamins C and E, beta-carotene, Se, and zinc, while the supplement increased skin cancer in women. Supplementation with vitamins C and E plus Se in Shandong, China did not affect the development of gastric cancer in persons with precancerous gastric lesions. Finally, Se supplementation in SELECT did not affect the incidence of prostate, lung, colorectal, or other cancers. Se remains a promising cancer chemopreventive agent with demonstrated efficacy against some cancer sites in selected populations. Intervention dose, form, and duration, as well as subgroup susceptibility should be considered in interpreting results of completed trials and in planning future efforts.

Keywords: Cancer, Prevention, Trials

Selenium and type-2 diabetes: rationale for, and results of, a randomised trial of selenium on type-2 diabetes risk, as assessed by plasma adiponectin

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Evidence that selenium (Se) affects the risk of type-2 diabetes (T2D) is conflicting with observational studies showing both lower and higher risk or prevalence linked to higher Se status. Importantly, however, a *post-hoc* analysis of the NPC trial carried out in the US showed a significantly increased risk of T2D in those supplemented with Se (200 µg/day as Se-yeast), the increased risk being driven by those in the highest tertile of plasma selenium at baseline (>121.6 µg/L). Stored plasma samples from the UK PRECISE Pilot study, in which 501 elderly volunteers were randomly assigned to a six-month treatment with 100, 200 or 300 µg Se/d as high-Se or placebo yeast, provided an opportunity to investigate the impact of Se supplementation on the risk of T2D in a lower-Se population. Plasma adiponectin concentration, a recognised independent predictor of T2D risk, was the biomarker chosen as the plasma samples were non-fasted, precluding the measurement of glucose or insulin. Adiponectin concentration was measured at baseline and at the six-month follow-up by ELISA in 473 participants who had one or both plasma samples available. Mean plasma Se increased significantly from baseline in all Se-supplemented groups. Multivariable linear regression based on log-transformed adiponectin data showed a cross-sectional inverse association between plasma Se and adiponectin concentration at baseline. However, results from linear mixed models on untransformed and log-transformed adiponectin concentrations, adjusted for study centre, showed no effect of Se supplementation on adiponectin concentration. Study limitations were the high variability in baseline adiponectin concentrations in the population, the short duration of supplementation and the narrow age range of the participants (60-74 yr). Potential mechanisms by which Se may affect the risk of T2D, including effects on insulin signalling, oxidative and ER stress and the role of selenoprotein P will be discussed.

Keywords: Selenium, Adiponectin, Type 2 Diabetes, Randomised Controlled Trial

Progress in chemical mimics of glutathione peroxidase

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Among the mammalian selenoenzymes, glutathione peroxidase (GPx) is a chemically and structurally well-studied selenoenzyme. It functions to catalyze the reduction of hydroperoxides (ROOH) by glutathione (GSH). Therefore it plays an important role in the organism antioxidant for protecting cells from oxidative stress. Various organo-selenium compounds have been developed as GPx models. Here we introduce three kinds of model compounds as chemical mimics of GPx which are ebselen (2-phenyl- 1,2-benzisoselenazole-3(2H)-one) and its derivatives, cyclodextrin derivatives and selenium-mediated micelles. Their mimicing of GPx activity were compared, their advantages and disadvantages as chemical mimics of GPx were evaluated. At the same time, the interaction mechanisms of selenium with reactive oxygen species (ROS) are discussed in this report.

Keywords: Glutathione Peroxidase, Chemical Mimics, Reactive Oxygen Species

Symposium 1(A)

Title: Fe and Zn Homeostasis across Pregnancy,
Lactation and Early Childhood: Translational
Implications of Recent Research

Sponsor: Micronutrient Initiative, Canada and TEMA-14

Location: Conference Room 1

Iron, inflammation, and infection

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Iron deficiency anemia remains a public health challenge and is associated with impaired neuro-motor development, cognition, and immunity. Excess iron intake and status could also be linked to poor health outcomes perhaps through damaging reactive oxygen species (ROS). The dual burden of iron deficiency and excess on inflammation can be important and challenging at both the individual and population-level. Iron supplementation can improve iron status but is not always accompanied with improvement in immune function or reduction in infections. These mixed findings can be related to limitations in design of studies concerning sample size, variability in immune function tests, nutrient and health status and age of study participants, differential mode of iron supplementation, and nature of infections examined. Literature on iron supplementation and infections consists primarily of studies in anemic subjects or those at risk for iron deficiency; few studies have evaluated responses in relation to baseline iron status in iron-replete versus iron-deficient participants. The results of oral iron supplementation trials on risk of infections vary from no effect, to protective and even adverse effects particularly among iron-replete individuals in malaria-endemic areas. Iron excess can occur following parenteral iron, or bolus of oral iron in situations where the host is compromised (e.g. deregulated iron absorptive mechanisms, impaired protein status, etc.). This can result in a greater non-transferrin bound “labile” or free iron pool that is readily available to pathogens for their growth and proliferation and an increased risk of infections. Because of the role of iron at the center of host-pathogen interactions; the challenge is to maintain iron balance while avoiding iron excess. In populations with a high prevalence of iron deficiency universal iron supplementation is indicated with the long term goal of improving iron status via sustainable strategies. On the other hand, targeted interventions to iron-deficient individuals would be prudent in malaria-endemic regions coupled with anti-malarial programs to maintain host-pathogen interactions for reducing risk of infections.

Keywords: Iron, Immunity, Infection

Challenges of zinc (Zn) assessment in women and young children

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The assessment of Zn status remains a vexing challenge, including in particular for women during the reproductive cycle and in infants and young children. Plasma Zn concentration is the most commonly used biomarker to assess Zn status, but its low sensitivity results in limited usefulness for individuals. In addition to the need for careful handling to avoid contamination of sample, potential confounders include age, gender, pregnancy, inflammation or infection, and effects of fasting. We have examined the utility of the exchangeable Zn pool (EZP), defined as the mass of Zn that exchanges with the Zn in plasma within 2-3 days, as an index of Zn status. EZP is determined with the application of stable isotope methodology. In both adult and infant cohorts, we find EZP size correlates significantly with habitual dietary Zn intake; responds to change (especially depletion) in Zn intake; and is correlated with the amount of absorbed Zn from the diet, and with body weight and fat free mass. Similar relationships have not been consistently identified with plasma Zn. Limited data are available for assessment of Zn status in pregnant or lactating women but the changes body composition, hormonal milieu and Zn homeostasis complicate further the interpretation of EZP measurements and plasma Zn concentrations. The presentation will consider outstanding questions about the interpretation of EZP as an indicator of Zn status and future research needs for identification of biomarkers of Zn status in these important physiologic conditions.

Keywords: Zn Assessment, Zn Homeostasis, Exchangeable Zn Pool (EZP)

Bioavailability of heme and non-heme iron: implications for maternal and child health

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Iron deficiency anemia during pregnancy is associated with multiple adverse maternal and neonatal outcomes. Increasing data links suboptimal neonatal iron stores at birth with both acute and persistent alternations in neurophysiological and cognitive outcomes. To improve maternal and fetal iron utilization during pregnancy, further characterization of iron bioavailability from both heme and non-heme iron sources is needed. Hepcidin is now known to be the systemic Fe regulatory hormone but little is known about its association with either non-heme, or heme iron utilization during pregnancy. Recent stable isotope data indicates hepcidin is significantly related to non-heme iron absorption, but is not associated with heme iron absorption during pregnancy. New findings also suggest that there may be preferential fetal utilization of maternally ingested heme iron suggestive of differences in enterocyte export, early partitioning or placental uptake of maternally ingested heme iron compared to maternally ingested ferrous sulfate. The ability of the fetus to utilize heme iron is supported both by the high expression of the heme trafficking protein, FLVCR (Feline Leukemia Virus Subgroup C Receptor) and by the presence of heme catabolic enzymes in the human placenta. The need to fully endow the neonate with optimal iron stores is increasingly recognized due to the low iron content of breast milk and the developmental immaturity of the neonatal gut with respect to regulation of iron absorption. Iron repletion of anemic women during pregnancy is often unsuccessful which may in part be associated with the limited ability to upregulate non-heme iron absorption even when iron demands are high. Because heme iron absorption is less dependent on iron status and the placenta may preferentially utilize maternally ingested heme iron, additional investigation of bioavailability of heme iron sources among pregnant women is warranted. To date, studies assessing the bioavailability of heme iron have primarily been carried out among dialysis patients or non-pregnant populations and only a handful of studies have assessed the utility of heme-iron supplementation during pregnancy. Improved understanding of iron bioavailability and molecular mechanisms of heme iron transport is needed to inform interventions in support of maternal, fetal and pediatric iron demands.

Keywords: Placenta, Hepcidin, Heme

Absorption of Fe and Zn during infancy and childhood and their interactions

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Both Fe and Zn are well absorbed from breast milk, partly due to the presence of factors facilitating their uptake, partly to the absence of inhibitory factors. Absorption of Fe and Zn is lower from cow's milk formula, most likely due to cow's milk casein which is difficult to digest and the formation of casein phosphopeptides, which are inhibitory of Fe and Zn absorption, during digestion. Absorption of Fe and Zn from soy formula is even lower, due to the presence of phytate, a well-known inhibitor of both Fe and Zn absorption. When infants are weaned, the composition of complementary foods will have an impact on Fe and Zn absorption, and the presence of phytate in such foods often causes low absorption. The presence of meat can have an enhancing effect on Fe absorption, but meat intake in infants is usually very low. Thus, a combination of low intake and the presence of phytate in staple foods often contribute to a high prevalence of Fe and Zn deficiency in infants and young children. Supplementation with Fe and Zn is often used to combat these deficiencies; however, when they are taken on an empty stomach, there is an interaction between these two micronutrients with each one inhibiting the absorption of the other. The molecular mechanism behind this interaction is not yet fully known. This interaction is not found when Fe and Zn are added to the diet by food fortification, suggesting that absorption may occur via different mechanisms when dietary ligands are present. Excess absorption of Fe and Zn is generally not considered in this age group, due to homeostatic regulation of their absorption. Isotope studies suggest, however, that Fe homeostasis is poorly developed in young infants, which may explain why adverse effects of Fe are observed in this age group. Less is known about homeostatic regulation of Zn homeostasis in infants and young children.

Keywords: Iron, Zinc, Interactions

Relationships between iron intake, status and health: the EURRECA systematic review approach

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The EUROpean micronutrient RECommendations Aligned (EURRECA) Network of Excellence (www.eurreca.org) is attempting to address disparities in micronutrient Dietary Reference Values (DRVs) between European countries, using standardized systematic review (SR) and meta-analysis methodologies. The relationships between intake, status and health were assessed for prioritized micronutrients; the process for iron is presented here. The SR protocol included structured searches on OvidSP MEDLINE, EMBASE (OvidSP) and Cochrane CENTRAL, rigorous inclusion/exclusion criteria, data extraction, quality assessment, and meta-analyses. Iron status measures were limited to hemoglobin, ferritin, transferrin receptor (TfR) and body iron; and prioritized health outcomes included physical performance, immune function, tiredness, cognitive function, thermoregulation and restless legs syndrome. The search resulted in the identification of 3000 potentially relevant randomized controlled trials (RCTs), and 51 full-text articles were included following selection processes. Of these, 48 measured the relationship between supplement intake and hemoglobin, 38 measured ferritin, 16 TfR and 6 body iron. Meta-analyses and dose-response analyses were carried out, and some of the variability between studies was addressed using subgrouping and sensitivity analyses. Overall, no dose-response relationships were observed between intake and status. Few studies were identified for the prioritized health outcomes and analyses were limited by the scarcity of data for most outcomes. Physical performance was an exception with 20 included studies, but there was large variation in the outcome measures reported. Preliminary analyses showed that most markers of physical performance remained unchanged after iron supplementation. Despite the amount of literature, limited high quality and comparable data are available to clearly define the addressed relationships. In addition, important confounders, such as bioavailability, complicate their assessment. *This work was completed on behalf of the EURRECA Consortium and funded under the EU 6th Framework Food Quality and Safety programme, project number FP6-036196-2. This report does not necessarily reflect the Commission's views or its future policy in this area.*

Keyword: Iron, Intake-Status-Health Relationship, Systematic Review

Haem and non-haem iron absorption and iron status after sleeve gastrectomy and Roux-en-Y gastric bypass

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Iron status and iron absorption are impaired after bariatric surgery. Nevertheless, more information is needed regarding the effects of different types of surgery. Also, it is not known whether haem and non-haem iron absorption is equally affected. In morbidly obese patients undergoing Roux-en-Y gastric bypass (RYGBP; a restrictive and malabsorptive surgery) and sleeve gastrectomy (SG; a restrictive surgery) the effects of such interventions on hem and non-haem iron absorption and iron status 12 months after the surgery were evaluated. Thirty-one women enrolled in an ongoing study have completed the evaluations before and 12 months after surgery (initial age 36.5±8.4y, BMI 40.4±4.3 kg/m²). Twenty-two underwent RYGBP and nine SG. Hemoglobin, zinc-protoporphyrin, transferrin saturation, serum ferritin, serum transferrin receptor as well as iron absorption tests for hem and non-hem iron were carried out in both occasions. RYGBP patients were supplemented with 60 mg/d of Fe; SG patient received 36 mg/d of supplemental Fe. Serum ferritin was decreased one year after surgery (<0.001), although the type of surgery was not significant. Zinc protoporphyrin increased in the RYGBP group only. The rest of iron status parameters were unchanged. Hem iron absorption decreased from 20.9% to 5%, while non-hem iron absorption was reduced from 11.7% to 4.9%. No effect of the type of surgery was observed. In conclusion, regardless the type of bariatric surgery (RYGBP or SG), the patients present decreased iron deposits and reduced iron absorption capacity one year after surgery. Haem iron absorption is more affected by these surgeries than non-haem iron absorption. *Research leading to this abstract was provided by FONDECYT project 1080576*

Keywords: Iron, Obesity, Bariatric Surgery

Zinc and copper status after sleeve gastrectomy and Roux-en-Y gastric bypass

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Bariatric surgery produces major alterations of gastrointestinal anatomy. The effects on zinc and copper status have not been fully studied. In severe and morbidly obese patients undergoing Roux-en-Y gastric bypass (RYGBP; a restrictive and malabsorptive surgery) and sleeve gastrectomy (SG; a restrictive surgery) the effects of such interventions on zinc and copper status were determined. Also, some exploratory studies on intestinal zinc and copper transporters were carried out. Thirty-four women enrolled in an ongoing study have completed the zinc/copper status evaluations before and 12 months after surgery. Twenty-two underwent RYGBP and twelve underwent SG. RYGBP patients received 25 mg of Zn and 3 mg of Cu as supplements, while SG patients received 15 mg of Zn and 1.8 mg of Cu. Plasma and hair zinc, as well as plasma copper were available for all cases. The expression of zinc and copper transporters (ZIP4 and CTR1), and proteins related to Zn and Cu metabolism (MT and CCS) were determined by real-time PCR in intestinal biopsies in a subsample of the subjects. Plasma zinc but not hair zinc was reduced ($p < 0.001$) one year after bariatric surgery with no effect of the type of surgery. Plasma copper was also reduced ($p < 0.002$), and RYGBP tended to a greater decrease ($p = 0.007$) than SG. After the experimental period, trends ($p = \text{NS}$) of changes observed in mineral transporters or related proteins were: CTR1 increased, CCS no change, ZIP4 and MT decreased. Thus, regardless the type of bariatric surgery (RYGBP or SG), zinc and copper status is adversely affected. Intestinal zinc and copper transporters present some modifications one year after the surgery. *Research leading to this abstract was provided by FONDECYT project 1080576*

Keywords: Zinc, Copper, Bariatric Surgery

Inhibitory action of analytical grade zinc oxide and of a new potentiated ZnO on the in vitro growth

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Pharmacological dosage of zinc oxide in piglet weaning diets is a common practice for growth performance and gut health. The mode of action of this dietary fortification is still hypothetical. Among recognized effects, the antimicrobial activity of zinc oxide compounds is one key mode of action. A new and potentiated feed grade zinc oxide product (ZinPot, Animine) is compared to analytical grade zinc oxide for their growth repressing effect on two pathogenic bacterial *E. coli* strains : *E. coli* PS79 (O47:K88) and *E. coli* PS7 (O138:K81). Strains were incubated in Brain-Heart Infusion Medium (BHI). Saturated Zn-containing media were produced by adding 10 g Zn-source to a total of 100 ml BHI media at pH 4.6 and pH 6.5, then incubated, autoclaved, centrifuged and finally adjusted with BHI media to identical Zn-concentration at different dilution levels. Measurements during incubation were taken every 2 minutes over a period of 8h for media at pH 6.5 and every 4 minutes for 16h at pH 4.6. Growth curves were obtained from data and regression analysis was employed to calculate coefficients for maximum growth in the stationary phase and lag time for each individual incubation. In comparison to MIC determination which defines complete bacterial inhibition, this kinetic assay measured the influence of ZnO source on growth of enterobacterial strains at sub-inhibitory Zn-concentrations. Below the MIC of 0.32 µg/ml at pH 6.5, lag phase, exponential growth and stationary phases could be distinguished. Compared to analytical grade ZnO, the lag time was significantly ($p < 0.05$) higher in ZinPot for the two *E. coli* strains at all Zn concentrations and at both pH, but only at low Zn-dosage for *E. coli* PS7 at pH 6.5. At pH 4.6, both *E. coli* strains showed higher maximum growth for standard ZnO compared to ZinPot at all sub-inhibitory Zn-concentrations. These results suggest that this potentiated zinc oxide may be utilised at a lower dosage than the standard form. In order to assess the impact of ZinPot on bacterial communities in the weaned piglet intestine, further ex-vivo studies should explore the effects of these two types of ZnO on bacterial fermentation and bacterial cell number.

Keywords: Zinc Oxide, Piglet, *E. coli*

Nanoparticulate iron: a quick-to-clinic strategy to address iron deficiency anaemia?

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Over one third of the world's population suffers from anaemia, mostly due to iron deficiency, and current iron supplements and fortificants aren't particularly effective. Existing barriers to successful treatment of this disease are: (i) high adverse effects and poor compliance and (ii) lack of discrimination between those needing iron and those who do not. Current treatment is almost always based on soluble ferrous (Fe^{2+}) iron salts. These are cheap and reasonably well absorbed but cause significant adverse effects, in particular associated with gastrointestinal disturbances because they are completely different from the iron forms present in our food. Therefore, even in subjects with iron deficiency only about 20-30% of oral iron is absorbed and the remainder transits through the gut lumen undergoing redox cycling and inducing free radical mediated damage to the gut mucosa. Ferric iron (Fe^{3+}) supplements are better tolerated but, due to their low solubility, are poorly absorbed. To tackle the problem, our approach is to use cheap, synthetic analogues of the ferritin core which could have both supplemental or fortificant potential. We consider this more practical to develop and implement and considerably cheaper than widespread gene modification of cereal plants to induce ferritin synthesis and abnormal iron storage. Our ferritin mimics are nanoparticulate ferric iron oxides wrapped in a coat made from organic acids naturally found in food, such as tartaric and adipic acids. Preliminary cellular and animal studies look promising and show that the novel nano-iron is able to be taken up by intestinal cells and shows equivalent bioavailability to ferrous sulphate (the gold standard of iron therapy) in iron deficient animals. The use of food-grade, dietary components in this material, its ease of cellular degradation into its component parts, and its intended downstream use as a nutritional supplement favour intervention studies directly in humans. Moreover, unlike ferrous sulphate, which is toxic to the intestinal mucosa and associated with significant adverse effects due to its role in redox cycling, any unabsorbed iron from this novel nanoparticulate material should remain insoluble in the intestinal lumen, thus preventing mucosal toxicity.

Keywords: Iron Deficiency Anaemia, Nanoparticles, Ferric Iron, Nano-iron, Iron Oxides

An intervention to improve the iron status of rural adolescent girls in Karnataka, India

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Iron deficiency anemia (IDA) is one of the major nutritional problems in India. Adolescent girls in rural India are one of the vulnerable groups prone to iron deficiency anemia. Farm women during adolescence suffer from anaemia due to increased body needs and routine activities at home and field. In view of this, a study was designed to assess the knowledge about iron rich foods and extent of anemia in adolescent girls. By participatory rural appraisal technique in a Cluster of village's viz., Mugali, Madanbhavi and Hosatti of Dharwad taluk, Karnataka state, India, revealed that the adolescent girls consumed less of iron rich foods and they also lacked knowledge regarding iron rich foods. It was also observed that 80% of the respondents were suffering anemia. They expressed the problem of tiredness, easy fatigue, inability to carry on work. In order to educate the adolescent girls and improve their blood hemoglobin an intervention study was further designed. Nutrition education was imparted through lectures, demonstrations of usage methods of iron rich foods, exhibitions showcasing iron rich foods, causes for deficiency and means to overcome the deficiency problems. Fifteen voluntary adolescent girls suffering from IDA were randomly selected for feeding trials. The health mix made of locally available foods - popped sorghum, wheat, puffed bengal gram, sugar, gum, garden cress seeds and milk powder developed was fed to the adolescent girls for three months. Each adolescent girl consumed 50g in two split doses per day. 50g of the health mix porridge provided 13% energy, 12% of protein, 25% of fat, 16% iron and 23% of folic acid of the recommended dietary allowance. The initial BMI of the girls which ranged from 14.72- 20.31 increased to 16.69 – 23.05. The blood hemoglobin levels which ranged from 10- 11.20 g/dl increased to 12- 12.4 g/dl indicating improvement in iron status. It can be concluded that creating awareness about the iron rich foods and consumption of combination of locally available foods can improve iron status in adolescent girls.

Keywords: Adolscent Girls, Iron Deficiency Anemia, Nutrition Education

Synthesis, structural characterization, safety and efficacy evaluation of zinc threoninate chelate

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To develop a safe, effective, nonpolluting and feed additives, zinc threoninate chelate ($C_8H_{16}N_2O_6Zn \cdot 2H_2O$) was synthesized by use of patented technology - "one step process. At the same time, safety and efficacy were tested by toxicological evaluation trials and a piglet feeding trial. The oral lethal dose 50% (LD50) was 3160 mg/kg in male rats and 2710 mg/kg in female rats. Moreover no genotoxicity was found by Ames test in *Salmonella typhimurium* strains TA97, TA98, TA100, and TA102, by bone marrow mouse micronucleus test and a sperm abnormality test in mice. It had no adverse effects on growth, blood biochemical parameters, ratio of organ to body and on organs in rats (thirty-day repeat dose toxicity study). It had no significant teratogenic effect at a daily dose of 42 mg/kg. Three hundred and sixty crossbred piglets (Duroc×Landrace×Large White, forty-day-old), with an average weight of (11.37 ± 0.42) kg, were randomly allocated into five dietary treatments with six replicates (twelve pigs per pen) by weight and gender. The basal diet was corn-soybean meal. The positive control diet included 100mg/kg zinc from zinc sulfate into the basal diet. The negative control group was fed with the basal diet. The other dietary treatments were supplemented with 50, 75, 100mg/kg zinc from zinc threoninate chelate in the basal diet. The results showed that the piglets fed zinc-amino acid complex as a zinc source had a statistically significant improvement in weight gain and feed conversion ratio. Meanwhile, in order to provide theoretical basis for research and application of new feed additives, the regulatory role of zinc threoninate chelate in the related gene of animals was studied by molecular biology techniques. After 28 days, the tissues of piglets were collected to study the effect of zinc source and zinc levels on gene expression. The levels of mRNA expression were quantified with PT-PCR. Zinc threoninate chelate can significantly up-regulate zinc transporter (ZnT1) and metallothionein (MT1) gene expression in the jejunum, ileum, jejunum mucosa and ileum mucosa of piglets. In the liver of piglets, it can significantly up-regulate MT1 gene expression.

Keywords: Zinc Threoninate Chelate, Synthesis, Growth Performance

Symposium 2(B)

Title: Trace Mineral Metabolism and Interactions:
Implications for Animal and Human Health

Sponsor: Novus International, Inc., USA and TEMA-14

Location: Conference Room 2

As sodium goes down - are we getting enough iodine?

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The normal adult human body contains about 15-20 mg of iodine, of which 70 – 80% is concentrated in the thyroid gland. Iodine deficiency can lead to adverse effects on growth and developmental abnormalities. Under the Canadian Food and Drug Regulations, all table salt must contain 76 µg iodine (as KI) per gram of salt; however, iodine is not added to manufacturing/food processing salt. In recent years there has been a great emphasis on reducing intakes of sodium, as part of population health strategies to reduce diseases associated with high sodium intakes. Recent national surveys in Canada have shown that 60-70% of Canadians never or rarely add salt to food at the table; hence it is important to determine if the diet contains sufficient iodine, since the majority of Canadians do not consume iodized salt. We analyzed iodine levels in Canadian Total Diet food samples that corresponded to the food composition data that were used in the recent national food consumption survey, Canadian Consumer Health Survey (CCHS 2.2, nutrition). Iodine levels were determined in 138 food sample composites from over 800 purchased foods, representing 15 food groups, which are representative of the foods most often consumed by Canadians. Food groups containing the highest amount of iodine included: dairy products 520 ± 201 ng/g (range: 99 – 947); fish products 159 ± 184 ng/g (range: 15-429); cereals and cereal products 99 ± 218 ng/g (range: ND – 991) and baby foods 105 ± 161 ng/g (range 3 – 488). Levels of iodine in Canadian foods remain high and levels in dairy products have not been reduced significantly since 1991, when the ban on ethylenediamine dihydroiodide (EDDI) use as a prophylactic agent for foot rot in cattle was introduced. These results suggest that the Canadian diet provides adequate amount of iodine, although obtaining sufficient amounts of iodine depends on consuming adequate amounts of dairy products. However, depending on inadvertent addition of iodine by the dairy industry is not consistent with a rigorous public health approach to food fortification. If the Canadian dairy industry should change production practices to reduce or remove iodophore sanitizers etc, as was done in other countries, the Canadian population would be vulnerable to insufficient intakes of iodine.

Keywords: Canada, Iodine, Salt, Intake

Impact of zinc deficiency, oxidative stress and DNA integrity- from cells to humans

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There is increasing evidence that micronutrient deficiencies may damage DNA and increase cancer risk. This is an important public health concern as a large proportion of the population has inadequate zinc intakes. Zinc is a component of over 300 proteins, including DNA-binding proteins with zinc fingers, Cu/Zn superoxide dismutase and DNA repair proteins such as p53, a zinc protein which is mutated in half of human tumors. It can be hypothesized that insufficient zinc intake can impair antioxidant defenses and compromise DNA repair mechanisms, making the cell highly susceptible to oxidative DNA damage. Both in vitro and in vivo, we have also found that zinc deficiency increases DNA damage in cells, increases several markers of oxidative stress and compromises DNA repair signal pathways including p53-dependent pathways. Consequently, zinc deficiency not only causes oxidative stress and induces DNA damage, but also compromises the cell's ability to repair this damage. In humans, increases in DNA damage precede losses in plasma zinc levels in response to dietary zinc depletion, and is reversed with zinc repletion. Interestingly, the prostate appears to be highly susceptible to zinc loss and zinc may play an important role in prostate health. In particular, the lobes of the prostate that are prone to developing cancer appear to be uniquely sensitive to zinc deficiency and DNA damage. This work strongly suggests that zinc deficiency has a detrimental effect on DNA integrity and emphasizes the importance of good nutrition in the prevention of cancer.

Keywords: Zinc, Oxidative Stress, DNA Damage

Chelation strengths of organic manganese and zinc on their absorptions and utilizations in broilers

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In vitro and in vivo experiments were conducted using primary culture of myocardial cells, inverted sacs and in situ ligated loops of the small intestine of broilers. Intravenous injections of Mn and Zn to broilers and diets investigated chelation strengths of organic manganese (Mn) and zinc (Zn) on absorption and utilisation in broilers. The ileum was the main site of Mn and Zn absorption in the small intestine of broilers. Manganese and Zn absorptions were carrier-mediated processes in the duodenum and jejunum, but a nonsaturable diffusion process in the ileum. The absorption of organic Mn and Zn with optimal chelation strengths were greater than inorganic forms in the small intestine of broilers, and increased with increasing chelation strengths. Organic Mn and Zn with higher chelation strengths were not easily dissociated in the gut, and had better resistance to precipitation and adsorption from high calcium and phytate in the digestive tract, thus showed higher Mn and Zn absorptions. Met was more effective in facilitating Mn absorption than Gly, but they were equally effective in facilitating Zn absorption. There was a close relationship between chelation strengths of organic Mn and Zn and their relative bioavailabilities for broilers, in which the organic Mn and Zn sources with moderate chelation strengths were the most available among organic and inorganic Mn and Zn sources. Although organic Mn and Zn with strong chelation strengths had the greatest Mn and Zn absorptions, they were harder to be mobilized and utilized at the target cell and tissue levels, therefore demonstrated lower or even the lowest bioavailabilities. The different mechanisms of Mn and Zn absorptions in different intestinal segments and among Mn and Zn sources with different chelation strengths might be due to different mRNA expressions of the divalent metal transporter 1 (DMT1) and metallothionein (MT) which play an important role in Mn and Zn absorptions in the small intestine of broilers. Further trials are needed to investigate factors other than Mn and Zn that would regulate the expressions of DMT1 and MT and transport-carriers other than DMT1 and MT which would be involved in the absorptions of Mn and Zn.

Keywords: Manganese Source, Zinc Source, Chelation Strength

Influence of dietary iron concentration on metabolism of other trace minerals in pigs and cattle

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Dietary mineral imbalance in animals can greatly influence the absorption and utilization of several trace minerals. In domestic livestock diets, iron is frequently found in concentrations well above that which is required by the animal. A number of proteins integral to iron absorption have been identified in pigs and cattle, including divalent metal transporter 1, and ferroportin. Metabolism of other trace elements may be influenced by excessive dietary iron because of competition for transport or storage proteins. In particular, divalent metal transporter 1 is a likely point of interaction between elements such as iron and manganese. In two experiments where weaned pigs were fed varying concentrations of dietary iron we observed a negative relationship between dietary iron and manganese concentration in tissues such as intestine, liver, and heart. Pigs fed 797 mg iron/kg DM demonstrated reduced mRNA expression of divalent metal transporter 1 in duodenal scrapings compared with pigs fed 97 mg iron/kg DM. This decrease likely explains the decrease in tissue manganese concentrations observed in these pigs. Similarly, young dairy cattle fed 810 mg iron/kg DM tended to have lower protein expression of DMT1 in duodenum compared with calves receiving 60 mg iron/kg DM. In this study duodenal manganese concentrations were decreased by 30% in cattle fed high iron compared to animals fed low iron diets. Zinc transport may also be influenced by high dietary iron, as we have observed decreased duodenal mRNA expression of zip14 in pigs fed high dietary iron compared with low iron control pigs. Interestingly, we have also observed a decrease in intestinal expression of zip14 mRNA as pigs increase in age from 21 to 63 days of age. Because feeds commonly fed to domestic livestock are often high in iron, animal status for trace elements such as manganese and zinc should be monitored and additional supplementation considered when necessary.

Keywords: Iron, Manganese, Animals

Effects of selenium source on productivity of dairy cows and their mechanism of action

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Selenium-enriched probiotics (SP) is a new type of organic Se source developed by our lab, (China patent patent number: ZL 20051 0040990.2). The SP can exert dual effects of organic Se and probiotics at the same time. The present study is to determine how a basal diet supplemented with Na₂SeO₃ or SP affects absorption and transformation of selenium, antioxidant ability, milk yield and milk quality in dairy cows. Effects of different forms of Se on mRNA level and activity of GPx1 were also studied in bovine hepatocytes. SP or Na₂SeO₃, when compared with control group, increased Se concentrations of blood, colostrum and milk, erythrocyte GPx1 activity and milk percentages of polyunsaturated fatty acids (PUFA) and cis-9,cis-12 linoleic acid and decreased milk somatic cell count and MDA level. Cows supplemented with SP had higher Se levels in blood and milk and percentage of PUFA in milk and lower GPx1 activity and milk somatic cell count when compared with those supplemented with Na₂SeO₃. Milk yield, milk component and serum GPx3 activity were not significantly affected by Se source. Primary cultured bovine hepatocyte monolayers from neonatal male Holstein calves (aged 1–2 days) were incubated for 24h with 0 (control), 0.5, 1, 1.5, 2, 3, 4 or 5 μM of Se from DL-selenomethionine (Se-Met), Na₂SeO₃ or Kappa-selenocarrageenan (Se-Car). Compared with controls, there was a significantly lower lactic dehydrogenase (LDH) release at 0.5–5 μM of Se-Met, 0.5–1 μM of Na₂SeO₃ and 0.5 μM of Se-Car, but significantly higher LDH release was observed at 2–5 μM of Na₂SeO₃ and 3–5 μM of Se-Car. Intracellular reduced GSH in all Se-treated cells was significantly lower than that controls. Significant increases in GPx1 mRNA were obtained in all Se-treated cells. Furthermore, 3 μM of Se from Se-Met resulted in peak levels of GPx1 mRNA. After reaching a maximal level, higher Se supplementation led to a reduction of GPx1 mRNA. The activity of GPx1 was showed similar patterns but of lower magnitude. Se-Met is better on regulation of mRNA level and activity of GPx1 in primary bovine hepatocytes than Na₂SeO₃. The optimal doses of Se to support the full expression of GPx1 in bovine hepatocytes when supplied as Se-Met, Na₂SeO₃ and Se-Car are 3, 1.5 and 2 μM.

Keywords: Selenium Source, Milk Productivity, Primary Bovine Hepatocytes

The effect of sublethal waterborne cadmium on several enzyme activities in gills of mud crab *Scylla Paramamosain*

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The aim of this study was to evaluate the effects of sublethal levels of waterborne cadmium on metabolic condition (including ionoregulatory, immune and antioxidants defense systems) in gills of mud crab *Scylla paramamosain*. For this purpose, crabs were submitted to 0.025, 0.05, 0.075, 0.1mg Cd L⁻¹. The results showed that antioxidant enzyme (superoxide dismutase, SOD) activity was stimulated significantly by higher level of cadmium (0.1mgL⁻¹) after 3 or 5 days, and also shown a significant reduction with the experimental time prolonging. Ca²⁺-ATPase activity was significantly inhibited by cadmium after 1 day. However, Na⁺,K⁺-ATPase revealed a much lower sensitivity to cadmium than Ca²⁺-ATPase. The increases of Ca²⁺-ATPase and Na⁺,K⁺-ATPase activities were found compared with controls after 5 days. The change depended on the cadmium concentration. For acid and alkaline phosphatase activities, their change to cadmium exposure was presented in different way. It may depend on features of themselves. These results demonstrated that a short-term sublethal cadmium exposure could lead to metabolic disturbance and provide important clues to further understanding of the biomarker responses of mud crab *Scylla paramamosain*.

Keywords: Cadmium, *Scylla Paramamosain*, Biochemical Parameter

Effect of varying selenium and iodine intake on feline thyroid function

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Novus International, Inc.

Se and I concentrations can be quite high in cat foods, especially canned diets containing fish and/or seafood. Se and I concentrations were measured in commercial canned cat foods w/ fish (n=64), canned cat foods w/o fish (n=37) and dry catfood (n=54). Se concentrations averaged 2.36, 1.42 and 0.72, ranging from 0.25–12.3 mg/kg diet (DM); I concentrations averaged 10.05, 5.5 and 2.63, ranging from 0.8-51 mg/kg diet (DM). A number of epidemiological studies indicate greater incidence of hyperthyroidism in cats consuming canned diets (2-4 fold greater incidence in cat populations consuming canned diets relative to cats consuming dry diets only), however, the cause of the disease is unknown. Two trials in normal healthy cats tested the effect of varying I and Se intake on thyroid function. In trial 1, cats were fed a basal diet supplemented with seven levels of KI for one year. Analyzed I concentrations ranged from 0.17 -8.8 mg I/kg diet (DM basis). Response variables included I concentrations in serum, urine, feces, urinary I:creatinine ratio, I balance, technetium 99m pertechnetate (Tc99m) thyroid:salivary (T:S) ratio, as well as serum thyroid hormone profiles. No significant changes in food intake, weight gain or clinical signs were noted. Serum I, urinary I, fecal I and urinary I:creatinine ratio were linear functions of I intake. An estimate of the I requirement (i.e., breakpoint) was determined from regression of Tc99m T:S ratio (scintigraphy) on I intake at 12 mo (0.46 mg I/kg diet); T:S ratio was elevated at I intakes \leq 0.23 mg/kg I. An I requirement was also determined using 9 mo I balance (0.44 mg I/kg diet). There were no significant effects of I intake on thyroxine (TT4) or triiodothyronine (TT3). However, free thyroxine (FT4), was lower at wk 48 for cats fed the highest I concentration (quadratic effect; $P=0.007$). In trial 2, cats were fed a basal diet supplemented with six levels of selenomethionine ranging from 0.04–8.4 mg Se/kg diet, DM to normal healthy cats for six month duration. A linear increase ($P=0.0003$) in uptake of Tc99m with increasing Se intake in cats was observed, however, no significant changes were observed for any of the thyroid hormones measured. In summary, I deficiency and Se excess increased thyroidal uptake, whereas I excess suppressed thyroid function. Avoidance of Se and I excess in cat foods is recommended.

Keywords: Selenium, Iodine, Cat, Thyroid

Impact of chelated trace minerals on immune function in farmed animals

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Zn deficiency impairs immunity including reducing the activity of both T and B lymphocytes and causes decreased antibody response to vaccination. We evaluated the effect of a new class of methionine hydroxy analogue chelated Zn, Cu and Mn on immune response in production species. In the first trial, gilts (50 per treatment) were fed diets supplemented with 165ppm Zn, 16.5ppm Cu and 38.6ppm Mn either as trace mineral salts, or an equal blend of salts and chelates. Gilts were vaccinated against *M. hyopneumoniae* on weeks 0 and 2 postweaning, and bled for antibody titers on weeks 0, 2, 4, 8 and 12. Log titers were measured by a commercially-available ELISA. Gilts supplemented with chelates exhibited positive titers on weeks 4 and 8, and titers were greater than in the controls ($P < 0.05$). Controls reached a positive titer by week 12. In the second trial, striped catfish (120/treatment) were fed a control practical diet containing 44ppm Zn, or diets supplemented with Zn sulfate or Zn chelate to contain 107 ppm Zn. After 6 weeks on diets, all 3 dietary treatments were split, and either mock-vaccinated with PBS, or vaccinated with a formalin-killed *E. ictaluri* vaccine. Titers were measured by agglutination assay prior to vaccination (day 0), and days 14 and 21. All 3 mock-vaccinated treatments remained negative for titers on all days, and all treatments were negative on day 0. On day 14, the vaccinated Zn sulfate and vaccinated chelated Zn treatments exhibited titers greater than unvaccinated treatments ($P < 0.05$), whereas the vaccinated control treatment did not. On day 21, all vaccinated treatments achieved titers greater than unvaccinated ($P < 0.05$), but titers in the chelated Zn group were higher ($P < 0.05$) than all other treatments. At least 42 fish per treatment were challenged by immersion with *E. ictaluri*, and survival measured for 14 days. Vaccination significantly increased survival across dietary treatments ($P < 0.0001$). While not significantly different than the other vaccinated treatments, relative percent survival of the vaccinated Zn chelate group was highest at 76% while the vaccinated Zn sulphate and control groups were 59% and 61%. These data indicate a more robust antibody response to vaccination in the chelated Zn treatments, in both swine and fish.

Keywords: Trace Mineral, Immunity, Catfish

The effect of copper and ATP7A overexpression on CTR1, ATOX1, ATP7B and ceruloplasmin in PMC42-LA human breast cells

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The proper growth and development of infants is dependent on their ability to obtain essential nutrients from their mother's milk. Copper is a crucial component of the milk and plays a role in a number of enzymatic reactions. Copper deficiency can lead to neurological degeneration, growth retardation, pale kinky hair and loose skin. These symptoms, particularly neurological degeneration can lead to infant death at an early age. In this study we have used the PMC42 cell line, model of human mammary epithelium, to over express ATP7A and analyse its impact on other copper transporting proteins within the cells. We used a previously developed ATP7A over expressing construct to transfect PMC42 cells and over express ATP7A. We then used Western blot analysis, quantitative real time PCR, immunofluorescence, biotinylation and AAS to measure changes to CTR1, ATOX1, ATP7B, Ceruloplasmin (Cp) mRNA levels and protein levels and localisation, and intracellular copper levels. Results showed that copper and ATP7A overexpression influenced CTR1 protein levels, while localisation was unaffected. Ceruloplasmin (Cp) mRNA and protein levels showed an increase in response to ATP7A overexpression and there was also a change in band pattern on the western blot following the alterations of copper concentration. Small changes in ATOX1 and ATP7B protein levels were observed in response to ATP7A overexpression. ATP7B and Cp showed no changes in localisation in response to ATP7A overexpression, however ATP7B did relocalise in response to copper. The data obtained in this research has increased our knowledge on the role of ATP7A in cells and its impact on the regulation of cellular copper homeostasis in the breast epithelium.

Keywords: Copper Transporters, Breast Epithelium, Minerals in Milk

Copper chelation reduces HIF-1 α accumulation induced by dimethyloxallyl glycine in human umbilical endothelial cells

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Cytosolic accumulation of hypoxia-inducible factor-1 α (HIF-1 α) is a critical regulatory mechanism of HIF-1 transcriptional activity. Dimethyloxallyl glycine (DMOG), by inhibiting the prolyl hydroxylases, causes HIF-1 α accumulation so that it is under the drug development for HIF-1 transcriptional activation. Previous studies have shown that copper is required for the transcriptional activity of HIF-1 and copper is functional deficient under ischemic conditions. The present study was undertaken to examine the effect of copper deficiency on HIF-1 α accumulation induced by DMOG to better understand the regulatory mechanism of HIF-1 under disease conditions. Human umbilical vein endothelial cells (HUVECs) subjected to the treatment with 100 μ mol DMOG for 4 hrs resulted in an accumulation of HIF-1 α in the cells, determined by Western blot analysis of HIF-1 α protein. Along with the DMOG treatment, a copper chelator, tetraethylenepentamine (TEPA), at 50 μ mol blocked the intracellular accumulation of HIF-1 α . Further analysis revealed that TEPA reduced both DMOG-elevated nuclear levels of HIF-1 α and the cytosolic accumulation. This study thus demonstrates that although inhibition of prolyl hydroxylases by DMOG can lead to accumulation of HIF-1 α in the cells, copper is critical for the stability of HIF-1 α . Copper might affect the nuclear translocation process leading to decreased nuclear levels of HIF-1 α , but it cannot be excluded that copper also affects other processes leading to the reduced stability of HIF-1 α in the cells.

Keywords: Copper, HIF-1 α , Prolyl Hydroxylases

Organic selenium supplementation improved growth performance of buffalo (*Bubalus bubalis*) calves

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Eighteen male buffalo (*Bubalus bubalis*) calves (88.8±2.62 kg) were divided in to three equal groups and supplemented either with 0 (control, Gr I) or 0.2 ppm selenium (Se) from inorganic (sodium selenite, Gr II) or organic (Jevsel-101, Gr. III) sources. All the animals were fed a common basal diet consisting of concentrate mixture and wheat straw in 52: 48 ratio. Concentrate mixture was comprised of 30% maize grain, 42% wheat bran, 25% soybean meal, 2% mineral mixture and 1% common salt. Experimental feeding was for a period of 180 days during which body weights were recorded at 15 days intervals. A metabolism trial was conducted after 120 days of experimental feeding. The selenium content in the basal diet was 0.20 ppm. Results revealed no significant ($P>0.05$) difference in the intake of CP, DCP, TDN and digestibility of different nutrients viz. dry matter, organic matter, crude protein, ether extract, neutral detergent fibre, acid detergent fibre, cellulose, hemicelluloses. Balance of nitrogen, calcium and phosphorus was also not affected due to Se supplementation as it was comparable in the three groups. However, average daily gain (ADG) was higher in Gr II and III being 433.3 g and 450.7 g, which was 6 and 10 percent more as compared with 408.8 g in the control group (Gr I). It indicated that supplementation of 0.2 ppm Se in the diet of buffalo calves, having 0.2 ppm Se, improved the growth performance of these animals. It was also deduced that between the two sources of Se, organic Se was more effective than inorganic Se.

Keywords: Organic Selenium, Buffalo Calves, Growth and Nutrient Metabolism

Symposium 3 (C)

Title: Trace Elements on Cell Death, Tumor, and Cancer

Sponsor: TEMA-14

Location: Conference Room 3

Selenium, selenoproteins, sulforaphane and colon cancer

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Chronic inflammation and selenium-deficiency increase the risk of colon cancer, however, it is not known, whether the selenium effect is based on the expression of specific selenoproteins such as glutathione peroxidases (GPx). Also, a wide range of dietary chemopreventive agents, comprising phytochemicals like glucosinolates and derived metabolites such as sulforaphane (SFN), have been demonstrated to prevent carcinogenesis via activation of the Nrf2 system. Since SFN also induces the expression of the selenoproteins GPx2 and TxR1, a synergistic action of selenium and SFN has been proposed. In contrast, GPx2 is also induced by the key player of the Wnt pathway, TCF/ β -catenin, which rather points to a pro-cancerogenic action. Thus, the function of GPx2 in carcinogenesis remains unclear. GPx1 and -2 double-knockout, but not single knock-out mice, develop spontaneous ileocolitis and intestinal cancer. We, therefore, tested whether GPx2-single-KO mice are more susceptible to inflammation-promoted colon carcinogenesis mediated by azoxymethane and dextran sulfate sodium (AOM/DSS) and whether the tumor-suppressing effect of selenium and SFN depends on GPx2 [1]. Wild-type and GPx2-KO mice were adjusted to selenium-poor, -adequate, or -supranutritional status before AOM/DSS treatment combined with and without SFN-feeding. Severity of inflammation and SFN target-gene expression was tested 3 weeks after AOM, tumorigenesis after 12 weeks. Both, GPx2 and selenium suppressed AOM/DSS-induced inflammation and tumorigenesis. A beneficial SFN effect was only observed when selenium was available, which did not require GPx2. Loss of GPx2 most probably was compensated by GPx1, which was highly increased in GPx2-KO mice in each selenium status in areas where GPx2 is expressed in wild-type mice.

[1] Krehl S, Loewinger M, Florian S, Kipp A, Banning A, Wessjohann LA, Brauer MN, Iori R, Esworthy RS, Chu F-F, and Brigelius-Flohé R. GPx2 and selenium decrease AOM/DSS-induced colitis and tumorigenesis, whereas effects of sulforaphane depend on selenium. 2011, submitted.

Keywords: Selenium, GPx2, Sulforaphane, Inflammation, Colon Cancer

Selenium induces apoptosis and blocks tumor invasion

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Anticarcinogenic functions of selenium can be classified as chemoprevention and inhibition of tumor invasion. Recent studies have implicated that apoptosis is one of the most plausible mechanism of chemoprevention by selenium and matrix metalloproteinases (MMPs) are a crucial factor involved in tumor invasion and metastasis. In these studies, it was shown that Se-methylselenocysteine (MSeC), one of highly effective selenium compounds for chemoprevention, induced apoptosis in HL-60 cells and that reactive oxygen species (ROS) played a crucial role in MSeC-induced apoptosis. N-Acetylcysteine, glutathione, and deferoxamine blocked cell death, DNA fragmentation, and ROS generation induced by MSeC. Moreover, N-acetylcysteine effectively blocked caspase-3 activation and the increase of the sub-G1 population induced by MSeC. It was demonstrated that nontoxic level of selenite (less than 3 μM) inhibited invasion of HT1080 cells and also adhesion of the tumor cells to the collagen matrix. Moreover, selenite reduced activity and expression of matrix metalloproteinase-2,-9 and urokinase type plasminogen activator, which are involved in matrix degradation and tumor invasion. This inhibitory effect of selenite on the proteases' expression was mediated by the suppression of transcription factors, NF- κ B and AP-1. Another experiment showed that methylseleninic acid inhibited PMA-stimulated proMMP-2 activation mediated by MTI-MMP expression and further tumor invasion through suppression of NF- κ B activation. Further animal study have shown that administration of MSeC or selenite to c57Bl/6J mice increased survival rate and reduced tumor metastasis by injection of melanoma into the tail vein. These results suggest that Se compounds may be useful for both chemoprevention and therapeutic application for cancer patients.

Keyword: Se, Apoptosis, Tumor Invasion

Synergistic interactions between isothiocyanates and selenium in the up-regulation of TR-1 and GI-GPx and protection against free radical-mediated cell death

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In the human genome, 25 genes for selenoproteins have been identified. Among the 25 selenoproteins, only two of them, thioredoxin reductase (TR-1) and gastro-intestinal glutathione peroxidase (GI-GPx or GPx-2), were found to possess antioxidant response element (ARE) in their gene promoter. This suggests that activation of Nrf2 signaling may result in the upregulation of these two selenoproteins. Dietary isothiocyanates are potent inducers of Nrf2 and have been extensively studied as chemopreventive agents from cruciferous vegetables. It has been previously shown that isothiocyanates sulforaphane and selenium have a synergistic effect on the upregulation of TR-1 in human hepatoma HepG2 cells. Here, further evidence is presented to show that sulforaphane and selenium synergistically induce TR-1 and GI-GPx expression in immortalised human hepatocytes and colon cancer Caco-2 cells. Sulforaphane can protect against hydrogen peroxide-induced cell death and this protection was enhanced by co-treatment with selenium. Using siRNA to knock down TR-1 or GI-GPx, sulforaphane-protected cell viability was significantly reduced. Sulforaphane-induced TR-1 or GI-GPx expression was positively associated with significant levels of Nrf2 translocation into the nucleus, but co-treatment with selenium showed no significant increase on Nrf2 translocation suggesting that selenium mainly act as translational level. Moreover, MAPK (ERK, JNK and p38) and PI3K/Akt signaling pathways were found to play no significant role in sulforaphane-induced Nrf2 translocation into the nucleus. However, blocking ERK and JNK signaling pathways decreased sulforaphane-induced TR-1 mRNA by about 20%; whereas blocking p38 and PI3K/AKT increased TR-1 transcription. In summary, isothiocyanates are potent inducers of selenium-dependent enzymes such as TR-1 and GI-GPx, the induction occurs mainly *via* the Nrf2-ARE pathway. A combination of sulforaphane and selenium resulted in a synergistic upregulation of TR-1 and GI-GPx that contributed to the enhanced protection against free radical-mediated oxidative damage in cultured cells. Therefore, we believe that an optimal combination of selenium and Nrf2 inducers such as isothiocyanates may provide a promising strategy to maximize beneficial effects of selenium and isothiocyanates whilst minimizing their potential adverse effects at higher doses.

Keywords: Selenium, Sulforaphane, Selenoproteins

Deficiency of the 15kDa selenoprotein inhibits colon cancer risk

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The role of the 15kDa selenoprotein (Sep15) in colon cancer was assessed by preparing and using mouse colon CT26 cells stably transfected with shRNA constructs targeting Sep15. Metabolic ⁷⁵Se-labeling, Northern and Western blot analyses revealed that more than 90% of Sep15 was down-regulated. Growth of the resulting Sep15-deficient CT26 cells was reduced ($p < 0.01$) and cells formed significantly ($p < 0.001$) fewer colonies in soft agar compared with control CT26 cells. Whereas most (14/15) BALB/c mice injected with control cells developed tumors, few (3/30) mice injected with Sep15-deficient cells developed tumors ($p < 0.0001$). The ability to form pulmonary metastases had similar results. Mice injected with the plasmid-transfected control cells had >250 lung metastases/mouse; however, mice injected with cells with down-regulation of Sep15 only had 7.8 ± 5.4 metastases. The effect of Sep15 knockout in mice *in vivo* was also evaluated. After four weekly injections of azoxymethane (10 mg/kg) weanling, Sep15 knockout mice had significantly ($p < 0.001$) fewer carcinogen-induced aberrant crypt foci (ACF), a putative preneoplastic lesion, in their colon than littermate control or heterozygote mice. To investigate molecular targets affected by loss of Sep15, gene expression patterns in colonic mucosal cells of knockout and wild type mice were examined. Subsequent analyses verified that guanylate binding protein-1 (GBP-1) mRNA and protein expression were strongly upregulated in Sep15 knockout mice. GBP-1, which is expressed in response to interferon- γ , is considered to be an activation marker during inflammatory diseases, and up-regulation of *GBP-1* in humans has been associated with a highly significant increased five-year survival rate in colorectal cancer patients. In agreement with these studies, we observed a nearly two-fold higher protein expression of interferon- γ in plasma of untreated Sep15 knockout mice. Our results demonstrate for the first time, that Sep15 knockout mice are protected against chemically-induced ACF formation and that Sep15 appears to have oncogenic properties in colon carcinogenesis both *in vitro* and *in vivo*.

Keywords: 15kDa Selenoprotein, Colon Cancer Risk, Mice

Zinc depletion, intracellular calcium disturbance, and apoptosis

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It is well established that zinc can function as an inhibitor of apoptosis. Depletion of cellular zinc induces apoptosis while elevated level of cellular zinc inhibits apoptosis. However, the exact mechanisms whereby zinc modulates apoptosis remains to be elucidated. We have previously shown an elevated expression of GADD45, a family of growth arrest and DNA damage gene, in zinc depletion-induced apoptosis in breast cancer MDA-MB-231 cells. The objectives of this study were to investigate whether DNA damage played a role in zinc depletion-induced apoptosis in MDA-MB-231 cells and to explore the possible cause of DNA damage associated with zinc depletion in MDA-MB-231 cells. The cells were cultured in DMEM supplemented with FBS (10%) followed by treating the cells with TPEN to deplete intracellular zinc. Zinc depletion significantly induced apoptosis, increased single-strand DNA break, and oxidative stress-induced DNA damage. Interestingly, zinc depletion resulted in a time-dependent increase in the generation of reactive nitrogen species, but not reactive oxygen species. Inhibition of eNOS activity suppressed zinc depletion-induced apoptosis. Furthermore, decreasing intracellular calcium level through chelation significantly reduced apoptosis. Similarly, interrupting intracellular calcium trafficking also reduced significantly zinc depletion-induced apoptosis. In summary, these results suggested that zinc depletion altered intracellular calcium homeostasis, resulting in an elevated intracellular calcium level, which promoted generation of reactive nitrogen species. This elevated reactive nitrogen species, in turn, induced DNA damage and consequently, resulting in an elevated apoptotic death of breast cancer MDA-MB-231 cells. (*Supported by NSERC*).

Keywords: Apoptosis, Calcium, Zinc

Selenium-induced senescence as an early barrier of tumorigenesis

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Selenium (Se) chemoprevention by apoptosis has been well studied, but it is not clear whether Se can activate early barriers of tumorigenesis, namely senescence and DNA damage response. In response to clastogens, the ataxia-telangiectasia mutated (ATM) and DNA-PKcs proteins are rapidly activated, which in turn initiates a cascade of DNA damage response. In a cancer prevention perspective, we reason that Se could in principle counteract tumorigenesis at the precancerous stage, preventing progression towards full-blown cancer. To test this hypothesis, we treated normal and cancerous cells with a gradient concentration of sodium selenite, methylseleninic acid (MSeA) and methylselenocysteine (MSeC). Here we show that Se compounds at doses \leq LD50 can induce cellular senescence, as evidenced by the expression of senescence-associated β -galactosidase and 5-bromo-2-deoxyuridine incorporation, in normal but not cancerous cells. We found that the ATM and DNA-PKcs are activated by the Se compounds, and the kinase activities are required for the Se-induced senescence response. ATM is upstream of DNA-PKcs in the Se-induced DNA damage response. Pretreatment of the MRC-5 non-cancerous cells with antioxidants, N-acetylcysteine and tempo, suppresses the Se-induced ATM and DNA-PKcs activation and senescence. Interestingly, DNA-PKcs plays a feed-forward role to sustain oxidative stress induced by Se compounds. Taken together, the results suggest a novel role of Se in the activation of early tumorigenesis barriers specific in noncancerous cells, whereby Se induces an ATM- and DNA-PKcs- dependent senescence response that depends on ROS. These results provide a new direction for understanding Se chemoprevention that targets genome maintenance at the precancerous stage.

Keywords: Selenium, Senescence, DNA Damage

A novel molecular mechanism of cancer chemoprevention by selenium: p53-mediated DNA repair

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Selenium is an essential trace element in mammalian organisms. Among several selenium compounds, selenomethionine (SeMet) has been studied for chemopreventive effect via stimulating DNA repair towards various genotoxic stresses. However, its chemopreventive mechanism is not well clarified. In this study, we examined the mechanism of SeMet in terms of p53-mediated base excision repair (BER). Our data showed that the amount of DNA damage was rapidly decreased in the presence of SeMet when methyl methanesulfonate (MMS), a BER-inducing agent, was added to the cells. In addition, the removal of apurinic/aprimidinic sites was significantly enhanced in p53 wild type cells in response to SeMet. Furthermore, we observed the Gadd45a, known to be involved in BER as one of the p53 downstream genes, responde to SeMet in p53 wild-type RKO cells. Indeed the interaction of BER-mediated repair proteins including PCNA (proliferating cell nucleus antigen) and APE/Ref-1 with Gadd45a was notably decreased by SeMet in p53 siRNA-treated cells. In vivo studies, the frequency and size of polyp was decreased in response to SeMet in an AOM/DSS animal model for colitis-related carcinogenesis. Moreover, proteins related to DNA repair including Trx (thioredoxin), p53 and Gadd45a were increased in SeMet treated AOM/DSS model. These results suggested that BER activity might be dependent on wild-type p53 under the modulation of protein complexes with Gadd45a and repair protein including PCNA and APE/Ref-1 as distinct chemopreventive mechanisms of SeMet activity. Our study might provide important evidence for the development of chemopreventive strategies against various oxidative stresses.

Keywords: Selenomethionine, DNA Rrepair, p53

Methylselenol, a selenium metabolite, plays a critical role in inhibiting colon cancer cell growth

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Methylselenol is hypothesized to be a critical selenium (Se) metabolite for anticancer activity. In this study, submicromolar methylselenol was generated by incubating methionase with seleno-L methionine, and both colon-cancer-derived HCT-116 cells and noncancerous colon NCM460 cells were exposed to methylselenol. Methylselenol exposure inhibited cell growth and led to an increase in the G1 and G2 fractions with a concomitant drop in the S-phase, and an induction of apoptosis in HCT116, but to a much lesser extent in NCM460 colon cells. The examination of mitogen-activated protein kinase (MAPK) and c-Myc signaling status revealed that methylselenol inhibited the phosphorylation of extracellular-regulated kinase1/2 (ERK1/2) and p38 MAPK, and the expression of c-Myc in HCT116 cells, but also to a lesser extent in NCM460 cells. The other important finding is that methylselenol inhibits Src phosphorylation in HCT116 cells. In sharp contrast, methylselenol up-regulated the phosphorylation of both Src and FAK survival signals in NCM460 cells. In addition to the above findings on human colon cells, we also found that methylselenol inhibited the growth of MC-26 colon cancer xenografts in Balb/c mice. Taken together, methylselenol's strong potential of inhibiting colon cancer cell proliferation, may be a critical mechanism by which selenium exerts its anticancer activity.

Keywords: Selenium, Cell Growth, Colon Cancer

Selenoprotein gene variants and risk of esophageal and gastric cancer in a Chinese population

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We previously found that selenium supplementation reduced cancer mortality, particularly gastric cancer mortality, and that low serum selenium concentration was associated with increased risks of esophageal squamous cell carcinoma (ESCC) and gastric cardia adenocarcinoma (GCA). Selenium may exert some of its chemopreventive actions through selenoproteins. Thus, we conducted a study to examine genetic variants in selenoprotein genes and risks of ESCC and GCA. We included 1027 ESCC and 753 GCA cases plus 1452 controls from two epidemiologic studies in China. We genotyped the 25 known human selenoprotein genes and four selenium metabolism genes using 272 tag single nucleotide polymorphisms (SNPs). Logistic regression assuming a log-additive model was used to estimate odds ratios (OR) and 95% confidence intervals (CI) for each SNP with ESCC and GCA. For each gene, we calculated a standardized summary p-value using the adaptive rank truncated product (ARTP) method. In gene-based tests adjusted for multiple comparisons, the selenoprotein gene *SELS* (selenoprotein S) was associated with ESCC risk (p=0.00070), and *TXNRD2* (thioredoxin reductase 2) showed borderline non-significant associations with both ESCC (p=0.063) and GCA (p=0.051). In SNP-based tests for these two genes, rs8029790 (tagged to upstream noncoding region of *SELS*) was associated with a 1.30-fold increased risk of ESCC (CI=1.14-1.47, p=0.000052); rs2073750 (tagged to intron in *TXNRD2*) was associated with risks of both ESCC (OR=0.84, CI=0.74-0.94, p=0.0029) and GCA (OR=0.82, CI=0.72-0.93, p=0.0026). Our study strengthens the hypothesis that selenium plays a role in cancer development, and our findings warrant further research on elucidating the functional effects of these SNPs on upper gastrointestinal (UGI) carcinogenesis.

Keywords: Esophageal and Gastric Cancer, SNPs, Selenoproteins

Selenium status and advanced/aggressive prostate cancer risk reduction: results from dose-response meta-analysis

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The evidence regarding the relationship between selenium and prostate cancer risk indicates dose- and species-specific effects of selenium, and a potential narrow range of optimal selenium intake and status. The objective of this study was to undertake a systematic review to assess the relationship between selenium status and prostate cancer risk, in particular to investigate the dose-response relationship to determine the 'optimal range'. Data from a meta-analysis of studies included in the World Cancer Research Fund/American Institute for Cancer Research Continuous Update Project database, updated to Sept. 2010, will be presented. Meta-analyses were performed and study validity, heterogeneity and publication bias were assessed. Dose-response meta-analyses were undertaken, with fractional polynomials for nonlinear trends, to investigate the association between selenium status and prostate cancer risk. Criteria for inclusion included an adult population, assessment of selenium intake or selenium status (including toenail, plasma or serum selenium) as an exposure with >2 categories, assessment of prostate cancer cases (number of events) and relative risk as an outcome. There were 8 studies included in the meta-analysis, with >11,000 participants and >4,000 incident cases of prostate cancer. The relationship between plasma/serum selenium and prostate cancer was non-linear and risk decreased with increasing plasma/serum selenium up to ~175ng/ml. Study validity and nonlinear fractional polynomial plots displaying the relationship between plasma/serum selenium and total or advanced prostate cancer risk will be presented. Relationships between micronutrient intake/status and health outcomes are being assessed as part of the ongoing work of the EURRECA (www.eurreca.org) Network of Excellence, with a primary objective of collating evidence that can be used for deriving dietary reference values.

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Keyword: Selenium, Prostate Cancer, Toenail Selenium, Plasma/Serum Selenium

Efficacy and safety of different phyto-selenocompounds in the prevention and control of stomach cancer

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More and more selenocompounds in selenium(Se)-enriched organisms are identified, and the relationship between natural selenocompounds and prevention and therapy of human diseases are of interest. For last ten years, about 1000 Se-enriched wild plants grown in naturally seleniferous areas or with by Se-fertilizer were analyzed for more than 9 families of selenocompounds. For the prevention of stomach cancer, studies of in vivo, in vitro and primary human intervention were conducted with some of these compounds. Four different Se species showed significantly different efficacy in the inhibition on the development of rat aneuploid cells in mucosal epithelium of the gastric antrum in N-Methyl-N'-Nitro-N- nitrosoguanidine (MNNG) Wistar rat model. Phytomethylsellanol precursor seleno compounds have much higher activity in eliminating the multidrug resistance to *Helicobacter pylori*. For the study of anti-oxidative mechanism in the MNNG rat model, blood and liver GPx activities of rats with Se added were significantly higher than those controls. No significant differences of blood and liver GPx occurred in rats with 150µg/g BW and 300µg/g BW of Se supplementation by four Se-enriched plants. For the safety study of seleno compounds, the tissue Se accumulation and distribution as well as regular toxicological indices in rats, dogs and mice were compared by use of selenite or Se-enriched soybean protein as control Se compounds, respectively. The accumulation of Se primarily had taken place in red blood cell and spleen of rats, mice and dogs supplemented by Se-enriched garlic, and in liver and kidney of rats fed with selenite, Se-enriched broccoli and kales. Selenite is 4-fold more toxic than Se-enriched plants mainly containing phytomethylsellanol precursor selenocompounds in rat model. Se-enriched plants are one of important bio-resources for the screen of new Se species; Phytomethylsellanol precursor selenocompounds have the highest activity and safety in the preventing of stomach cancer among all identified phyto-selenocompounds. Further Se species analysis and healthy value evaluation of more Se-enriched plants are necessary for screening new selenocompounds with high healthy values.

Keywords: Se-enriched Plant, Efficacy, Safety, Stomach Cancer, Se-compounds

Symposium 4(D)

Title: Link between Trace Elements in Soils and Their
Deficiencies in Animals/Humans

Sponsor: HavestPlus, Washington DC, USA and TEMA-14

Location: Conference Room 4

The role of soils in trace element deficiencies in animals/humans: an overview

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The underlying cause of many animal and human deficiencies of essential trace elements is closely linked to low levels of these nutrients in the soils upon which the agricultural systems operate. For example, iodine, selenium and cobalt deficiencies in many world regions are the result of not enough of these nutrients in the soils that are farmed to produce the foods and feeds eaten. Solutions to these deficiencies are best found in eliminating the root cause of the deficiencies, i.e. too low available amounts in the soil. Thus, fertilizing soils with available forms of essential trace elements can correct the source of the problem. Doing so supplies these nutrients for both livestock and humans dependent on these soils to produce the products eaten. It is a food systems approach and benefits all organisms dependent on the system.

Zinc-deficient soils are also widespread globally as is zinc deficiencies in animals and humans. Here too, the use of zinc fertilizers applied in sufficient amounts at the right time to soils or to plant leaves could contribute greatly to helping eliminate zinc deficiencies from these regions. Unfortunately, correcting deficiencies of highly insoluble trace elements such as iron is difficult to do using inexpensive inorganic fertilizer salts because of their limited solubility. Further, applying excessive amounts of any essential trace element can lead to toxicities to the crops. Therefore, using a fertilizer approach to reduce trace element deficiencies has to be done with knowledge of how to most efficiently apply the fertilizer and how to avoid applying excessive amounts.

Using agricultural approaches to reduce trace element malnutrition should become a primary intervention strategy for the world because deficiencies of these nutrients are always linked to dysfunctional food systems that are dependent on agricultural systems that do not meet the nutritional needs of the societies they support. Correcting low soil levels of Se and I have proven to be effective in eliminating these deficiencies in humans. Importantly, many agriculture tools can be used to improve the nutrition and health of everyone and these tools should be integrated into more commonly used strategies, such as fortification and supplementation programs.

Keywords: Agricultural Strategies, Deficiencies, Fertilization, Food Systems, Trace Elements

How much iron deficiency anemia in people is the result of zinc deficiency in soils?

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The post war explosion in the human population put great stress on our food systems in the 1950s but the Green Revolution (1960-1980), using new high-yielding cereal varieties and NPK fertilizers, more than doubled world food production and mass starvation was avoided. Instead, there was in the 1980s and 1990s a massive rise in micronutrient deficiencies, especially iron deficiency anemia in subsistence farming systems, which are still unresolved today. It appears that the Green Revolution emphasis on cereal production at the expense of pulses and other nutrient-rich foods is the cause, and new food systems capable of addressing all human nutritional needs are being developed, a multi-factor challenge. Recent molecular physiology of the human gut sheds new light on this problem and indicates that zinc deficiency may be the most fundamental change in these food systems and other deficiencies may be aggravated by low zinc status. Dealing with the complex nutritional requirements of new and effective food systems for the future is demanding and among other resources, new analytical capability will be required to support plant breeders and agronomists in the field.

Keywords: Zinc, Iron, Deficiency, Anaemia

Efficiency of different fertilizer application on Fe and Zn accumulation and bioavailability in rice and pakchoi

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Rice (*Oryza sativa* L.) is a poor source of minerals, especially iron (Fe) and zinc (Zn). Polished rice contains an average of only 2 mg kg⁻¹ Fe and 12 mg kg⁻¹ Zn (target 14 Fe mg kg⁻¹). Approx 24% of all Chinese children suffer from a serious anemia, while over 50% show a sub-clinical Zn deficiency. We examined the effects of spraying foliar Fe and Zn containing solutions on Fe and Zn accumulation in rice grains. In Longyou County of Zhejiang Province in 2008, iron concentration in brown and polished rice were increased by 14.47% and 15.08% after spraying foliar Fe (II)-AA fertilizer while iron concentration of different rice varieties increased differently. The in brown and polished rice of mutant “Nipponbare” Fe was increased by 29.62% and 25.91%. In Shaoxing County of Zhejiang Province (2009), nicotinamide added to the Fe solutions accelerated Fe accumulation in rice grains. The Fe concentration was increased by 24% when 1% nicotinamide was added to the foliar Fe solutions. Zn accumulation was increased by 16.0% when 0.5% ZnSO₄·7H₂O added to the sprays with no negative effects on Fe accumulation. Also in Shaoxing County, spraying new zinc fertilizer OMEX-I-Zn and OMEX-II-Zn increased Zinc concentration in brown rice by 14.01- 19.99% and 33.17-43.62% in 2008 and 2009. A Caco-2 cell culture model was used to investigate the effects of amino acids on iron bioavailability of Pakchoi (*Brassica chinensis* L.), Amino acids could improve soluble Fe content in the shoot. 20% replacement with Glu treatment got the highest soluble Fe content, followed by Met, Arg, Gln, Asp, and ammonium compared with the nitrate control, which was increased by 76%, 71%, 47% 30%, 10% and 10%,. Sulphur-containing amino acids such as the Asp treatment got the highest iron ferritin content. However, there was a negative correlation between soluble Fe content and the Caco-2 cell ferritin formation and it seemed to be necessary to add ascorbic acid in order to increase ferritin formation above baseline.

Keywords: Rice, Iron, Zinc, Biofortification, Bioavailability, Nicotinamide

Plant-based biofortification from phytoremediation to selenium-enriched agricultural products

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Selenium has a greatly uneven distribution in the world. For example, there are Se-deficient places with the Keshan disease whilst by contrast, in other places of China the levels of Se concentration are toxic to humans and animals. Se accumulation and distribution in plants varies among species, and as a function of chemical forms and concentrations of Se supplied.. One option is to add Se-containing plants to soils in Se-deficient areas as a source of bio-organic fertilizer supporting forage crops. Proper amounts of this bio-organic fertilizer can improve the condition of Se deficiency in the local soil to provide crops with Se. These will improve the dietary intake of Se of the local animals and people. Secondly Se is an essential trace element for proper nutrition and sound health in humans and animals. In this regard, one solution is to use seleniferous plant materials as forage for animals. As a result, Se-enriched plants are able to play an important role in improving the Se dietary intake of animals in the Se-deficient areas. In addition, plants used for the phytoremediation of Se, may be used to generate heat by the combustion of dried plant material and bioenergy by fermentation to methane and/or ethanol. A large variety of chemical compounds (e.g., oil, sugars, fatty acids, proteins, pharmacological substances, and vitamins) are naturally produced by plants and may be useful as by-products of the phytoremediation process. Se in soil, plants, crops, and animal products can be utilized for the biofortification need. The concept of biofortification, inherently stemming from the concept of green chemistry, embodies the transfer and delivery of high Se resources. From being toxic inorganic or organic Se compounds to some specific local residents, to the regions that are deficient in Se to increase the Se content in higher plants, animals, food, and ultimately to enhance human Se intake. In order to ensure the concentration and speciation of Se in agricultural products to be within the safe or recommended amounts of human Se intake through biofortification, additional field studies should be conducted in the future.

Keywords: Biofortification, Phytoremediation, Selenium-Enriched

***Adenocaulon himalaicum*, a novel selenium-hyperaccumulating plant in Enshi, Hubei, China**

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Adenocaulon himalaicum, a species of the genus *Adenocaulon* H., was collected in Enshi, Hubei, China. The underneath soils of the plants were also sampled. The results showed that the total Se in soils varied from 8935 to 99090 ug/kg with a mean of 42238 ug/kg, in which the un-bioavailable Se, such as HCl-soluble fraction and remain fraction, were predominant with a proportion of 82 - 83 %. The bioavailable Se-fraction (including water-soluble fraction and exchangeable fraction) and the transferable Se-fraction (organic-bind fraction) in soils were 2 - 5 % and 13 - 15 %, respectively. The total Se in plants varied from 298706 to 2277757 ug/kg with a mean of 760433 ug/kg in leaf, from 267735 to 1611849 ug/kg with a mean of 580480 ug/kg in stem, and from 227208 to 8391123 ug/kg with a mean of 1743851 ug/kg in root. Overall, the Se contents in different organs of plants were as follows: root > leaf > stem. Furthermore, the SeCys2 fraction was predominant in leaf part with a proportion of 70 - 98 %, and the SeMeCys fraction and the SeMet fraction in it were 7 - 19 % and 3 - 11%, respectively, which is quite different with common plants dominated by SeMet fraction. Similar pattern occurred in the stem part and the root part. It should be pointed out that the SeCys2 fraction would be more when the underneath soil had higher content of Se. To evaluate the accumulation of Se in *Adenocaulon himalaicum*, the accumulation coefficient (AC) was employed between organs of plants and their corresponding underneath soils. For leaf part, the AC_L ranged from 6.13 - 66.47 with a mean of 29.25 compared with the total Se content in soil, from 34.10 - 136.75 with a mean of 97.76 compared with the sum of bioavailable and transferable Se content in soil, and from 187.56 - 687.03 with a mean of 463.01 compared with the bioavailable Se content in soil. For stem part, the corresponding AC_S ranged from 6.86 - 39.15 with a mean of 17.11, from 38.17 - 96.79 with a mean of 73.35, and from 225.39 - 616.65 with a mean of 394.71, respectively. For root part, the corresponding AC_R ranged from 6.17 - 84.68 with a mean of 26.13, from 34.33 - 503.79 with a mean of 118.41, and from 63.54 - 2230.50 with a mean of 567.07, respectively. Overall, the AC was as follows: root > leaf > stem.

Keyword: Adenocaulon Himalaicum, Selenium-hyperaccumulating Plant, SeCys2, Enshi

Leaching characteristics and co-combustion characteristics of a Chinese high-selenium stone coal

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The leaching behaviour and co-combustion characteristic of a Chinese high-selenium stone coal was investigated in this study. The effects of different pH value, liquid-solid ratio and leaching time on selenium leaching characteristics were measured by ICP-AES. The leaching-out rate of selenium decreased from 2.25% to 0.75% as the increased pH value from 2.3 to 3.5. The leaching-out rates were approximately 0.75-0.80% and shown no significant different between the ranges of 3.5-9.37 of pH value. The increasing the liquid-solid ratio and the leaching time could improve the leaching-out rates of selenium. The co-combustion characteristics of blend stone coal with bituminous coal were carried out by numerical simulation. The distributions of velocity, temperature and heat load in furnace were investigated to evaluate the utilization feasibility of high-selenium stone coal in power plants.

Keyword: Selenium, Stone Coal, Leaching Experiment, co-Combustion Characteristics

Symposium 5(E)

Title: Trace Elements on Cardiovascular Function and
Disease

Sponsor: TEMA-14

Location: Conference Room 4

Copper in cardiovascular pathogenesis and regeneration

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Vascularization is vital in the regeneration of ischemic myocardium. Depressed activity of hypoxia-inducible factor (HIF)-1 α in myocardial infarction, although it is activated in the early response to ischemia, is a key factor for the refractory response of vascular regeneration. Copper is required for HIF-1 α activation and under ischemic conditions copper efflux from the heart occurs. In a study examining the efficacy of localized copper supplementation on vascular regeneration in ischemic myocardium, we have produced myocardial ischemic injury in a rabbit model. After the establishment of myocardial infarction, an ultrasound targeted microbubble destruction copper delivery specifically to the infarcted myocardial tissue was developed for myocardial regenerative therapy. This treatment significantly increased the density of blood vessels, and importantly, caused regeneration of the infarct area, as determined by increased myocardial cells, reduction in myocardial fibrosis, improved cardiac contractility, and increased long-term survival. The expression of vascular endothelial growth factor was significantly increased and the activation of HIF-1 α . In addition, stromal cell-derived factor-1 was overexpressed in the copper-treated myocardium, along with increased accumulation of endothelial progenitor and hemotoprogenitor cells. Further analysis revealed that copper treatment increased bone marrow derived mesenchymal stem cell homing to the infarcted myocardium. Therefore, a localized copper supplementation by an ultrasound targeted microbubble destruction delivery mechanism significantly promotes the recovery of myocardial infarction and this recovery is likely related to copper activation of HIF-1 α , which promotes vascular regeneration and homing of progenitor cells.

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Keywords: Copper, Heart Disease, Vascular Regeneration

Modeling human pancreatic disease in thioredoxin reductase knockout mice

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Thioredoxin reductases (TXNRDs) are selenoproteins and, together with thioredoxins and NADPH, constitute the thioredoxin-system, which is a ubiquitous thiol-dependent oxidoreductase system controlling cellular redox balance, and thus cell fate. Altered redox homeostasis has been linked to various diseases, such as cancer, metabolic and cardiovascular disease. The role of the nutritional selenium status in this context is under debate. We studied the influence of nutritive selenium on pancreatic carcinogenesis by use of two genetic mouse models based on p53+/? and TGF- α or an activated KRas, both leading to invasive pancreatic carcinoma. The nutritive selenium status did not alter pancreatic carcinoma incidence or latency but influenced cellular differentiation and unraveled a novel type of precancerous lesion pointing towards an alternative cellular origin of ductal adenocarcinoma. Se depletion might not be the ideal means of influencing thioredoxin reductase expression, because expression is rather robust under selenium deficiency compared to other selenoproteins. When we measured the impact of Se depletion and of genetic haplo-insufficiency on TXNRD enzyme activity, we found that haploid insufficiency in Txnrd1+/- and Txnrd2+/- mice decreased TXNRD activity to an extent that can be further decreased by Se deficiency, but not to levels below those observed for Se depletion alone. Ubiquitous homozygous knockout (ko) is the ultimate means to eliminate gene expression. Ko of cytosolic (Txnrd1) and mitochondrial thioredoxin reductase (Txnrd2) turned out to be embryonic lethal. For further studies focusing on the role of thioredoxin reductases in pancreas diseases we established mice where the thioredoxin reductase alleles can be inactivated in an organ-specific fashion. While inactivation of Txnrd1 in the exocrine pancreas induces a mild metabolic phenotype, pancreas-specific Txnrd2 ko induces fibrotic remodeling and pancreatitis. We are about to establish more genetic tools using the recently described Dre/rox recombination systems. Allowing the simultaneous activation and deactivation of thioredoxin reductases in the pancreas the system will help us to discriminate chronic and acute effects.

Keywords: Thioredoxin Reductase, Pancreas, Cancer

Zinc status related to vascular function, inflammation and atherosclerosis

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Atherosclerosis is initiated and promoted by vascular inflammation and oxidative stress. We therefore hypothesised that zinc may influence the pathogenesis of atherosclerosis (Beattie & Kwun, Br. J. Nutr. 2004, 91:177-181). While zinc status is an obvious candidate to influence atherogenesis, it has received scant attention. This is partly because epidemiological evidence showing a relationship between status and cardiovascular disease is lacking, due partly to an absence of reliable zinc status biomarkers. In addition, rats and mice are not good models of atherosclerosis, and appropriately large, long-term and well-controlled studies with suitable animal models and zinc intake levels are also lacking. We have therefore utilised vascular cell cultures, a mutant mouse model of atherosclerosis, and a human intervention study with zinc to evaluate the significance of zinc intake and status in maintaining vascular health. In a preliminary 13-week study with apoE-null mice, which develop atherosclerosis, we found that more plaque was present in aorta of animals consuming a low zinc (3 mg/kg), compared with an adequate zinc (35 mg/kg) high fat diet. More recently in a 25-week study, we have demonstrated that aortas from apoE-null mice contain significantly more plaque, which is more highly calcified, than Zn-adequate controls, even at dietary zinc levels of 8 mg Zn/kg. Significantly elevated circulating IL-1 β , IL-6 and VCAM-1 at 3 mg Zn/kg diet compared with the zinc adequate diet was associated with raised plasma total cholesterol and total protein levels, suggesting that low zinc status promotes atherogenesis through increased circulating levels of proatherogenic lipoprotein particles. Vascular smooth muscle cell (VSMC) phenotype and function is influenced by inflammatory cytokines such as IL-1 β and we previously noted that markers of VSMC differentiation, such as sm22 α , were significantly affected in Zn-deficient rats. We are therefore investigating the direct and indirect influences of zinc and inflammation on rat VSMCs in primary culture. Our work supports a role for adequate zinc nutrition in protecting against inflammation and atherogenesis. This work was supported by the Scottish Government Rural and Environment Science and Analytical Services and also by the national Research Foundation of Korea (Grant No. NRF 220-2008-1-F00013)

Keywords: Zinc Deficiency, Atherosclerosis, Inflammation

Role of zinc in osteogenic and vascular calcification

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One of the major characteristic sign of zinc deficiency is retarded skeletal growth, which implies zinc involvement for osteogenic action and bone formation. Our previous studies using osteoblastic MC3T3-E1 cells showed that zinc deficiency decreased osteogenic activity by decreasing extracellular matrix calcification mainly through inhibition of ALP action (Mol Nutr & Food Res, 2011, accepted) and by decreasing osteoblast differentiation marker gene transcription through reduced and delayed bone transcription factor Runx2 expression (Bone, 2010;46:732-41). In bone tissue, zinc can be a stimulator for bone formation which includes bone matrix calcification. Meanwhile, there is emerging evidence that zinc can protect against vascular damage and therefore may decrease the incidence of atherosclerotic plaques and calcification. While mineralization is a normal physiological process in bone tissue, anywhere else in the body, like the blood vessels, it is a pathological process. Thus, it is of interest to clarify how zinc can differentially modulate calcification in these two different tissues. Our recent study using rat aortic smooth muscle cell line (A7r5) and rat primary vascular smooth muscle cells (pVSMC) showed that zinc deficiency increased vascular smooth muscle cell calcification and this calcification is parallel with the apoptotic pattern, rather than osteogenic calcification. Under atherosclerotic conditions in mice (ApoE null mouse), zinc deficiency promotes aorta Ca and P deposition (vascular calcification), while it decreases Ca and P contents in femur (bone calcification). The in vitro and in vivo findings from these two studies of osteoblast and vascular smooth muscle cell models suggest that zinc may have a reciprocal role for the mechanism of calcification in bone (hard tissue) and blood vessel (soft tissue). It is suggested that zinc can have a significant influence on therapeutic strategies aimed for osteoporosis and atherosclerosis, both of which involve calcification.

Keywords: Zinc, Bone Formation, Vascular Calcification

Selenium suppressed oxidative stress-induced vascular smooth muscle cells calcification via regulation of the ERK signaling pathway

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Atherosclerosis is frequently associated with vascular calcification. Increasing evidences underline that the essential micronutrient selenium may prevent atherosclerosis, but the role of selenium in vascular calcification remains unknown. In this study, we assessed the effect of sodium selenite (Na_2SeO_3) on oxidative stress-enhanced vascular smooth muscle cells (VSMCs) calcification and examined the involvement of extracellular signal-regulated kinase (ERK) signaling pathway. Oxidative stress was induced by treating calcifying VSMCs with H_2O_2 or xanthine/xanthine oxidase (X/XO), confirmed by an increase in intracellular reactive oxygen species production and malondialdehyde levels, and the decrease of total protein thiol content and the activity of antioxidant selenoenzyme glutathione peroxidases. These effects of H_2O_2 or X/XO were suppressed by pretreatment of the cells with selenite for 24 h. Hydrogen peroxide or X/XO enhanced vascular calcification by inducing osteoblastic differentiation of VSMCs, as shown by up-regulating the mRNA expression of type I collagen, osteocalcin, and Runx2, a key transcription factor for osteoblastic differentiation, increasing alkaline phosphatase activity and calcium deposition. In addition, H_2O_2 or X/XO activated the phosphorylation of ERK1/2 and inhibition of activated ERK signaling by MEK inhibitor PD98059 blocked the effect of H_2O_2 or X/XO on osteoblastic differentiation of VSMCs. Selenite pretreatment significantly attenuated H_2O_2 or X/XO-induced osteoblastic differentiation and ERK activation. These results suggested that selenite suppressed oxidative stress-enhanced osteoblastic differentiation and calcification of VSMCs through inhibiting ERK activation, indicating a potential preventive role for selenium in vascular calcification.

Keywords: Selenium, Vascular Calcification, Oxidative Stress

Zinc deficiency promotes calcification in rat vascular smooth muscle cells independent of alkaline phosphatase

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Zn deficiency has long been associated with retarded skeletal growth, and more recently in the development of cardiovascular diseases, both of which involve aberrant mineralization. ALP is a key regulator of osteogenic calcification and acts by modulating local inorganic phosphate (Pi) concentrations by hydrolyzing pyrophosphate. Vascular smooth muscle cells (VSMCs) generally do not express alkaline phosphatase (ALP) but its presence has been reported on calcified VSMCs. However, under Zn deficiency, our initial findings showed undetectable level of ALP activity at calcifying conditions. We therefore hypothesized that Zn deficiency-induced calcification may not be initiated by ALP in VSMCs. To test this hypothesis, we cultured rat aortic A7r5 VSMCs using β -glycerophosphate (β -GP, ALP substrate, 0-15 mM) or Na phosphate (non-ALP substrate, 0-7 mM) under Zn deficiency (1 μ M) as sources of Pi for up to 22 days. Normal growth medium and Zn adequate level (15 μ M) were used as controls. Ca and P accumulation was examined by Alizarin red and von Kossa staining, respectively. We also measured ALP activity by staining the products of ALP activity in cellular matrix. Our findings demonstrate that under Zn deficiency, P accumulation increased with increasing Na phosphate concentration (3-7 mM) but not with β -GP treatment which requires ALP activity to generate Pi. Ca deposition also increased with Na phosphate in a dose-dependent manner, in contrast, β -GP did not affect Ca deposition. ALP activity was neither affected by β -GP nor by Na phosphate concentrations. In addition, Zn status did not affect ALP activity in VSMCs. Taken together, our results illustrate that Zn deficiency-induced calcification in VSMCs is not initiated by ALP action and other Zn-sensitive mechanisms may be involved.

Keywords: Zinc, Alkaline Phosphatase, Vascular Calcification

Vascular smooth muscle protein responses and gene expression in zinc deficiency

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Our recent research suggests that zinc status influences vascular health. Zinc has antioxidant and anti-inflammatory properties in biological systems. In rat aorta proteomic studies, we have found that markers of vascular smooth muscle cell (VSMC) differentiation responded to zinc deficiency. We therefore hypothesised that increased inflammation in low zinc status impacts on VSMC phenotype. Our objective was to define how VSMCs are targeted and affected. Male rats were given diets that were either Acutely Zinc Deficient (AZD, <1 Zn mg/kg), Zinc Deficient (ZD, 3 Zn mg/kg) or Zinc Adequate (ZA, 35 mg Zn/kg). Two Pair-fed groups were used to control for reduced food intake in AZD and ZD rats and food intake and body weight changes were monitored. After 2 weeks, significant decreases ($p < 0.05$) in food intake and body weight were found in AZD group compared to the ZA group. Plasma zinc decreased significantly in AZD and ZD compared to their respective pair fed groups and also the ZA group. Transgelin 1 (sm22 α) and calponin 3 were analysed as markers of VSMC differentiation in aorta. By Western blotting we observed 3 main isoforms for transgelin 1 and the major band decreased significantly in the AZD group compared to that in the pair fed control and ZA groups. This indicates that VSMCs may be changing from a differentiated to a proliferative phenotype. Analysis of proliferation markers (e.g. PCNA) are in progress. Furthermore, rat primary VSMCs were pre-incubated in low zinc DMEM until 95+% confluence, and the medium was then changed to DMEM containing plasma from either Pair-fed, ZA, and AZD or ZD, with or without Zn added back. After 24 hours, cell viability was significantly reduced in AZD plasma medium but not in its counterpart with Zn added back, suggesting that Zn protects VSMC from potential cytotoxins within the AZD plasma. Affected pathways are being studied using microarray. *This work was funded by the National Research Foundation of Korea (Grant No. KRF-2008-220-F00013) and the Scottish Executive Rural and Environment Research and Analysis Directorate.*

Keywords: Zinc, VSMC, Differentiation

Symposium 6(F)

Title: Trace Elements on Brain Function and Neural
Disease

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The role of zinc in neurotransmission

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Centre de recherche Université Laval Robert Giffard

We have studied the mechanism by which vesicular zinc regulates synaptic transmission in the CNS. We tested the possibility that vesicular zinc acts on presynaptic release mechanisms. This hypothesis is clearly supported by our data demonstrating that vesicular zinc has a major role in defining calcium sensitivity of release in a subgroup of vesicles during increased synaptic activity. Broader implication of our work lies within the fact that our findings challenge the common assumption that glutamatergic vesicles in individual terminals have identical vesicular content and molecular composition. We show not only that heterogeneity among vesicles exists, but also how diverse vesicle pools are generated and what the functional implications of this diversity are. We also tested the possibility that presynaptic zinc could alter postsynaptic signaling. We used the membrane-impermeable zinc chelator CaEDTA to determine if synaptically released zinc has any influence on postsynaptic calcium signals. Our data show that postsynaptic calcium signals measured in CA3 pyramidal cells are not sensitive to the presence of this zinc chelator. Similar results were obtained using ZnT3 knock-out animals. Our data indicate that vesicular zinc in hippocampal mossy fibers has no influence on the amplitude of postsynaptic calcium signals in CA3 pyramidal cells. Our data suggest that vesicular zinc plays a role in the regulation of presynaptic release dynamics, while postsynaptic calcium signals are not affected by the presence of zinc in the presynaptic terminal.

Keywords: Synaptic Transmission, Synaptic Plasticity, Neurotransmitter Release

Cu, Zn and Fe in Alzheimer's disease: from bench to clinic

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The brain houses high concentrations of Zn, Cu and Fe, used for specialized neurochemistry like the regulation of neurotransmission and heme synthesis. Neuronal flux of these metal ions is extreme. Zn and Cu are released during glutamatergic neurotransmission, and their reuptake, which is normally very rapid fatigues with age. This increases the average concentration of extracellular Zn and Cu (a phenomenon called "metallostasis") leading to A β aggregation and downstream pathologies. Intraneuronal cortical Fe metallostasis is a feature of aging, and is exaggerated in AD where Fe is trapped by tangles. We hypothesized that the main proteins implicated in the pathology of AD are in proximity to these metals because they function to regulate aspects of neuronal metal homeostasis. The major results to date show that 1. APP is the neuronal ferroxidase partner of ferroportin and is needed for Fe efflux. It is inhibited by Zn, which transfers from amyloid collections in AD tissue. 2. In mouse models, PBT2, a Zn/Cu ionophore that improves cognitive function within 12 weeks in AD patients, reverses metallostasis and restores neuronal Fe homeostasis by preventing Zn-Abeta complexes from inhibiting APP ferroxidase activity. Recapitulating the findings in AD patients, PBT2 treatment improves memory function in APP transgenic mice within days of treatment. 3. Tau knockout mice accumulate Fe in the cortex and nigra, causing neuronal loss, parkinsonism, and memory loss with advancing age. The nigral pathology and Parkinson phenotype is reversed with Fe-chelator treatment. APP trafficking defects caused by tau loss prevent it from being able to reach ferroportin. 4. Loss of Zn flux in the glutamatergic synapse causes accelerated age-dependent cognitive decline in ZnT3 ko mice, a phenocopy of AD. 5. Presenilins 1 and 2 play major roles in the uptake and turnover of Zn and Cu. The SOD1 activation pathway is sensitive to PS loss. Metallostasis may be the upstream factor that leads to proteostasis in AD. Major proteins implicated in AD pathogenesis are important components of metal trafficking, so that their failure may cause metallostasis. Metallostasis is an upstream target for new pharmacological approaches, and PBT2 is a promising potential therapeutic that advances to further clinical testing.

Keywords: Alzheimer's disease, Zn, Fe

Role of the trace element selenium in brain development and function

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Proteins containing the rare amino acid selenocysteine (Sec) are called selenoproteins. Sec is incorporated into proteins co-translationally, and is encoded by UGA codons. Hence, Sec is the 21st amino acid in mammals. A dedicated metabolic pathway consisting of Sec biosynthetic enzymes and trans-acting factors needed to re-code UGA has recently been delineated. Among selenoenzymes are glutathione peroxidases (GPx), thioredoxin reductases (TrxR), and iodothyronine deiodinases (Dio). Selenoprotein P (SePP) plays a central role in Se transport into target proteins. We have inactivated SePP in mice and observed reduction in selenoprotein expression in the brain and associated, Se-responsive neurological phenotypes including seizures and ataxia. In order to define (i) Se target cells in the brain, (ii) critical selenoproteins in the brain, and (iii) critical selenoprotein-dependent processes, we have specifically inactivated tRNA^{[Ser]Sec} in neurons. Cerebral expression of selenoproteins was significantly diminished in the mutants and histological analysis revealed progressive neurodegeneration. Developing interneurons specifically failed to express parvalbumin (PV) in the mutants. Electrophysiological recordings supported spontaneous epileptiform activity *in vitro*, in accordance with observation of seizures in mice. We then analyzed animals with neuron-specific inactivation of *Gpx4* and observed a similar phenotype with failure of PV interneuron development. Mice expressing a hypomorphic allele of tRNA^{[Ser]Sec}, *Trsp^{AE}*, likewise display reduced PV interneuron numbers and a phenotype similar to *Sepp^{-/-}* mice. Recently, two syndromes have been described in humans involving inherited defects of selenoprotein biosynthetic factors. Mutations in *SECISBP2* lead to a milder, but pleiotropic phenotype involving the thyroid hormone axis and, in more severe cases, neurological and neuromuscular defects. Mutations in *SEPSECS* lead to *Progressive Cerebello Cerebral Atrophy*, a severe neurodegenerative disorder in infants. Reports on the alleged responsiveness to Se supplementation of intractable childhood seizures associated with low plasma Se may, in retrospect, have involved children with inherited disorders of selenoprotein biosynthetic enzymes.

Keywords: Se, Gpx4, SePP

Selenoprotein-protein interactions in human brain indicate their possible roles in Alzheimer's disease

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Selenium has been reported to prevent cognitive impairment and Alzheimer's disease (AD), but its mechanism remains to be clarified. Study on the interaction between selenoproteins in human brain will help understanding of the role of selenium in the onset and progression of AD. Human selenoprotein genes including SelR, SelM, and SelP were cloned, site-directedly mutated and used to screen human fetal brain cDNA library by the yeast two-hybrid system. Four pairs of selenoprotein-protein interaction were found, including SelR and clusterin (CLU), SelM and cytochrome c oxidase (COX6C), SelM and galectin-1 (Gal-1), SelP and tubulin (TUBA1A). The acquired selenoprotein-protein interactions were verified by fluorescence resonance energy transfer (FRET), coimmuno-precipitation (co-IP), or GST pull-down assay. Co-IP results revealed that the central region of CLU, spanning amino acids 315-381 and containing a dynamic, molten globule domain with an amphipathic α -helix, is required for binding to SelR. This interaction is very strong that site-directed mutation of the Cys residues in SelR cannot prevent the interaction. As gene mutation in CLU is closely associated with AD, the interaction between SelR and CLU in human brain indicates that SelR may mediate the onset and progression of AD through CLU. Based on the interactions between SelM and COX6C, SelM and Gal-1, further study was performed on the relationship between SelM and COX6C activity. N2a cells treated with 0.1-0.2 $\mu\text{mol/L}$ Na_2SeO_3 were found to have significantly higher cell livability and COX activity than the control. Cells transfected with SelM mutant and overexpressing this protein had higher COX activity than the control. In addition, Na_2SeO_3 could increase the expression of full-length SelM and decrease the expression of truncated SelM. Full-length SelM had stronger antioxidative function than SelM mutant, whereas the truncated SelM had an adverse effect. Transfection of SelM or its mutant into the cells significantly decreased the aggregation rate of $\text{A}\beta$ and recovered the mitochondria from intumescent to normal state. Those results imply that SelM plays an important role in preventing AD in its early stage. *This project is financially supported by the National Natural Science Foundation of China (No. 31070731, 30901182).*

Keywords: Selenoprotein R, Selenoprotein M, Alzheimer's disease

Involvement of metal transporters, ZnTs and DMT1, in Alzheimer's disease

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Pathological accumulation of β -amyloid peptide ($A\beta$) is one of the pathological features in Alzheimer's disease (AD). Bivalent metals such as iron, copper, and zinc can initiate the deposition of $A\beta$ and lead to the formation of senile plaques. However, the underlying mechanisms are obscure. With immunofluorescence and confocal microscopy, we found that six members of the zinc transporter (ZnT) family, ZnT1, 3, 4, 5, 6, 7, and two isoforms of the divalent metal transporter 1 (DMT1), DMT1-IRE and -nonIRE, were extensively present in the $A\beta$ -positive plaques of postmortem AD brain. Using the APP/PS1 transgenic mouse model, we found that the protein levels of all the ZnTs and DMT1 tested were significantly increased in the cortex and hippocampus compared with wild type-control. Zinc-specific immersion autometallography (AMG) was performed to detect the distribution of zinc ions in the human and transgenic mouse brain. The density of silver enhanced zinc-sulphur nanoparticles was much higher in the plaques than in the surrounding zinc enriched terminals. Thus bivalent metal transporters, ZnTs and DMT1, may be involved in plaque formation in AD brain. To verify whether DMT1 might be involved in APP processing and $A\beta$ secretion, a human neuroblastoma SH-SY5Y cell line stably overexpressing human APP Swedish mutation (APP^{sw}) was used as an in vitro model. Both DMT1-IRE and -nonIRE were mainly distributed in a punctate pattern and colocalized with $A\beta$ within the cytoplasm of APP^{sw} cells. There was a significant increase in the protein levels of both DMT1-IRE and -nonIRE following APP^{sw} transfection. Importantly, silencing of endogenous DMT1 by RNA interference, which reduced bivalent ion influx, led to reductions of APP mRNA and protein expression. Further, silencing of DMT1 significantly reduced $A\beta$ 1-42 level in the conditioned medium of APP^{sw} cells incubated with ferrous iron. Thus bivalent metal transporters, may play a critical role in ion-mediated neuropathogenesis in AD.

Keywords: Alzheimer's disease, Divalent Metal Transporter, Zinc Transporter

Role of selenium on molecular pathways of TRPM2 cation channels and Ca²⁺ signaling in neuronal cells

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Ca²⁺ signaling is important for developing epilepsy and pain. The Ca²⁺-permeable melastatin related transient receptor potential 2 (TRPM2) channels can be gated either by ADP-ribose (ADPR) in concert with Ca²⁺ or by hydrogen peroxide (H₂O₂), an experimental model for oxidative stress. Since the mechanisms that lead to TRPM2 channel activation/inhibition in response to oxidative stress, glutathione (GSH) depletion, selenium supplementation in neuronal cells are not understood, I summarized our findings and important recent advances in the understanding of Ca²⁺ influx via TRPM2 channels in dorsal root ganglion (DRG), PC12 neurons and epilepsy. GSH is the most abundant thiol antioxidant in mammalian cells and maintains thiol redox in the cells. Selenium dependent glutathione peroxidase (GSH-Px) enzyme uses GSH as substrate. GSH depletion has been implicated in the neurobiology of sensory neuron. In a recent study we observed activation of TRPM2 channels in DRG neurons by intracellular GSH depletion through buthionine sulfoximine incubation. H₂O₂-induced TRPM2 channels currents and Ca²⁺ signaling were modulated in DRG neurons by selenium. In recent studies we also observed protective effects of selenium with epileptic drug topiramate on Ca²⁺ signaling, electroencephalography records, GSH-Px and GSH values in PC12 neuronal cells and rat brain. In conclusion, selenium and glutathione seem to important components on regulation of Ca²⁺ signaling and TRPM2 channels currents in DRG neurons and epilepsy pathogenesis. It seems to that the exact mechanisms between selenium and TRPM2 channels inhibition in neuronal cells still remains to be determined.

Keywords: Selenium, Dorsal Root Ganglion Neurons, TRPM2 Cation Channels

Putative pathological mechanism of neurodegenerative disease Friedreich ataxia, caused by frataxin deficiency

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Friedreich ataxia (FRDA) is an autosomal recessive neurodegenerative disease caused by reduced expression levels of the frataxin gene (FXN) due to expansion of triplet nucleotide GAA repeats in the first intron of frataxin. The important roles for frataxin were played in mitochondrial iron storage, regulation of intracellular iron trafficking, iron-sulfur (Fe-S) cluster and heme biogenesis, removal of reactive oxygen species, and reactivation of the labile Fe-S cluster of mitochondrial aconitase. The central and peripheral nervous systems and heart are among the most severely affected tissues, and more than half of those afflicted eventually succumb to cardiac-related complications. However, mitochondria-demanding tissues, like kidney and liver, are not affected, although the level of FXN in these tissues is high and mitochondrial function is active. We tried to address the nervous systems and heart-specific mechanism how FXN deficiency raises FRDA disease in these tissues. Our recent work revealed that expression of two novel transcripts of FXN existed in specific tissues such as cerebellum and heart, respectively. NCBI database and other bioinformatic database support the existence of the transcripts in those tissues. Therefore, we put forward a hypothesis that tissue-specific transcripts may translate into new isoforms and the tissue specific lesion occurs if their expression is in imbalance. Functional assay showed that each isoform could interact with the core proteins including ISCS, ISD11, and ISCU to form a four-component complex, which can promote Fe-S assembly in vitro. Expression of these isoforms in mammalian cell lines showed that one of the isoforms, heart-specific, can enhance the mitochondrial and cytosolic aconitase activities significantly in any cell types even though the localization of the isoform is cytosolic. Another two isoforms showed very similar effects on iron-sulfur cluster biogenesis to the canonical one. The putative counterparts of mouse Fxn were observed in mouse tissues. The complexity of frataxin expression observed here provides mechanistic insights into how low expression levels of FXN causes FRDA disease with tissue-specific pathology.

Keywords: Friedreich Ataxia, Frataxin, Tissue-specific Isoform

EGCG Protects against 6-OHDA induced neurotoxicity in a cell culture model

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Parkinson's disease (PD) is a progressive neurodegenerative disease causing severe dopamine depletion in the striatum which induces clinical signs such as tremor, rigidity, akinesia, immobility and frequent falls. Disruption of iron metabolism may be associated with PD, resulting further damage through iron-induced oxidative stress. Our objective was to test the protective effect of (-)-epigallocatechin-3-gallate (EGCG) against 6-hydroxydopamine (6-OHDA) induced neurotoxicity and to understand whether the protective effect was by regulating iron homeostasis in N27 cells. Protection of EGCG from 6-OHDA neurotoxicity was assessed by cell viability (MTT), cell death (SYTOX Green) and cell apoptosis (Caspase-3 activity) assays. Additionally, we also performed primary neuron assay to test the protective effect of EGCG on neurotoxicity. To determine whether EGCG exerted its protective effect by regulating iron associated genes, we performed real-time PCR to quantify mRNA levels. In the normal and iron excess condition (100 μ M Fe), pretreated N27 cell with 100 μ M EGCG for 2h showed significant protection against 6-OHDA induced neurotoxicity. The mRNA expressions of divalent metal transporter-1 (DMT1+IRE), hepcidin, transferrin receptor-2 (TfR2), H-ferritin were increased and ferroportin-1 (FP1) was decreased suggesting that iron accumulation results with 6-OHDA (25 μ M for 24h) administration. However, EGCG exerted its protective effect by reversing the effect of 6-OHDA by decreasing DMT1+IRE (130%, $p < 0.0001$), hepcidin (70%, $p < 0.0001$), H-ferritin (105%, $p < 0.0001$), TfR2 (37%, $p < 0.05$), increasing FP1 (55%, $p < 0.001$) and thus, may reduce iron burden in the cells. The TH cell count (59%, $p < 0.0001$) and neurite length (91%, $p < 0.0001$) of primary neuron were also improved with EGCG compared with 6-OHDA treatment. Similar results were obtained under iron excess condition. In conclusion, our results suggest that EGCG protects against 6-OHDA induced neurotoxicity by regulating genes involved in brain iron homeostasis. However, future studies are warranted to determine whether the mechanism of neuroprotection of EGCG is by the regulation of iron homeostasis or by reducing oxidative stress.

Keywords: EGCG, Iron, 6-OHDA

Depletion of intracellular zinc induced apoptosis in cultured hippocampal neurons through RAF/MEK/ERK pathways

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An experiment was performed to observe changes of Raf-1 kinase/Mitogen-activated protein kinase ERK (MEK)/Extracellular signal-regulated kinase (ERK) signaling pathways in cultured hippocampal neurons and the correlation with neuron apoptosis induced by intracellular zinc depletion. Cultured hippocampal neurons were exposed to a cell membrane-permeant zinc chelator TPEN (2 μ M), and to TPEN plus zinc sulphate (5 μ M) for 24 h. Cultures were then processed to detect neuronal viability by the methyl thiazolyl tetrazolium (MTT) assay and apoptosis rate was observed simultaneously by flow cytometric analysis. Raf-1, pMEK, pERK1/2 and pCREB protein levels were examined by Western blot assays. Viability in TPEN-incubated neurons was notably decreased and apoptosis rate significantly increased compared with non-treated controls. Significant down-regulation of Raf/MEK/ERK signalling pathways and expression of pCREB were decreased in TPEN-treated neurons. Co-addition of zinc almost completely reversed the TPEN-induced alterations. The results demonstrated zinc modulated apoptosis and the expression of Raf/MEK/ERK at the protein levels in hippocampal neurons, which implies a possibility that intracellular zinc depletion-induced apoptosis in cultured hippocampal neurons may be relevant to the changes of Raf/MEK/ERK signaling pathway.

Keywords: Zinc Depletion, Raf/MEK/ERK, Apoptosis, Hippocampal Neurons

Zinc and adaptation of army conscripts to intensive military service

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In the present work a complex investigation of mineral status and functional state of internal troops, servicemen, and the effect of the zinc preparation, was carried out. We studied a group of 40 military men of internal troops (20 persons within 2 months (the basic group) took 40 mg of zinc a day, 20 persons didn't take a Zn (control group)). Mineral profile was estimated by hair and blood serum multielement analysis, which was made by ICP-AES/ICP-MS using instruments Optima 2000 DV and Elan 9000 (Perkin Elmer Corp., USA) in the test laboratory of ANO "Centre for Biotic Medicine" (Moscow, Russia). With the treatment Zn content was increased in both hair ($P < 0.05$) and serum ($P < 0.05$). In addition, overall shift towards normalization were observed for concentration of Ca in both hair ($P < 0.1$) and serum ($P < 0.1$), Mg ($P < 0.05$), Co ($P < 0.1$), Fe ($P < 0.1$) – in hair and Se ($P < 0.05$) – in serum. The investigation of functional state included an assessment of physical and functional state of the subjects along the course of military service, including service under exposure to combustion products. The study showed that two months after the application of Zn the number of persons with positive changes in physiological status became increased. Among functional parameters, we found an increase of relative lung capacity, chest volume, Erismann's index, heart rate (resting, after load, after breath-holding), index of functional state level. Administration of Zn had a positive effect on a variety of parameters, increased overall adaptability of the soldiers. It was also notable that the soldiers, who took the medication under study, felt the improvement in overall health. Thus, Zn is an effective corrective remedy that increases the level of functional reserves of the organism and its adaptation to the stressful conditions of military service and can be recommended for widespread use in restorative medicine as a mean for functional reserves enhancement. In this study we looked at the unique ability of Zn to provide universal sanogenetic effect, manifested in restoration of mineral homeostasis and improvement of many laboratory and clinical parameters in persons initially characterized by Zn insufficiency.

Keywords: Zinc, Adaptation, Regeneration Medicine

Symposium 7(G)

Title: Zinc intakes world wide – are we making any progress towards reducing the prevalence of zinc undernutrition?

Sponsor: TEMA-14 and IZiNCG

Location: Conference Room 1

Plasma zinc concentration as a biomarker of zinc status

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Serum (or plasma) zinc concentration (SZC) has been promoted as the best available biomarker of population risk of zinc deficiency. However, some researchers doubt whether SZC truly reflects zinc status because multiple other factors modify SZC and a clear relationship between individual SZC and physiological function is generally lacking, except in the case of severe zinc deficiency. This presentation will review recent evidence on the relationships between dietary zinc deprivation/supplementation and SZC. Also, specific factors that confound the relationship between zinc intake and SZC will be discussed.

SZC remains stable among adults consuming their habitual diet. However, SZC declines rapidly following severe dietary zinc restriction, although it responds less rapidly or non-detectably following moderate dietary restriction among previously well nourished volunteers. SZC increases in dose-dependent fashion within a few days of initiating zinc supplementation in both adults and children, regardless of the initial SZC, thereby suggesting that a positive response to supplementation should not be interpreted as evidence of pre-existing zinc deficiency. Contrary to the experience with supplementation, SZC often fails to respond to zinc fortification, possibly because of less efficient zinc absorption from mixed diets and/or insufficient levels of fortification.

SZC changes throughout the day in response to meals. SZC is highest in fasting individuals in the early morning, falls abruptly after each meal and then after several hours increases somewhat until the next meal. Specific cutoffs for low SZC have been proposed in relation to the time of day that the specimen is collected and the fasting status of the individual, as well as age and sex. Systemic infection or inflammation also lowers the SZC, so simultaneous measurement of indicators of the acute phase response is recommended.

In conclusion, SZC is a useful biomarker of zinc intake and can therefore serve as a suitable indicator of population risk of zinc deficiency. However, care must be taken to avoid major pitfalls when analyzing and interpreting SZC, namely sample (exogenous and “endogenous”) contamination, the effects of meals and time of day, and the presence of systemic inflammation.

Keywords: Zinc, Nutritional Assessment, Serum Zinc Concentration.

Dietary assessment of zinc status

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Nutridemics and IZiNCG

The inadequate intake of bioavailable forms of dietary zinc is the most likely cause of zinc deficiency globally. Despite the widespread prevalence of zinc deficiency across the developing world, there is relatively little information on the adequacy of zinc intakes in representative populations. Information on zinc intakes, and its primary food sources, would enable the identification of subpopulation groups at elevated risk of dietary zinc deficiency, and the appropriate design of food-based interventions. There are several important considerations for the application of population dietary zinc intake assessment: i) quantification of dietary zinc intakes; ii) estimation of zinc bioavailability; iii) determination of the adequacy of zinc intakes by comparison to dietary reference intakes. Zinc tends to be ubiquitously distributed in the food supply, and hence quantitative methods such as direct weighing or 24-hour recalls are recommended. The 24-hour recall method has been validated for quantifying zinc intakes in rural Africa. Several models for estimating the bioavailability of zinc, as a percent of total zinc intake, have been proposed, most of which consider only total zinc and phytate as covariates. As these models were derived from isotope tracer studies in adults and take into account total daily zinc intakes, they cannot be directly applied to children's dietary intakes. External validation of the algorithm with epidemiological data would be useful. Several sets of dietary reference intake data for zinc have been presented in the last decade. These include the WHO/FAO RNIs, the IOM (USA/Canada), and IZiNCG. Each of these has limitations for international application. The WHO/FAO estimates do not use currently accepted models for determining physiological requirements for absorbed zinc, but do present different requirement options for diets with low, moderate, or high bioavailability. While the IOM pioneered a more appropriate model for estimating physiological zinc requirements, the bioavailability of zinc was assumed to be high and suited for the North American population, but may not be appropriate for other diet types. IZiNCG applied the accepted model for estimating zinc requirements, and presented options for low and moderate zinc bioavailability diets, but it may have underestimated zinc physiological requirements. A harmonized set of dietary zinc reference intakes, suitable for international use, is needed. A comparison of clinical indicators of zinc status in adult participants of zinc depletion/repletion studies suggests that current values need to be revised.

Keyword: Zinc, Diet, Bioavailability

Evaluation of zinc status and community perceptions in Pakistan: the National Nutrition Survey 2011

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Over a third of the global population is at risk of zinc deficiency, based on population level dietary intake and prevalence of stunting. Zinc deficiency is the fifth leading risk factor for disease in the developing world and several systematic reviews of preventive and therapeutic strategies have highlighted potential benefits of zinc for growth and health outcomes in childhood. Pakistan is recognized as a country with a significant proportion of its population at risk of zinc deficiency and a previous National Nutrition Survey in 2001 identified over a third of the women and children as zinc deficient on the basis of plasma zinc. In the last decade, other than the introduction of zinc for the management of diarrhea, no large scale preventive interventions have been put in place. In order to understand the population prevalence of zinc deficiency as well as community perceptions of zinc and health, we specifically evaluated these components as part of the recently concluded National Nutrition Survey 2011. The survey was conducted on a national and provincial sampling frame weighted for urban and rural populations and targeting women of reproductive age (WRA) 15-49 years and children under 5 (U5C) 0-59 months. All seven provinces of the country were included in a two stage stratified survey. Altogether 30,000 households surveyed and 12,000 blood specimens each from WRA and U5C analyzed for a range of micronutrients using standard procedures in a CDC certified central micronutrient laboratory. Additional household level information was obtained on the community knowledge about zinc and health and potential consequences of deficiency. Preliminary findings from the survey indicate that overall nutritional status of children in Pakistan has not improved since 2001. Stunting rates range from 37-54% and between 5-9% of children are severely wasted. Among WRA 5-18% have BMI < 18.5. Preliminary findings of the overall prevalence of zinc deficiency suggest that 38% of U5C and 48% of WRA have serum zinc concentrations < 60 µg/dL). Only 7.7% of WRA were aware of any health benefits associated with zinc. The public dissemination of the project is planned for Sept 17 2011 in Islamabad and detailed findings from the survey will be shared at the Zinc seminar at the TEMA conference on Sept 21 this year.

Keywords: Zinc, Deficiency, Status, Nutrition Survey, Pakistan

Higher risk of zinc deficiency in New Zealand Pacific school children compared to their Māori and European counterparts: a New Zealand national survey

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Few multi-ethnic national surveys have examined Zn nutriture, despite its importance for optimal growth and development during childhood, in part because of the lack of consensus on appropriate indicators of zinc status. Biochemical, dietary, and functional indicator – have been recommended for assessing risk of zinc deficiency in populations and for identifying subgroups at elevated risk. We used these indicators to assess the Zn status of urban and semi-urban children 5–15 years from three ethnic groups in New Zealand (NZ) in the 2002 Children's National Nutrition Survey (CNS02) and investigated factors predisposing them to Zn deficiency. Anthropometry, serum Zn, and Zn intakes via 24-hour recalls (repeated on a sub-sample) were measured. Serum Zn was collected from a non-fasting venipuncture blood sample, and analyzed and interpreted using IZiNCG procedures. Intake distributions were adjusted for intra-subject variability, and the prevalence of usual Zn intakes estimated by the Estimated Average Requirement (EAR) cut-point method based on the Australian and NZ EARs. In a 10-month cross-sectional survey, Pacific and Māori children were over-sampled permitting ethnic-specific analyses. Anthropometric *z* scores were highest in Pacific children. Overall mean adjusted serum Zn (95th CI; $\mu\text{mol/L}$) at 11years were: M:11.9 (11.5,12.3) F:12.5(12.0,12.9) in NZ European and Other (NZE0) (*n* 395); M:11.9(11.4,12.4) F:12.0(11.4,12.5) in Māori (*n* 379); and M:11.5 (11.1,11.9) F:11.4 (11.1,11.8) in Pacific (*n* 589). Predictors of serum Zn were: age, serum selenium, and sex for NZEO; serum selenium and age for Pacific; none for Māori. Pacific children had the highest prevalence of low serum Zn (% , 95% CI) 21 (11,30), followed by Māori 16 (12,20), and NZEO 15 (9,21). Prevalence of inadequate Zn intakes, although low, reached 8% for Pacific children who had the lowest Zn intake per kg body weight. Pacific boys but not girls with low serum Zn had a lower mean height-for-age *z*-score ($P < 0.007$) than those with normal serum Zn. We conclude that the biochemical risk of Zn deficiency in Pacific children indicates a public health problem. However, a lack of concordance with the risk of dietary Zn inadequacy suggests the need for better defined cut-offs in children. *The CNS02 was funded by the NZ Ministry of Health.*

Keywords: Zinc, Deficiency, Schoolchildren, New Zealand

Assessment of zinc status in the national survey in Cameroon

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Prior to initiating a mass fortification program including zinc, this study aimed to assess zinc status and risk of zinc deficiency among Cameroonian preschool children and women of reproductive age. This was a nationally-representative, multi-stage cluster survey. We randomly selected 30 clusters in each of 3 zones (North, South, and Large Cities) and 10 households (HH) per cluster, each with a child 12-59 mo and a woman 15-49 y (n = 904 HH). IZiNCG recommendations for blood collection and processing procedures for zinc measurement were followed. The time of day of blood collection, time elapsed since previous meal, and time from blood collection to centrifugation were recorded. Plasma zinc was measured by ICP-AES, and plasma C-reactive protein (CRP) and α 1-acid-glycoprotein (AGP) were measured by ELISA. Plasma zinc concentrations were adjusted mathematically for the presence of elevated acute phase proteins (CRP > 5 mg/L and/or AGP > 1 g/L). Adjusted mean plasma zinc concentrations were 54.7 μ g/dL among children (95% CI: 53.6 – 55.8 μ g/dL, n = 812) and 53.4 μ g/dL among women (95% CI: 52.1 – 54.7 μ g/dL, n = 853). Low plasma zinc concentration was present in 69.1% of children (adjusted plasma zinc < 65 μ g/dL in AM samples and < 57 μ g/dL in PM samples) and 76.9% of women (adjusted plasma zinc < 70 μ g/dL for AM fasting samples, < 66 μ g/dL for other AM samples, < 59 μ g/dL for PM samples, and < 50 μ g/dL for pregnant women). Mean plasma zinc concentration was lower in the North than in the South and the Large Cities and was positively related to SES among both children and women. Stunted children (n = 240) had lower adjusted plasma zinc concentration than did non-stunted children (n = 507) (52.6 vs. 56.1 μ g/dL, p < 0.001). The prevalence of low plasma zinc concentration and risk of zinc deficiency are high among both women and children in Cameroon. Programs to improve zinc nutrition, including food fortification, are needed.

Keywords: Zinc, Deficiency, Africa

Expression of genes that encode zinc transport proteins suggest that zinc deficiency is not real in hemodialysis patients

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Zinc (Zn) deficiency or hipozincemy is highly prevalent in hemodialysis (HD) patients. The equilibrium of Zn in the cell is finely regulated by Zn transporters and Zn binding proteins. The input of Zn into the cytosol from extra- or intracellular space vesicles is performed by ZIP proteins. On the other hand, the Zn output from the cytosol is performed by ZnT proteins and cytoplasmic Zn distribution is performed by metallothionein (MT). The aim of this study was to determine the expression profile of genes that encode Zn transport proteins in micro-inflamed HD patients with known levels of Zn and evaluate if low plasma Zn levels reflect a real deficiency of the mineral. The expressions of ZIP1, 3, 4, 14, ZnT1 and MT (1,2) genes were measured by cDNA coming from a biobank of HD patients that had low plasma Zn (ref. value <70µg/dL) and normal plasma Zn (≥70µg/dL), also called hypozincemics (HZn) and normozincemics (NZn), respectively. Samples were collected at two points: in moment of defining the nutritional status of Zn and after 60 days of HD with 30mg of Zn replacement for HZn. The qPCR was performed using SYBR green assays. Comparisons among groups of data were done using paired t test. The plasma Zn concentration is an accepted parameter for evaluating the nutritional status of the mineral and adopted for supplementation indications. Thus, was expected in HZn, a high expression of ZIP1, 3 and 4 and decreasing MT mRNA levels to practically undetectable amounts. It was expected also after Zn supplementation a change in the ZIP4 expression, allowing us to conclude that there is no stimulus differences between HZn and NZn individuals for intestinal absorption of the mineral, which has not happened in this study. The unique gene of the ZIP family that had high expression was ZIP14 in both groups, probably because of the patients inflammation degree, since ZIP14 is regulated by IL-6. Meanwhile, the gene with the highest expression was ZNT1, whose function is to reduce the Zn cytosolic level. Its action is antagonistic to the ZIP14. Was also observed that patients who has ZIP14 higher also presents ZNT1 and MT higher and vice versa. In Conclusion, although many HD patients have low plasma Zn, the real Zn deficiency and necessity of supplementation may be questioned, since the gene expression profile showed that there was a situation of normality to excess of intracellular Zn in the studied patients.

Keyword: Zinc Deficiency, Zinc Transporters, Hemodialysis

MINTREX-Zn improves tibia zinc deposition and antioxidant status of broilers under stress with coccidiosis infection

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An experiment was conducted to evaluate the effect of supplementing an organic source of Zn (Mintrex-Zn) to a corn-soybean meal diet on broiler growth performance, tibia Zn content and bone breaking strength, oxidative status, and immune responses with or without coccidiosis challenge during a 0-42 day test period. A total of 480 day-old Arbor Acres male chicks were randomly placed into 80 cages with 6 chicks each cage. The basal diet supplemented with reagent-grade Zn sulfate at 40 mg/kg Zn served as a positive control and supplemented with Mintrex-Zn to provide 20, 40, and 60 mg/kg organic Zn as the testing diets. On Day 21, bird from half of the replicates (cages) of each dietary treatment were inoculated by gavages with 1.5×10^4 E. tenella sporulated oocysts. Results showed that no difference in mortality, Lymphocyte proliferation, and organ weights as a percentage of BW (Thymus, bursa and spleen) was affected by either the level of zinc or the challenge status. There was no difference in body weight gain, feed intake as well as FCR footpad score, intestinal relative weight to body weight and breast yield among treatments. However, the tibia Zn deposition and bone breaking strength of chicks fed with MINTREX-Zn was higher ($P < 0.05$) than that fed with inorganic Zn at the same levels (40 mg/kg). GSH-Px activity of chicks consuming MINTREX-Zn at 40 mg/kg was significantly elevated ($P < 0.001$), conversely lipid peroxide (LPO) and ceruloplasmin (CP) were markedly decreased ($P < 0.05$). Also, anti-NDV antibody level was significantly enhanced in chicks fed diet supplemented with 40 and 60 mg/kg of MINTREX-Zn as compared with inorganic source at 14 d ($P < 0.05$) and 21 d of age ($P < 0.001$), respectively. It can be concluded that MINTREX-Zn enhanced tibia Zn deposition and could be considered to be more protective than zinc sulfate in terms of reducing the negative effect of oxidative stress induced by coccidiosis infection.

Keywords: MINTREX-Zn, Broilers, Coccidiosis Challenge

Evaluation of metallothionein as a biomarker of zinc status in a human dietary intervention study

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Zinc deficiency affects a third of the World's population and although plasma zinc is a useful biomarker of zinc status for population groups, there are no reliable biomarkers for individual status evaluation. Many years ago, on the basis of rat studies, plasma metallothionein (MT) was proposed as a potential biomarker of zinc (Zn) status but this idea has never been properly evaluated in human subjects due to lack of a good sensitive bioassay. MT analysis in blood cells has also been challenging for various reasons. As part of the Human Biomarkers of Zinc Status (HuBZS) project, we have used a new immunoassay for human MT in plasma to investigate the response of plasma MT to consumption of a low and a high Zn diet by human volunteers. We have compared the utility of MT as a zinc status biomarker with that of plasma Zn analysis, which is the most practical and widely used method. These and other biomarkers were analysed in up to 100 healthy men aged 18-45 whose dietary intake of Zn was manipulated in an intervention study. At the start of the study, habitual dietary zinc intake was estimated by standard methods and volunteers were then given high (17 mg/d, HZD) or low (4.4 mg/d, LZD) zinc diets for 5 weeks. Although plasma Zn significantly decreased after 5 weeks of Zn depletion, Plasma MT was unaffected. There was no correlation between plasma Zn and plasma MT. We conclude that plasma MT does not appear to be a good biomarker of Zn intake, and that plasma zinc and MT levels are unrelated to each other. Analysis of the exchangeable zinc pool is on-going to confirm the actual Zn status of volunteers.

This study was funded by the Food Standards Agency/Department of Health.

Keyword: Zinc, biomarker, human, dietary intervention

Symposium 8(H)

Title: Trace Element Biomarkers of Body Status
and Responses

Sponsor: TEMA-14

Location: Conference Room 2

Body trace element responses to human depression and strenuous soccer training

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The 40 member multielement profile (MP) was studied in the human depression and in the strenuous exercise. The study adhered to the ethical principles of Helsinki Declaration on human subject research; written consent was mandatory. The elemental content of all the tested biological matrix samples of hair (H) and whole blood (WB) was analyzed by the ICP MS at the ISO certified Center for Biotic Medicine, Moscow, Russia. MP profile was assessed in the H of 48 depressed subjects (D; 33 ♀ and 15 ♂) and 48 control subjects (C; 25 ♀ and 23 ♂). The difference of $\pm 15\%$ between the median of C and D was considered to be significant. The depressed subjects showed increased hair retention of $\text{La} > \text{W} > \text{K} > \text{Na} > \text{Rb} > \text{Ag} > \text{Ba} > \text{Ti} > \text{Pb} > \text{Ga} > \text{Mn} > \text{Al} > \text{Ge} > \text{Mg} > \text{B} > \text{Ca} > \text{Fe}$, decreased retention of $\text{Hg} > \text{Bi} > \text{I} > \text{Se} > \text{Zr} > \text{Zn} > \text{Cu}$, whereas the elements (in the decreasing order) P, Li, As, Sb, Au, Ni, Tl, Pt, Co, Be, Cr, Mo, Sn, Cd, V, Si were not affected. Apparently, hair Ca and Mg increase followed their mobilization from the bones, that of K (Rb) and Na (La) from the muscles, and that of Fe (Mn) from the erythrocytes, due to the underlying physical/metabolic inactivity, whereas the lack of the essential elements I, Se, Zn, and Cu may generate the overall metabolic slowdown. The depression dependent changes of MP demonstrated the presence of the overall body inactivity, where the respective deficit of essential elements may be either the cause or the trigger that activates the basic failure of the body energy control mechanism. MP in the H and WB, and 7, 8-dihydro-8-oxo-2'-deoxyguanosine (8-oxodG) in the peripheral lymphocytes of 17 men professional soccer players were assessed before and after the simulated match. After the match the WB Mg was decreased ($p < 0.01$) and 8-oxodG increased ($p < 0.01$); the rest of the elements appears statistically unaffected. The professional strenuous exercise damages the DNA and the stress bearing capacity of the body is reduced due to the high Mg internal metabolic consumption. The study of MP networks should replace the single element cause-effect model for the study of the complex dynamic of elements entangled in the intricate web of simultaneous physiological and metabolic events in the human body in health and disease.

Keywords: Multielement Profile, Depression, Exercise

Dietary exposure assessments of heavy metals and trace elements in China

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The dietary intakes of sixteen trace elements in Chinese adult males have been obtained using the 2000 Chinese Total Diet Study. This included twelve provinces, divided into four regions: North One (Heilongjiang, Liaoning and Hebei), North Two (Henan, Shanxi and Ningxia), South One (Shanghai, Jiangxi and Fujian), and South Two (Hubei, Sichuan and Guangxi). The research steps of the Chinese Total Diet Study included food consumption survey, food aggregation, food sampling, cooking and preparation, sample analysis and dietary exposure assessments. The elements surveyed in this study were Fe, Zn, Se, Cu, Mn, Cr, Ni, B, V, Li, Mo, Pb, Cd, Hg, Al, total and inorganic arsenic. The dietary safety of these trace elements was assessed by using their respective provisional tolerable weekly intake (PTWI) recommended by WHO. The nutritional status of essential elements was evaluated by the RNI and AI as established by the Chinese Nutrition Society. Chinese dietary Pb, Cd, Hg, Al, total arsenic and inorganic arsenic average intakes (% of PTWI) in adult males were 0.081 mg/d (36.1%), 0.022 mg/d (35.3%), 0.007 mg/d (15.2%), 22.9 mg/d (36.3%), 0.276 mg/d and 0.079 mg/d (58.6%), respectively. The main dietary sources of these harmful elements were cereals and vegetables. Chinese average dietary intakes of Fe, Zn, Cu, Se, Mn, Cr, Mo, Ni, B, V and Li (% of AI or RNI) in adult male were 13.0 mg/d (87.0%), 10.4 mg/d (69.3%), 1.7 mg/d (84.5%), 0.064 mg/d (128.6%), 3.838 mg/d (127.9%), 0.116 mg/d (233.8%), 0.257 mg/d (428.9%), 0.235 mg/d, 1.42mg/d, 0.034 mg/d, and 0.054 mg/d, respectively. The dietary intake of selenium was higher than the RNI in most provinces, but the intakes in Ningxia (0.037 mg/d) and Jiangxi (0.040 mg/d) were lower than the average level. Harmful elements in most food groups of the surveyed provinces were well below the National Standard Limit (NSL) of China except a few samples in some areas, such as lead in eggs in South 1 region (NSL exceeded by 8.1%) as well as cadmium in aquatic foods in regions of North 1 and South 1 (NSL exceeded by 49.0% and 27.6%, respectively). The results indicate that dietary lead, cadmium, total mercury, total arsenic and inorganic arsenic intakes were safe in the different regions. The dietary intakes of iron and zinc were insufficient in Chinese people.

Keywords: TDS, Trace Elements, Dietary Exposure, Assessment

Determinants of selenium status in healthy adults

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Determinants of Selenium Status in Healthy Adults Gerald F. Combs, Jr. and Matthew I. Jackson Grand Forks Human Nutrition Research Center, USDA-ARS, Grand Forks, ND, USA It is well established that Se-deficient individuals show subnormal levels of several Se biomarkers, including some with functional significance, such as the selenoproteins, and others that indicate the amounts of Se in the body, such as the Se contents of tissues and body fluids. However, non-deficient individuals, however, have maximal selenoenzyme expression, rendering those parameters non-informative regarding changes in Se intake. Thus, the total Se content of plasma has become the default biomarker of Se status in non-deficient cohorts. The problem of characterizing the Se status of a non-deficient cohort is that plasma and other biomarkers of Se status yield discordant results. Plasma Se, while easily measured, is not a single entity. It has several components: two selenoproteins (selenoprotein P [SEPP1] and the extracellular glutathione peroxidase [GPX3], which specifically contain selenocysteine (SeCys); Se incorporated non-specifically as SeMet in lieu of methionine in albumin and other proteins; and a small amount of non-protein bound Se. In non-deficient individuals, differences in food-Se (selenomethionine) intake affect only the non-specific component of plasma Se, and factors other than Se intake that can contribute to variance in those and other Se biomarkers. Healthy individuals show plasma Se levels of which specifically associated with selenoproteins (glutathione peroxidase, GPX3; selenoprotein P, SEPP1) comprise as little as 20% and 35%, respectively. The balance, comprised of non-specific components, account for virtually all interindividual variation in plasma Se in such individuals. These and other biomarkers of Se status are affected by BMI, sex and genotype. SEPP1 can be depressed in individuals with body mass index (BMI) greater than 25-30. Urinary Se varies with metabolic body weight (kg^{0.75}) but increases more in women than men upon Se-supplementation. GPX1 genotype is a determinant of plasma Se, with individuals of the 679T/T type having lower plasma Se levels than those with other allelic variants. Such factors may contribute to heterogeneity in biomarker responses to Se-supplementation.

Keyword: Selenium, Biomarker, Genotype

Deficient iodine status and its correlates in a developed European country: the UK

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Historically, the increase in iodine concentration of milk since the 1930s has been pivotal in improving iodine intake and eradicating the goitre that was endemic in the UK until the 1960s, since milk is the principal source of iodine in the UK diet. Unfortunately, UK consumption of milk has decreased in recent years and furthermore, organic milk (iodine concentration 42% lower than conventional milk) consumption has increased over the last decade. Because universal salt iodisation (USI) was never introduced in the UK, fewer than 20% of supermarket shoppers in the UK have iodised salt available for purchase and it is considerably more expensive than standard table salt. Given these factors, it is hardly surprising that iodine deficiency has re-emerged. By measuring 24-hr urinary iodine excretion by ICP-MS, we found mild-to-moderate iodine deficiency (median concentration 63 mcg/L) in our study of 57 UK women of childbearing age in 2007-2008. A further investigation of 100 UK pregnant women using spot urine samples also revealed iodine deficiency (median concentration 85 mcg/L). We carried out a pilot study in 1,000 women of the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort who were recruited in the 1990s, measuring their spot urinary iodine concentration at 12-weeks' gestation and investigating the relationship of those values to their child's IQ at age 8, reading ability at age 9 and school scores at age 11. Using creatinine concentration to correct for urine volume, we showed that the 8-year-old children of women deficient in iodine (iodine to creatinine ratio < 150 mcg/g) at 12-weeks' gestation were significantly more likely to have an IQ below the 25th centile [unadjusted OR=1.42, 95% CI 1.05, 1.94]. After adjustment for relevant confounders, the odds increased [OR=1.57; 95% CI 1.08, 2.30; P=0.02]. Stronger results were found for reading accuracy using the lower quartile of the reading accuracy assessment at age 9 [adjusted OR=1.88, 95% CI 1.24, 2.84; P=0.003]. School scores at age 11 showed strong adjusted associations for the lower quartiles of the maths score [OR=1.68; 95% CI 1.10, 2.56] and the science score [1.43; 0.96, 2.13]. We plan to extend our investigations to the whole ALSPAC cohort and will investigate the links with other aspects of neurocognitive impairment, including behavioural aspects. We thereby hope to persuade the UK Department of Health to take action, such as universal salt iodisation, to improve UK iodine status.

Keywords: Iodine, Pregnancy, IQ, Reading Ability, ALSPAC

Research into the safe intake levels of iodine in adults

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Health concerns over the widespread use of Universal Salt Iodization (USI) in a population with adequate iodine natural supply, coupled by the increase of iodine excess disorders in China have highlighted the necessity for a systematic evaluation of iodine safe levels. The objective of the study was to explore the safe upper level of total daily iodine intake among adults in China.

A four-week, double-blind, placebo-controlled, randomized controlled trial was conducted in 256 euthyroid adults. Participants were randomized to 12 intervention groups with varying iodine supplement doses ranging from 0 to 2000 µg for 4 weeks. All subjects were followed up for at least 4 additional weeks after iodine withdrawal. Total iodine intake included iodine from both supplements and diets. Multiple outcome measures were used to evaluate possible adverse effects including thyroid function, thyroid size, and urinary iodine. In comparison with the placebo group, all the iodide-supplemented groups responded with a significant rise in median urinary iodine (MUI) ($p < 0.05$) and sensitive thyroid stimulating hormone (sTSH) concentrations ($p < 0.05$). Thyroid volume decreased after 4 weeks in high iodine intervention groups (1500-2000µg). Subclinical hypothyroidism appeared in groups receiving 400µg iodine (5%) or higher (15-47%). However, no clinical hypothyroidism was observed. This study showed the subclinical hypothyroidism appeared in subjects at the 300 µg/day iodine supplement dose whose total ingested iodine was approximately 700µg/day. Thus, we raise caution for a total daily iodine intake that exceeds 700µg/day in China, recommending further research to determine a safe daily upper limit.

Keywords: Euthyroid people, Iodide Supplementation, Subclinical Hypothyroidism

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Iodine status of the Canadian population

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Iodine is an essential element required by the thyroid gland to produce the thyroid hormones, which are essential for normal growth and development. Severe iodine deficiency can lead to diverse effects including mental retardation, hypothyroidism, goitre, cretinism, stillbirths and varying degrees of other growth and developmental abnormalities. Thus, women have an enhanced requirement for iodine during gestation and lactation to support neuro-intellectual development of infants and children. The Canadian Health Measures Survey measured indicators of health and wellness on a nationally representative sample of approximately 5600 Canadians aged 6 to 79 years during 2007 – 2009. Biological samples were measured for indicators of general health, chronic disease, infectious disease, nutritional status and environmental biomarkers. Spot urine samples were analyzed for urinary iodine concentration (UIC) following a two step method, consisting of a digestion step, followed by the colorimetric determination of urinary iodine using a microplate reader. The median UIC for the Canadian population aged 6 to 79 was 130.4 µg/L (95% confidence interval (CI): [120.1, 140.7]); the proportion of the population with a UIC <100 µg/L was 35.2% [30.5, 40.0], < 50 µg/L 14.3% [11.3,17.4], while 12.8% [9.5,16.1] had UIC ≥ 300 µg/L. The median UIC for children aged 6 – 11 was 176.6 µg/L [160.2, 193.0]; the proportion of this population with a UIC < 100 µg/L was 24% [18.8, 29.2], < 50 µg/L was 9.3% [5.6,13.1], while 21.0% [16.7, 25.3] had UIC ≥ 300 µg/L. Women of child-bearing age (15-45) had a median UIC of 123.4 µg/L [110.8, 136.0]; the proportion of this population with a UIC < 100 µg/L was 39.5% [32.4, 46.6], < 50 µg/L 18.3.3% [14.7, 21.8], while 11.6% [7.2, 16.1] had UIC ≥ 300 µg/L. These findings suggest that Canadians have adequate intakes of iodine, although women of child-bearing age have lower median intakes and higher proportions with low UIC, while in young children, median intakes were substantially higher and 21% had UIC exceeding 300 µg/L. The distributions of UIC vary quite widely in the Canadian population and likely reflect differences in dietary intakes of iodine. Thus measurements of UIC in school-aged children are unlikely to adequately reflect the iodine status of national populations.

Keywords: Iodine, Canada, Status

The estimated prevalence of iron deficiency in Cameroon differs greatly depending on the iron status indicator used

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Available iron status indicators reflect different aspects of iron metabolism. We compared the prevalence and distribution of iron deficiency (ID) and iron-deficiency anemia (IDA) among Cameroonian women and preschool children as measured by plasma ferritin (F), soluble transferrin receptor (sTFR), body iron stores, and hemoglobin (Hb), and evaluated the impact of adjustments for concurrent infection on these measures. This was a nationally-representative, multi-stage cluster survey. We randomly selected 30 clusters in each of 3 zones (North, South, and Large Cities) and 10 households (HH) per cluster, each with a woman 15-49 y and a child 12-59 mo (n = 904 HH). Plasma F, sTFR, C-reactive protein (CRP) and α 1-acid-glycoprotein (AGP) were measured by ELISA. Hb was measured by portable photometer. Body iron stores were calculated using F and sTFR concentrations. Plasma F concentrations and body iron stores were adjusted mathematically for infection (CRP > 5 mg/L and/or AGP > 1 g/L). Infection was present in 20.8% of women and 48.0% of children, and 38.9% of women and 57.8% of children were anemic. The prevalence of ID ranged from 11.5 – 31.9% among women and 14.2 – 68.4% among children, and the prevalence of IDA ranged from 9.0 – 19.2% among women and 11.9 – 47.4% among children, depending on the iron status indicator. Moreover, the proportion of anemia that was associated with iron deficiency ranged from 25.7 – 49.5% among women and 20.6 – 82.0% among children. Adjustment of F and body iron stores for infection slightly increased the estimated prevalence of ID and IDA. The prevalence of ID and IDA was consistently greater in the North than in the South and Large Cities. In contrast, the relationship between socio-economic status and prevalence of ID and IDA varied by indicator and by group (women vs children). In this population, the prevalence of ID, IDA, and the proportion of anemia due to ID varied greatly depending on the iron status indicator used. Research is needed to clarify the relationships between existing iron status indicators, particularly in the presence of infection.

Keywords: Iron Deficiency, Anemia, Biomarker

Is serum ferritin <15 µg/l appropriate for identifying iron deficiency among marginal anemia populations in China?

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So far, the generally accepted cut-off level for serum ferritin, below which iron stores are considered to be depleted and hence the precondition for iron deficiency, is <15 µg/l, this study is aiming to assess whether the threshold is appropriate for identifying iron deficiency among marginal anemia populations in China. Methods: Data from an original cross-sectional survey, a published population-based intervention trial and a published diagnostic test were collected. As with the cross-sectional survey, 426 anemic subjects screened from a nutritional survey were measured on their body iron status, their dietary intakes of iron and iron modifier were investigated using methods of weighed diet records, 24h diet recall and food frequency questionnaire respectively according to different populations with different characteristics. For the intervention trial of iron fortification, 418 anemic students in four schools aged 11-18 years were randomly assigned with four kinds of treatments in cluster: a control school supplied with non-fortified wheat flour, the other three schools given flours fortified with electrolytic iron, FeSO₄ and NaFeEDTA, (fortification level of 60, 30 and 20 mg Fe/kg) respectively. Blood samples were obtained at 0, 2, 4 and 6 months, hemoglobin and iron status indicators were measured, respectively. For the third study, 476 patients in People's hospital of Guangdong province who were highly susceptible to iron deficiency anemia were taken serum ferritin measurement and bone marrow iron staining, then Receiver Operating Characteristic curve was used to assess the accuracy of different cutoff points in iron deficiency diagnosis. Results: From the cross sectional survey, it was found that the overall prevalence of iron deficiency anemia was much lower than reported if WHO criterion was used, however, a typical plant-based diet background with high fiber, phytate and polyphenol content, and low bioavailability of dietary iron was identified, also we find the percent of subjects with serum ferritin <15µg/l in severe and moderate anemia was significantly higher than that in marginal anemia. In the iron fortification trial, the average levels of serum ferritin in four groups were all far beyond the threshold value of 15µg/l, however, significantly positive response of serum ferritin to three chemical forms of iron fortificants could be clearly found after 2 months' consumption of iron fortified wheat flour. Through the study of diagnostic test accuracy evaluation, 36µg/l was determined as the optimal cutoff point for iron deficiency anemia, with its sensitivity 85.1% (79.4%-90.8%) and specificity 80.2% (75.3%-85.1%). Conclusion: Serum ferritin <15µg/l seems not an appropriate criterion for identifying iron deficiency among marginal anemia populations in China.

Keywords: WHO Criterion, Iron Deficiency, Marginal Anemia

The effect of inflammation and iron overload on the expression of iron-sulfur protein and thio-modification tRNA in microglial BV2 cells

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Microglia is a macrophage-like cell and plays an important role of immune function in the central nervous system. Neurodegenerative diseases are associated with iron dys-homeostasis and microglial hyper-activation, and these reactions result in iron-sulfur protein damage and mitochondrial dysfunction. However, whether these situations affect on the metabolism of iron-sulfur cluster biogenesis and thio-modification of tRNA in microglial cell is uncertain. Mitochondrial IscS protein is need for iron-sulfur cluster biogenesis, and thio-modification of tRNAs in eukaryotic cell. Mitochondrial IscS protein expression is modulated by iron deficiency in skeletal muscle of rats, and the inflammation also demonstrated has a similar effect. The aim of this study is to investigate the expression of mitochondrial IscS protein, iron-sulfur protein and thio-modification of tRNA in the inflammation and iron overload, and the need for IscS in thio-modification of tRNAs. After microglial BV2 cells were treated with 100 μ M ferrous sulfate (iron overload), the H-ferritin content was increased \sim six fold, and with the LPS and IFN-gamma co-stimulatio \sim nine fold compared with untreated cells. While LPS and IFN-gamma (IFN- γ) stimulation alone also did not significantly increase H-ferritin content. In addition, the expression of mitochondrial IscS protein was decreased by 60%, and enzyme activities of iron-sulfur proteins c-aconitase, m-aconitase and succinate dehydrogenase were decreased by 40%, 36% and 33%, after microglial BV2 cell stimulated by lipopolysaccharide (LPS) and IFN- γ . Similarly, the level of thio-modification of cytosolic tRNA^{lys}(UUU), tRNA^{glu}(UUC), and tRNA^{arg}(UGU) were significantly decreased by 18%, 13%, and 8%, in LPS and IFN- γ activated microglial BV2 cells. However, the thio-modification of mitochondrial tRNAs were not affected in LPS and IFN- γ activated microglial BV2 cell., This indicates mitochondrial IscS protein expression, the activity of iron-sulfur protein, and thio-modification of cytosolic tRNAs is regulated by inflammation in microglial BV2 cell and suggests mitochondrial IscS protein may be involved in regulation of biosynthesis.

Keywords: Inflammation, tRNA Thio-modification, Iron-sulfur Protein

Non-heme iron does not interact with heme iron absorption in humans

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Non-heme iron does not interact with heme iron absorption in humans. Absorption of heme iron has been described as distinctly different from that of non-heme iron. Whether heme and non-heme iron compete for absorption has not been well established. Our objective was to investigate the potential competition between heme and non-heme iron for absorption, when both iron forms are ingested on an empty stomach. Twenty-six healthy non-pregnant women were selected to participate in two iron absorption studies using iron radioactive tracers. We obtained the dose-response curve for absorption of 0.5, 10, 20, and 50 mg heme iron doses, as concentrated red blood cells. Then, we evaluated the absorption of the same doses, but additionally we added non-heme iron, as ferrous sulfate, at constant heme: non-heme iron molar ratio (1:1). Finally, we compared the two curves by a two-way ANOVA. Iron sources were administered on an empty stomach. One-factor analysis showed that heme iron absorption was diminished just by increasing total heme iron ($P < 0.0001$). The addition of non-heme iron did not have an effect on heme iron absorption ($P = \text{NS}$). We report evidence that heme and non-heme iron do not compete for absorption. The mechanism behind the absorption of these iron sources is not clear. However, it may imply differences in membrane transporters, as well as the traffic and storage of iron in to enterocytes.

Keywords: Heme Iron, Non-heme Iron, Absorption

A Randomized Controlled Trial Investigating the Effect of Calcium Supplementation on Iron Status in Chile

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Despite that it is widely accepted that calcium inhibits iron absorption from a meal. We found no inhibitory effect of 800 mg calcium on the absorption of 5 mg iron, when minerals were ingested on an empty stomach (Ca:Fe molar ratio ~ 220:1). On the other hand, a calcium-iron supplement for children would have a Ca:Fe molar ratio around 16:1, and it may be ingested on an empty stomach. Thus, in terms of anemia reduction, the efficacy of calcium-iron, or iron supplements would be similar. The aim of this study was to evaluate if the supplementation of 700 mg of calcium plus 30 mg of iron during 3 month has the same effect on iron status in children aged 6 to 8 years old compared with the supplementation of 30 mg of iron. We included 194 apparently healthy children (6-8 y). It was conformed two groups that were randomly assigned to receive 700 mg of calcium as calcium carbonate and 30 mg of iron as ferrous sulphate. The second group received 30 mg of single iron as ferrous sulphate. Follow up was for a duration of 3 months. The prevalence of anemia was evaluated pre and post-supplementation period. At the base line, the prevalences of anemia in the iron and the calcium-iron supplemented groups were 21.5 and 15.5 %. After follow up, the prevalence of anemia was 3.3 % in both groups (χ^2 ; NS). A combined calcium-iron supplement may be useful to increase calcium intake and to reduce the incidence of anemia in children.

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Keywords: Iron, Anemia, Calcium, Supplementation

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The role of selenium in metabolism and chronic disease

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Adequate supply of selenium (Se) is relevant for normal human development and health. Most of Se actions are mediated by selenoproteins, which contain selenocysteine as a catalytic component of their active site if they act as enzymes or as critical residue for their function as structural proteins. Two genetic defects have been reported which lead to impaired or complete loss of function of the corresponding selenoproteins. Several mutations in Selenoprotein N result in early onset, developmental severe myopathy (rigid spine disease, minicore disease). Selenoprotein N is expressed in myocytes and its cellular functions are involved in protections against oxidative stress and redox reactions relevant for calcium homeostasis. Several mutations were also reported for SECIS-binding protein 2, which initially manifest by impaired thyroid function due to decreased deiodinase and in severe cases several other (metabolic) impairments (delayed bone maturation, myopathy, mental and motor coordination, altered immune function, enhanced insulin sensitivity) were identified. Enhanced Se supply may only be partially effective as treatment. Inadequate Se status has also been associated with alterations in the thyroid hormone axis. Severe Se deficiency in combination with iodine deficiency is involved in development of myxedematous cretinism or Kashin-Beck disease. Iodine deficiency must be treated first before Se is supplemented in order to prevent further deterioration. Beneficial effects of Se supplementation occur in goiter prevention and two autoimmune diseases of the thyroid gland. 100 to 200 µg of Se compounds (selenite, selenmethionine or Se-yeast) for 3 or more months decreases thyroperoxidase (TPO) antibodies and improves health status in patients with M. Hashimoto, an autoimmune thyroid disease prevalent in adult females and similar results were also described for Graves`disease (M. Basedow). The underlying mechanism (Se deficiency?) or molecular targets (thyrocytes or the immune system) have not been identified. Molecular and cellular details of Se action on the immune system or its cellular components require more research.

Keywords: Selenoprotein, Thyroid, Metabolism

Roles of Se, GPX1 and SOD1 in insulin resistance, diabetes and obesity

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Trace elements such as Se, Cu, and Zn and enzymes containing these elements are considered to be protective against diabetes. Indeed, knockouts of Se-dependent glutathione peroxidase-1 (GPX1) and (or) Cu,Zn-superoxide dismutase (SOD1) impair insulin physiology and glucose metabolism. However, we have demonstrated a spontaneous development of type 2 diabetes-like syndrome in mice overexpressing GPX1. While this striking finding preceded reports on pro-diabetic potential of high body selenium status in a number of large human studies, it is unclear if high intakes of dietary Se alone induce insulin resistance or diabetes. Thus, we have conducted a two-generation rat experiment to determine if a prolonged high intake of dietary Se produced gestational diabetes in first-parity rat dams and insulin resistance in their offspring. A total of 55 female Wistar rats (67-day old) were fed a Se-deficient (0.01 mg/kg), corn-soy basal diet (BD) or BD + Se (as Se-yeast) at 0.3 or 3 mg/kg from 4 weeks before breeding to 2 weeks after farrowing. Offspring (n = 8) of the dams fed 0.3 and 3 mg Se/kg were fed with the same respective diet until age of 112 days. The 3.0 mg Se/kg diet induced hyperinsulinemia, insulin resistance, glucose intolerance, and decreased expression of 6 insulin signaling protein genes in liver or muscle in both dams and offspring. A second experiment was conducted to determine if high Se intake dys-regulated murine glucose metabolism and if knockout of GPX1 altered this effect of Se. A total of 40 weanling male GPX1^{-/-} and their wild-type (WT) mice were fed a Torula-yeast based diet supplemented with 0.3 or 1.0 mg Se/kg (as sodium selenite, n = 10 mice/treatment group) for 10 weeks. Both WT and GPX1^{-/-} mice fed 1.0 mg Se/kg exhibited higher (P < 0.05) fasting blood glucose concentrations and(or) lower (P < 0.05) insulin sensitivity and glucose tolerance than their respective controls fed 0.3 mg Se/kg. Glucose-stimulated insulin secretion was also elevated (P < 0.05) by feeding the high-Se diet to both genotypes. Knockout of GPX1 resulted in a reversal (P < 0.05) of all these trends. In conclusion, we have developed two rodent models illustrating the potential of over-supplementing dietary Se in inducing gestational diabetes and insulin resistance. Our data reveal a link between several selenoproteins, in particular GPX1, and the metabolic disorders (*NIH DK 53018*).

Keywords: Glutathione Peroxidase, Superoxide Dismutase, Diabetes

The current debate on selenium as risk factor for type 2 diabetes: Evidence for interplay of selenium and carbohydrate metabolism

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Selenium has a long track record for anti-diabetic and insulin-mimetic properties. Some data also point to pro-diabetic actions of Se, as supranutritional Se intake and high serum Se levels are associated with increased risk for development of type 2 diabetes in humans. Dietary Se compounds and/or abundantly expressed selenoproteins can impair both the regulation of pancreatic insulin secretion and the insulin sensitivity of target tissues, interfering with insulin-regulated metabolic pathways. To gain insight into the molecular mechanisms underlying an assumed interplay of selenium and carbohydrate metabolism, we investigated the transcriptional regulation of the serum Se transport protein selenoprotein P (SeP) by factors related to carbohydrate metabolism, and vice versa, the influence of Se compounds on insulin-regulated signalling pathways. We identified high glucose and glucocorticoids as positive regulators of hepatic SeP biosynthesis, whereas insulin and the anti-diabetic drug metformin attenuated SeP expression and secretion in hepatocytes. Thus, SeP is regulated virtually like a gluconeogenic enzyme by factors controlling the hepatic glucose factory under physio- and patho-physiological conditions. We also provided evidence that Se oversupply may cause disturbances in insulin-regulated carbohydrate metabolism in vitro and in vivo: Sodium selenite, inhibited the canonical insulin signalling cascade in cultured skeletal muscle cells by delaying insulin-triggered phosphorylation of protein kinase B (Akt) and FoxO transcription factors and attenuating insulin-stimulated glucose uptake. Supranutritional Se intake was not sufficient to induce overt diabetes in male pigs fed a high-Se diet (0.5 mg Se/kg) for 16 weeks. However, the glycolytic enzyme pyruvate kinase was down-regulated and the transcription factors FoxO1a and PGC-1alpha, both involved in the control of carbohydrate metabolism, were up-regulated in skeletal muscle of the high-Se animals. Taken together, epidemiological and mechanistic insights suggest a more careful handling of dietary Se supplements, as supranutritional Se intake may trigger adverse side-effects causing dys-regulation of carbohydrate metabolism.

Keywords: Type 2 Diabetes, FoxO, Transcription Factors, Insulin

Influence of SelR gene silence on peroxynitrite induced cell apoptosis in human lens cells

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Peroxynitrite (ONOO⁻) rapidly breaks down at physiological pH to yield the hydroxyl radical (\cdot OH) and nitrogen dioxide radical (\cdot NO₂). Endogenous peroxynitrite can be formed in various tissues of the eye, and then lead to the formation of cataracts. Methionine sulfoxide reductases (Msrs) including MsrA and MsrB, can reduce the methionine-S-sulfoxide and methionine-R-sulfoxide. MsrA plays an important role in protection of lens cells against oxidative damage and is required for the maintenance of lens transparency. However, MsrB1's (SelR) role in cellular protection against peroxynitrite-induced human lens epithelial (HLE) cell damage remains to be evaluated. Thus the effect of SelR gene silence on peroxynitrite-mediated cell apoptosis in HLE cells was examined. Cell viability was increased by low concentrations of peroxynitrite (50, 100 μ M) and decreased in a dose dependent manner by high concentrations of peroxynitrite (200-500 μ M) compared with normal cells. The apoptotic fraction of the group treated with 300 μ M peroxynitrite fore-and-aft SelR gene silence were 8.39% and 16.81%, respectively ($p < 0.01$); the Grp78 protein levels were significantly increased in HLE cells under peroxynitrite stress after SelR gene silence ($p < 0.001$), and the ROS and MDA levels were increased to approximately 4.4- and 3.8-fold after SelR gene silence, compared with untreated cells; the DNA strand breaks fore-and-aft SelR gene silence were 43.5% and 62.1%, respectively ($p < 0.001$); the activity of caspase-3 was increased to approximately 1.5- and 2.1-fold fore-and-aft SelR gene silence, ($p < 0.001$), compared with untreated control cells. The levels of ERK1/2 phosphorylation were significantly decreased ($p < 0.001$). Thus MsrB1 played important roles in regulating redox balance and mitigating ER stress induced by oxidative stress under physiological conditions as well as in protecting HLE cells against peroxynitrite-induced apoptosis by inhibiting activation of caspase-3 and oxidative damage of DNA, improving ERK phosphorylation under pathological conditions. *This work was supported by grant from the NSFC (Project No. 30870555)*

Keywords: SelR, ER Stress, Oxidative Stress, Cell Apoptosis, Cataract

Mice deficient in Se-dependent glutathione peroxidase-1 and -2 have inflammatory bowel disease

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Glutathione peroxidase (GPx)-1 is the first Se-dependent enzyme identified in mammals and is expressed ubiquitously. GPx-2 has similar enzymatic activity with predominantly epithelium expression pattern, especially high in the gastrointestinal (GI) tract. While mice with genetically targeted disruption of either GPx1 or GPx2 gene expression have no phenotype unless stressed, mice deficient in both GPx1 and GPx2 genes, GPx1/2-double knockout (DKO) have spontaneous ileitis and colitis. GPx1/2-DKO mice share the same disease etiology as human inflammatory bowel disease (IBD), which mainly consists of Crohn's disease and ulcerative colitis. The major factors affecting human IBD are genetic and environmental factors as well as dysregulated immune responses. We found that mouse genetic background has a huge impact on disease severity, C57BL/6 (B6) DKO mice have mild disease when 129S1Sv/J (129) mice have severe and life-threatening disease. Using a classic genetic approach, we have identified a colitis locus, GPx-deficiency-associated colitis-1, *Gdac1*, at mouse chromosome 2. We are in the process to identify the candidate genes affecting disease severity. Among the major environmental factors that we studied are luminal microflora and diet. Bacteria play an essential role in IBD, because germ-free mice are disease-free. Diet has a profound effect on disease severity; high-cholesterol diets exacerbate colitis, and mice on defined diets (without whole organisms such as extracts of beef, wheat, yeast, etc.) have better health than on rodent chows. Se supplementation has been shown to prevent chemical-induced mouse colon cancer or mice with *Apc* gene mutations. This effect is unlikely mediated through GPx1 or GPx2, because Se supplementation does not affect tumor incidence in the DKO mice, which have inflammation-associated intestinal tumors.

Keywords: Glutathione Peroxidase, Genetics and Diet, Intestinal Cancer

The essential role for Cu/Zn superoxide dismutase-dependent Ca²⁺ homeostasis in cellular thermotolerance

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Cu,Zn superoxide dismutase 1 (Sod1) is known to catalyze the cellular conversion reaction of O₂• free radicals for defense against oxidative stress, and mutations in the gene encoding Sod1 cause familial amyotrophic lateral sclerosis (fALS). However, the precise physiological function of Sod1 and how Sod1 mutations cause fALS have not been fully determined. We have found in the model organism *Saccharomyces cerevisiae* that Sod1 proteins not just defend cells against oxidative stress, but also balance intracellular Ca²⁺ level. We found that yeast mutant of *SOD1* deletion is defective in Ca²⁺ handling and unable to grow in the presence of 1 mM Ca²⁺ indicative of Ca²⁺ overloading; the Ca²⁺ balancing by Sod1 relies on its dismutase activity. Importantly, we have discovered that Ca²⁺ balancing by Sod1 is essential for yeast acquisition of thermo-tolerance, and the *sod1Δ* mutant was unable to grow at non-permissive temperatures of 37°C. The yeast analogous fALS-causing G85R mutation in Sod1 rendered yeast cells sensitive to high levels of Ca²⁺ at 30°C and unable to grow at 39°C. We found that the inter mitochondrial membrane space (IMS)-localized Sod1 is responsible for Ca²⁺ balancing and conferring thermo-tolerance. Our results revealed a physiological function for Sod1 of thermo-tolerance through Ca²⁺ balancing. The results also suggest that abnormal Ca²⁺ handling might underlie the cause of the deadly neurodegenerative disease fALS.

Keywords: Sod1, Ca²⁺, fALS

A novel correlation of hepatic p53 protein with Se- and glutathione peroxidase-1-mediated murine lipid metabolic disorders

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The well-known tumor suppress protein p53 has been found to be a novel regulator of lipid metabolism and involved in the development of obesity and fatty liver diseases. Because high body Se status was associated with adverse blood lipid profiles in humans and overexpression of Se-dependent glutathione peroxidase-1 (GPX1) induced type 2 diabetes-like phenotypes and obesity in mice, we conducted two experiments to determine responses of hepatic p53 protein to alterations of dietary Se intake and GPX1 expression. In Experiment 1, weanling wild-type (WT) and GPX1 overexpressing (OE) mice (n = 5 per genotype by diet) were fed a Torula yeast based diet (BD, <0.02 mg Se/kg) supplemented with 0 or 0.4 mg Se/kg (as sodium selenite) for 12 weeks. In Experiment 2, weanling WT, OE, and GPX1^{-/-} mice (n = 5) were fed the BD plus Se at 0.4 or 1.0 mg/kg for 5 months. Dietary Se deficiency resulted in 1.2-fold and 13% increase (P < 0.05) of the hepatic p53 protein level in the WT and OE mice, respectively. The OE mice fed the BD and 0.4 mg Se/kg had 19 and 54% lower (P < 0.05) of hepatic p53 protein than that of the WT mice, respectively. In contrast, elevating dietary Se from 0.4 to 1.0 mg/kg decreased (P < 0.05) hepatic p53 protein by approximately 90% in both WT and OE mice. Hepatic p53 protein in the GPX1^{-/-} mice was not affected by the high dietary Se supplementation, but was 53% higher (P < 0.05) than that of the WT mice fed 1.0 mg Se/kg. In conclusion, hepatic p53 protein seemed to be inversely related to dietary Se concentrations and GPX1 expression levels. This type of correlation may imply a novel role of p53 in the Se and GPX1-mediated lipid metabolic disorders (NIH DK53018).

Keyword: p53, Selenium, GPX1, Lipid Metabolism

Subclinical hypothyroidism and increased lipid peroxidation in mice lacking selenoprotein biosynthesis in thyroid epithelial cells

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Thyroid hormone biosynthesis requires the production of large amounts of hydrogen peroxide in the thyroid gland. Anti-oxidative enzymes expressed in thyroid epithelial cells are therefore protecting thyrocytes from damage through hydrogen peroxide. Among the expressed anti-oxidative enzymes are two families, thioredoxin reductases and glutathione peroxidases that contain selenocysteine in their active centre thus belonging to the family of selenoproteins. Selenoproteins are considered essential for thyroid function since low selenium status has been associated with thyroid disorders. We therefore set out to describe the physiological role of selenoproteins in the thyroid using a genetic loss-of function approach. The conditional inactivation of selenoprotein biosynthesis in thyrocytes via targeted disruption of selenocysteine tRNA was performed using two Cre-lines: Pax8^{Cre} for constitutive inactivation early in thyroid development and Tg^{CreER} as an inducible model during adulthood. Upon constitutive and inducible Cre/loxP-mediated recombination of tRNA^{[Ser]Sec}, we could detect a drastic reduction of glutathione peroxidase and type I-deiodinase activity in the thyroid gland. Immunohistochemical staining revealed increased 4-hydroxynonenal levels consistent with increased lipid peroxidation upon inactivation of glutathione peroxidase 4. Despite this fact and the detection of slightly increased thyrotropin levels suggestive of subclinical hypothyroidism, thyroid morphology remained intact for at least 6 months after recombination. Challenging mutant mice with low iodine diet increased thyrotropin, but did not lead to destruction of selenoprotein-deficient thyroids. Selenoproteins do protect the thyroid gland from oxidative damage and are involved in modulating thyroid hormone biosynthesis but are not essential for thyrocyte survival.

Keywords: Thyroid, Selenium, Iodine, Oxidative Stress

Study of Se-added ginkgo tea effect in mouse enzyme of stomach in alcoholic

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To study the influence of selenium-added Ginkgo tea, Zinc-added Ginkgo tea and common Ginkgo tea on mice malondialdehyde, glutathione peroxidase' and two kinds of activity. And to observe whether Ginkgo tea can play a useful role in Alcoholic stomach disease causing acute gastric mucosa damage, watching the experiment mice SOD, MDA and GSH - Px three of the enzyme activity in order to observe the changes of zinc and selenium and Ginkgo tea whether acute gastric mucosa damage to protect. Methods Kunming mice were male, only 60 24g 18 -, weight, by weight randomly divided into randomly divided into 6 groups of 10 only, respectively, which were model control group, selenium in low doses groups, selenium, selenium dose group of high-dosage groups, zinc low dose group, zinc of high dose zinc and dose group of group. Among them, and low selenium high-dosage groups respectively according to selenium 8.3 ug/kg ;zinc amount of low, and give high-dosage groups respectively according to 2.5 mg/kg. During the experiment, blank control, model control group, the rest of the group LiangKaiShui daily drinking LiangKaiShui add corresponding to the amount of selenium and zinc (selenium and zinc drink daily reference recommended intake by adults). Each mouse all use free drink way, successive and drinkable 30 days. During the experiment, weekly says, and observe a weight of the general situation in mice. The first 30 days each dose group and model control group to fill the stomach 12ml highly ethanol 12/ kg ? bw causes acute gastric mucosa damage model, fast after 12h death animals, take stomach tissue determined the mice are superoxide dismutase (SOD), malondialdehyde (MDA), glutathione peroxidase (GSH-Px) activity. Results Add selenium laboratory mice weight change is not significant, but add weight of zinc laboratory mice a significant increase trend. The control group experimental mice MDA value is the lowest, significantly lower than model control group and add selenium three groups ($P < 0.05$), model control group of laboratory mice is the tallest, MDA value significantly higher than the three groups add selenium ($P < 0.05$). The SOD is significantly higher than control group were model and selenium low dose group ($P < 0.05$). Model control group stomach tissue SOD significantly below the mice dose group of selenium and selenium in the high-dosage groups ($P < 0.05$), blank controls the highest, GSH - PX significantly higher than model control group and add selenium three groups ($P < 0.05$).

Keywords: Ginkgo Tea, Selenium, Alcohol, GSH-PX, MDA, SOD

Copper-homocysteine complex formation manipulates copper chaperone proteins

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Elevation of serum homocysteine levels is a risk factor for cardiovascular diseases. Previous studies suggested that interference with copper (Cu) metabolism is involved in the detrimental effect of homocysteine on cardiovascular system. Because Cu chaperones are critical regulators for intracellular Cu metabolism and distribution, the present study was undertaken to examine the effects of homocysteine on Cu chaperone levels and the possible underline mechanisms. Exposure of human umbilical vein endothelial cells (HUVECs) to concentrations of homocysteine at 0.01, 0.1, or 1.0 mM resulted in a dose-dependent increase in the concentration of intracellular homocysteine, along with the same pattern of a decrease in the cell viability and an increase in the necrotic cell. Western blot analyses revealed an increase in the protein of Cu chaperone for SOD-1 (CCS) and in the protein of Cu chaperone Atox1, but a decrease of the protein of Cu chaperone COX17. Interestingly, the mRNA levels for the three Cu chaperones were not changed by homocysteine, as determined by a real-time RT-PCR. Mass spectrometric analyses revealed that homocysteine formed complex with Cu, which was most likely responsible for the observed effects on Cu chaperones. Addition of excess Cu recovered the effects of homocysteine on Cu chaperones and a Cu chelator, tetraelenepentamine (TEPA), mimicked the same effects of homocysteine on Cu chaperones, which was also recoverable by excess Cu. This study thus demonstrated that the formation of Cu-homocysteine complexes resulted in a disruption in the equilibrium of Cu chaperones, leading to a disturbance of Cu metabolism and distribution.

Keywords: Copper, Homocysteine, Copper Chaperone

Ferroportin1 deficiency in mouse macrophages impairs iron homeostasis and inflammatory responses

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Systemic iron requirements are met predominantly through the recycling of iron from senescent erythrocytes by macrophages, a process in which the iron exporter ferroportin (Fpn1) is considered to be essential. Yet the role of Fpn1 in macrophage iron recycling and whether it influences innate immune responses is poorly understood *in vivo*. We inactivated Fpn1 in macrophages by crossing Fpn1-floxed animals with macrophage-targeted LysM-Cre or F4/80-Cre transgenic mice. Macrophage Fpn1 deletion mice were overtly normal, however, they displayed a mild anemia and iron accumulation in splenic, hepatic, and bone marrow macrophages when fed a standard diet. Iron loading was exacerbated following the administration of iron dextran or phenylhydrazine. When Fpn1LysM/LysM mice were challenged with an iron-deficient diet, they developed a more severe anemia and strikingly higher splenic iron levels than control mice, indicating significantly impaired iron mobilization from macrophages. Since immune responses can be altered by modulating iron status, we also examined the expression of pro-inflammatory cytokines. We found that expression levels of TNF-alpha and IL-6 were significantly enhanced in Fpn1LysM/LysM macrophages lacking Fpn1. These studies demonstrate that Fpn1 plays important roles in macrophage iron release *in vivo* and in modulating innate immune responses.

Keywords: Ferroportin, LysM-Cre, Macrophage

Features of hair and urine elemental composition of children with kidney malformations

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The study of 25 chemical elements in the hair of 60 children (29 healthy children - control group, 31 children with congenital kidney malformations) was carried out. The repeated investigation of 20 children with kidney malformations was carried out again after 5 years, and they also were examined as to the contents of 12 chemical elements in daily urine. The analysis was carried out in the laboratory ANO "Centre for Biotic Medicine" (Moscow) that is accredited by the Federal Centre for Sanitary Inspection Ministry of Health and Russia, with instruments Optima 2000 DV (Perkin-Elmer, USA) ELAN 9000 (Perkin-Elmer, USA) by standard methods of atomic emission and mass spectrometry. The analysis revealed that children with kidney malformations had increased level of toxicant elements from the group of heavy metals in the hair: cadmium (1.5 times), nickel (1.3 times), lead (1.2 times), tin (1.5 times) and relatively low - beryllium (below 2-fold) and zinc (1.2 times), from the other elements - increased level of aluminum (1.2 times higher). The dynamic showed the following: content of toxic elements in hair decreased, high incidence of zinc deficiency remained, revealed elevated levels of silicon. The study of chemical elements in the urine of children with kidney malformations showed that they had detected elevated level of mercury and decreased level of copper ($p < 0.05$). 25% of children had an increased excretion of zinc in the urine, 20% of children had concentration of zinc below the lower threshold age norm. It is concluded that children with different variants of the kidney malformations have a deficiency of essential trace elements and elevated levels of elements of pollutants at the stage of preexisting disease.

Keywords: Trace Elements, Children, Kidney Malformations

Symposium 10(J)

Title: Global Iron and Zinc Biofortification: Potential,
Success, and Challenge

Sponsor: HarvestPlus, Washington DC, USA and TEMA-14

Location: Conference Room 4

Zinc and iron biofortification: HarvestPlus crop development update

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HarvestPlus, Washington DC, USA.

Developing staple food crops (i.e. rice, wheat, beans, pearl millet) with high iron and zinc through biofortification requires combining high mineral content with characteristics that ensure acceptability by consumers. HarvestPlus plant breeding objectives for high iron and zinc for human nutrition include: 1) crop productivity equal or greater than conventional varieties; 2) stable genetic traits for high micronutrient levels across environments and climate conditions; 3) sufficient mineral concentration and bioavailability in the processed staple resulting in measurable impact on human nutritional status when intake \geq 30-40% the estimated average requirement (EAR); and 4) organoleptic characteristics that are acceptable to consumers. Germplasm screening and field evaluation of commercial varieties and breeding lines of beans and pearl millet from multiple countries have produced encouraging results for achieving nutritionally desirable Fe increases of 45 $\mu\text{g/g}$ and 17 $\mu\text{g/g}$, respectively. Increasing Zn concentrations in wheat and rice to nutritionally important levels is also feasible through traditional plant breeding. Lower phytate concentrations are highly desirable and may prove necessary. Genetic engineering is required to effectively increase iron levels in rice and wheat. In vitro and animal models for screening varieties for Fe and Zn bioavailability have added a useful dimension to the analysis of mineral concentrations. High Fe beans and pearl millet will be released respectively in Rwanda and India in 2011-2012.

Keywords: Food Crops, Rice, Wheat, Beans, Pearl Millet, High Iron and Zinc

Efficacy of iron biofortification: results from two human feeding trials of rice and beans

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Strategies to improve iron nutrition through biofortification (BF) of staple food crops have progressed towards tests of efficacy in human populations. The first test of efficacy was conducted in the Philippines with iron enhanced BF rice. A more recent feeding trial was completed in Mexico with iron enhanced BF beans. A sample of 192 religious sisters (age 19-50 y) living in 9 convents in greater Manila were individually randomized to consume either BF or control (Cx) rice (iron = 9.8 and 2.3 mg/kg, respectively). After consuming an average of 600 g of rice per day for 9 months, the women consuming the BF rice ingested 20% more dietary iron (10.0 versus 8.2 mg/d). While no group differences in hemoglobin (Hb), serum ferritin (Ft) and total body iron (BI) were seen for the entire sample, the non-anemic women who consumed BF rice (n=59) had a significant 6.7 µg/L increase in Ft and a 1.04 mg/kg increase in BI compared to Cx (n=59). Non-anemic women who consumed the greatest amount of BF rice had the greatest improvements in Ft and BI. In a feeding trial with BF beans in Mexico, 574 primary school children (age 6-12 y) attending 20 boarding schools were randomized by school to consume BF or Cx beans (iron = 95 and 55 mg/kg, respectively) for 6 months. After consuming an average of 52 g beans/d, the BF bean group ingested 100 µg/d more dietary iron, which resulted in a significant 0.38 µg/L decrease in soluble transferrin receptor (sTfR) compared to Cx. There were no significant differences in Hb and Ft between BF and Cx groups. Children in the BF group who were the most deficient at baseline showed the greatest improvement in sTfR. The significant positive results of these 2 feeding trials, while modest, demonstrate the efficacy of increasing iron status through long term consumption of a BF staple food. Studies of efficacy for iron enhanced BF beans and pearl millet are currently underway and studies of the effectiveness of iron enhanced BF are being planned in order to determine the impact of introducing BF staple food crops into populations that experience iron deficiency. *Supported by Asian Development Bank, DANIDA, AgroSalud and HarvestPlus*

Keywords: Biofortification, Iron, Efficacy

Assessment of iron and zinc bioavailability of biofortified wheat and maize in China

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Biofortified wheat and maize are an effective and economic ways for solving nutrient deficiency problems due to not only their carbohydrate and dietary fiber, but iron and zinc. With the support of HarvestPlus program, the biofortified wheat and maize varieties with higher iron and zinc levels have been screened out from hundreds of cultivars by CAAS in the past few years. However, their iron and zinc bioavailability (BV) have not been evaluated yet. Thus we aim to screen and provide wheat and maize cultivars with higher iron and zinc bioavailability for human beings. Iron and zinc levels in wheat flour with different extraction rates and maize were analyzed by ICP and AAS, with the bioavailability (BV) of biofortified wheat flours and maize screened to be assessed using an in vitro/ Caco-2 cell culture model. The wheat flours and maize with higher iron and zinc BV were further evaluated in hemoglobin regeneration trial in rats, and the maize cultivars recommended were evaluated with human trial. The results showed iron and zinc concentrations was significant affected by cultivar, milling extraction rate, and location, with milling extraction rate and cultivar being the predominant effects. Biofortified wheat cultivars was selected to study the impacting factors after establishing an in vitro digestion/ Caco-2 cell culture model, and iron bio-fortified maize cultivar zhongtie 2 and wheat cultivar Zhongyou 9507 was found to be able to maintain the iron store and iron level within normal levels even if rats were fed with low-iron forage. Maize cultivar zhongtie 2 was selected to be used in a 90 day human trial with improved nutritional status of children aged 9-13 year in intervention group than those in control group, but the difference was not statistically significant (P=0.059). Further analysis indicated that the improvement of girl students was more significantly effective (P=0.042), partly due to their better compliance than boys. The nutritional quality evaluation system of iron and zinc-biofortified wheat and maize needs to be further studied.

Keywords: Iron/zinc, Bioavailability, Wheat/maize

Importance and future of iron and zinc biofortification in Africa

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Nearly 200 million people in Africa are malnourished and at risk of disease, blindness, stunting and other illnesses. Most Africans rely on diets consisting of micronutrient poor staple foods and children under five years of age in Sub Saharan Africa bear the highest burden of micronutrient deficiency. There is therefore the need to breed varieties of staple food crops which are rich in vitamin A, zinc and iron in order to tackle the problem of micronutrient malnutrition, also known as hidden hunger. Hidden hunger impairs mental and physical development of children especially those under 5 years of age. Most people suffering from hidden hunger are poor and lack access to micronutrient rich foods on a regular basis. HarvestPlus an international research organisation has pioneered a process of breeding staple food crops with high micronutrient content of zinc, iron and Vitamin A in a process known as Biofortification. It fortifies foods habitually eaten and targets the rural poor who are often malnourished. In Africa the emphasis is on iron and vitamin A due to its high prevalence. Staple crops which are fortified include beans, maize, orange sweet potato and cassava. Beans are fortified with iron in D.R Congo and Rwanda; cassava with Vitamin A in D.R Congo and Nigeria; maize with Vitamin A in Zambia; and sweet potato with vitamin A in Uganda and Mozambique. Biofortification is sustainable because it improves the nutritional content of the staple foods that poor people already grow and eat and delivers micronutrients targeting the poorest people living in rural or remote regions of the world. It complements urban-based strategies such as supplementation and fortification and is a cost effective approach with low recurrent expenditures. Biofortification will help alleviate the problem of hidden hunger in developing countries in Africa.

Keywords: Vitamin A, Zinc, Iron, Africa

The importance of food composition data for a clear understanding of mineral nutrients in the food supply

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Food composition data is important for many endeavors from estimating nutrient intake for epidemiologic investigations to developing national health statistics to promulgating public policy. However food production is a complex biological practice that lacks the precision of manufacturing control for items such as pharmaceuticals or silicon chips. Most food is produced in an outdoor environment that is subject to climatic and geographical influences and food is derived from living organisms with a vast array of genetic, epigenetic and physiologic influences. Further complications include differing definitions for functional terms such as bioavailability, antioxidant and nutrient. A complete understanding of mineral elements in the food supply demands that these factors and influences be accounted for. The interaction of many of these factors on the accumulation of Se in plant and animal foods has been studied, and is an example of potential complications regarding food nutrient content. Incorporation of a clear picture of variability in the food supply may lead to alternative interpretations of epidemiologic data or development of regulatory controls.

Keywords: Food Composition, Selenium, Biofortification

Comprehensive utilization of selenium resources in black shales of Enshi

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Selenium (Se), as an important industrial material, are extensive applied in many fields, such as electronic industry, metallurgical industry, petroleum industry, and so on. However, Se is a typical dispersed element with a low crustal concentration (0.05-0.09 $\mu\text{g Kg}^{-1}$). Traditionally, Se was not considered to form independent deposits but instead occurs chiefly as an associated minor element in the ore deposits of other elements. In Enshi region, the huge independent deposit of Se with 5 billion tons of selenium resources, it is the only site in the world. The maximum Se concentration exceeding 80000 $\mu\text{g/ g}^{-1}$ in black shales has been reported, which is called stone coal. Nowadays, combustion is the major use form for stone coal. In coal combustion processes, Se is distributed in the vapors and particulate phases with different proportions. A significant portion of selenium escapes into the atmosphere in the form of vapors were resulted in the air pollution and waste of the scarce resources. Therefore, it is valuable work for comprehensive utilization of Se in Se-rich stone coal. One effective way to utilize Se in Se-rich stone coal is solidified and recovered the Se in the vapors from black shales combustion. Our work is focused on the adsorption and recovery of Se in the vapors from Se-rich stone coal combustion processes with calcium-based nano metal oxides. The adsorption efficiency of various calcium-based sorbents were evaluated at 700°C-1000°C. The results showed that the adsorption rate of selenium reached 90.9% at 800°C with CaO/nano-ZnO as sorbent. The XRD and FTIR indicated that Se were formed in CaSeO_4 species. Then selenium is recovered over reduction by Na_2SO_3 from sorbents of CaO/nano-ZnO.

Keywords: Black Shales, Comprehensive Utilization, Selenium

Improving iron bioavailability with ferritin overexpression in low phytate maize

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Insufficient dietary iron intakes as well as poor absorption of iron from cereal based diets high in phytate are major causes of iron deficiency anemia (IDA). Ferritin expression can be increased but may not overcome the inhibitory effects of phytate. We have exploited the low phytic acid 1-1 (*lpa1-1*) mutant of maize, which contains ~40% of the normal phytate content, to generate transgenic plants through the endosperm-specific overexpression of soybean ferritin. Iron and phytate contents were measured in both transgenic and non-transgenic seeds. Ferritin concentration was measured by using ELISA method and Caco-2 cell culture model was utilized to determine iron bioavailability. Phytate content in transgenic *lpa1-1* maize lines was similar to their parent line (1.17 mg/g). Several transgenic maize lines showed enhanced Fe content (20.7– 53.6 and 22.3– 37.9 µg/g in the *lpa1-1* and A188, respectively). Compared to the control non-transformed plants, some of these transgenic plants had 2-3-fold increase in Fe content. Ferritin concentration in transgenic maize ranged from 32.6 – 147.6 g/g DW, resulting in a maximum increase of 4-5 fold in some transgenic lines versus control. As expected, the non-transformed *lpa1-1* seeds showed 1.5-fold higher Fe bioavailability (31 ± 0.9 ng ferritin /mg protein) than non-transformed A188 (20 ± 0.5 ng ferritin/mg protein). Iron bioavailability of both transgenic *lpa1-1* (25 – 65 ng/mg protein) and A188 maize (19.8 – 44.7 ng/mg protein) was significantly higher (~2-fold, P=<0.001) than their respective non-transformed controls. A combined analysis of all transgenic lines shows that there is a significant correlation between ferritin concentration and Fe content for transgenic *lpa1-1* (R² = 0.63, P <0.05) and A188 (R² = 0.74, P <0.05) lines. Furthermore, Fe (R² = 0.84; P <0.001) and ferritin concentrations (R² = 0.56; P <0.05) were significantly correlated with Fe bioavailability in transgenic *lpa1-1* seeds, but not in transgenic A188 lines. Multiple regression analysis showed that iron and phytate contents are the significant predictors of iron bioavailability. In addition, high iron maize lines may overcome the negative effect of low phytate on seed germination. Our results suggest that transgenic *lpa 1-1* maize with high iron content is a potential approach to alleviate IDA.

Keywords: *lpa1-1*, Ferritin, Bioavailability

Daily selenium intake in high selenium area of Enshi, China

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Enshi is a typical high selenium area, where 477 cases of human selenosis have been reported from 1923 to 1987 and no occurrences of human selenium poisoning were reported again in recent years. In this study, to determine the daily dietary selenium intake in Enshi area and whether local residents still had potential risk of selenosis, typically consumed foods were collected and analyzed from 3 villages Beifengya, Laoxiongpo and Sangshupo of Shadi Town in Enshi. The daily selenium intake was 526.1 μg , 830.0 μg and 369.1 μg . For Shadi Town, the average daily selenium intake was 548.9 μg , close to the maximum safe selenium intake of 550 μg for an adult in high selenium areas. Guangqi Yang reported that selenium homeostasis was disturbed at intakes above 750 $\mu\text{g Se/day}$ and symptoms of selenosis occurred at dietary intake levels of greater than 910 $\mu\text{g Se/day}$. Therefore, there was no occurrence of human selenium poisoning in Shadi, but potential risk of selenosis for local residents, especially the residents of Laoxiongpo.

Keywords: Selenium, Daily Intake, Selenosis

Key issues and challenges of iron and zinc biofortification in Asia

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In early 2011, the FAO Cereal Price Index, including staples such as rice, wheat and maize rose to a record high compared with the value in 2008 and the increasing trend continues, due to the elevated demand for biofuel. This condition jeopardizes the diet quality of the poor and places women and young children at risk of hidden hunger or micronutrient malnutrition. Micronutrient deficiencies, especially those of iron and zinc, are prevalent among developing countries in Asia, leading to impaired physical and mental development; reduced work performance and increased risk of mortality due to severe infection. Since these communities are agricultural-based, a strategy of biofortification to increase micronutrient contents including iron and zinc in staple crops through plant breeding and enriched fertilizers with trace elements seem appropriate. The advantages of biofortification are the accessibility of micronutrient-rich crops among the malnourished groups in rural areas; relatively low cost and highly sustainable. Biofortification has been implemented under the HarvestPlus Challenge Program. So far, the nutrient targets and crop improvement have been set for iron and zinc in wheat, rice and pearl millet for Asian countries. The key issue at this stage is whether the retention and bioavailability of iron and zinc in these crops at consumption, will lead to improvement in status. A feeding trial of iron-biofortified rice led to increased iron stores among non-anemic Filipino women. Zinc in biofortified wheat has been shown to be bioavailable and need to be tested further in humans. In addition, under the HarvestZinc program, the use of zinc fertilizers in zinc-depleted soil or dressing the seeds with zinc resulted in markedly improved yield of wheat and rice in Turkey, Bangladesh, China, India and Thailand. Current effort involves examination of the species and form of zinc in these crops prior to bioavailability and efficacy trials. Key challenges include the length of time required for deliver of biofortified crops; the agronomic criteria for acceptance and applicability; the limited threshold of nutrient contents to generate impact; scientific evidence on efficacy and effectiveness studies etc.

Keywords: Iron, Zinc, Biofortification

Zinc biofortification of rice in Bangladesh

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In Bangladesh, 43% of under-five children have low height-for-age (Z-score <-2 compared with WHO standard), suggesting an elevated risk of zinc deficiency. Community-based studies indicate that dietary zinc intakes are inadequate among children and women (median zinc intakes 2.5 mg/d (95% CI: 2.1, 2.9) and 5.4 mg/d (4.8, 6.1) in children and women, respectively); and several investigators have reported a high prevalence of low serum zinc concentration among both infants and children.

Biofortification is an emerging strategy for controlling deficiencies of several micronutrients in lower income countries; and cultivars of rice with relatively high zinc content are now being produced in Bangladesh. Dietary studies in northern Bangladesh found that rice provided ~58% of energy intake among children 2-3 years of age and 84% of energy intake among women. Simulations of the potential impact of 70% population coverage with zinc-biofortified rice containing an assumed additional 0.8 mg zinc/100g dry weight indicate that this zinc-biofortified rice could reduce the prevalence of inadequate zinc intake from 22% to 9% in children and from 73% to 20% in women.

The ultimate nutritional impact of rice zinc-biofortification depends on the amount of zinc absorbed from high-zinc cultivars. We completed stable isotope tracer studies using the triple isotope ratio method to assess zinc absorption from conventional rice (CR: BR-28) and zinc-biofortified rice (ZnBfR: IR-68144). We compared total dietary zinc intakes (TDZ), fractional zinc absorption (FZA) and total absorbed zinc (TAZ) from mixed diets containing one of each of the two forms of rice on successive days. TDZ measured from all sources (rice, other foods, and zinc tracers) was 3.83 and 4.83 mg/d when the children were fed the CR- and ZnBfR-containing diets, respectively. The mean FZA (% of intake) was $25.1 \pm 4.1\%$ and $20.2 \pm 3.7\%$ from the respective diets ($p < 0.001$), and the mean TAZ was 0.96 ± 0.16 and 0.97 ± 0.18 mg/d ($p = 0.99$).

We conclude that zinc-biofortified rice has potential for improving zinc intake in rice-consuming populations, but the amount of additional zinc present in the ZnBfR we tested was insufficient to induce greater TAZ in young children. Thus, it appears that rice cultivars with higher zinc and/or lower phytate content will need to be developed to increase TAZ by young children.

Keywords: Zinc, Dietary Adequacy, Absorption, Biofortification, Rice

Symposium 11(K)

Title: Transporter, Systemic Control of Body Intake,
 and Homeostasis

Sponsor: TEMA-14

Location: Conference Room 5

Potassium in metabolism of copper and iron

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Metal ions play vital roles in the biological system, which is largely dependent on their incorporation into metalloproteins and subcellular compartmentalization. Given various implications of metal dyshomeostasis in health and disease, the mechanism underlying uptake and utilization of metal ions is highly significant research question. For instance, it is not known how extracellular copper (Cu)-containing proteins, such as ferroxidases (e.g., intestinal hephaestin, serum ceruloplasmin, and placental cytochrome b₅90), superoxide dismutase 3, lysyl oxidase and dopamine beta-hydroxylase, assemble Cu cofactor during their secretion. These cuproenzymes play critical roles for iron (Fe) metabolism, angiogenesis, antioxidant defense, extracellular matrix maturation and neurotransmission, respectively. Consistently, nutritional or genetic problems of Cu delivery to the secretory pathway lead to various disorders, such as anemia, cardiovascular disorders, cancer, and neuronal diseases. In the context of the fundamental roles of Cu and its implications in serious health issues, the mechanisms involved in synthesis of functional cuproproteins need to be defined. To gain a better insight into metal metabolism and metalloprotein synthesis, we have searched new genes involved in Cu and Fe utilization. Predicted potassium (K⁺)/proton (H⁺) antiporters were selected as new molecular factors necessary for activation of a Cu containing ferroxidase, a component of the cell surface Fe transport system. It is known that Cu serves as a cofactor of ferroxidases and both Cu and Fe are cofactors of respiratory chain electron transport; however, implication of K⁺ in Cu and Fe metabolism is an unanticipated finding. Several lines of our study indicate that the transporters mediate K⁺ import into the lumen of the trans-Golgi network, which is required for Cu metallation of ferroxidases. This exciting finding has opened new avenues by which we can elucidate the mechanisms underlying Cu metallation of cuproproteins at the secretory pathway, reveal a novel functional role of K⁺, and ultimately combat Cu, Fe and K⁺-related disorders, ranging from defects in normal growth and development to metabolic and degenerative diseases.

Keyword: Ferroxidase, Copper, Potassium

New insights into mammalian iron homeostasis

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Trace element iron is essential for nearly all living organisms. It is the key component of iron-containing enzymes and proteins, which participate in many cellular biological processes. It is estimated that nearly one quarter of population worldwide has been suffered from anemia due to iron deficiency. In contrast, iron overload induces a disease termed as Hemochromatosis, which the incidence is approximately 1/200 in Caucasians. Recently, the disease has also been reported in China. It is fatal if the disease progresses to late stage as the sign of heart, pancreas, and liver failures. Therefore, maintenance of iron homeostasis is crucial. It is believed that iron is uptake by small intestine, stored in liver, transported in blood, recycled by macrophages, and finally utilized by cells to fulfill the functions. In last “Golden Decade”, many novel iron metabolic genes have been cloned and functionally characterized to further understanding of regulation of iron metabolism and maintenance of iron homeostasis. However, more insights need to be learned considering the complexity of the processes. In this lecture, I summarize the recent findings (most from our own research) including in this field and discuss remaining questions, and provide our understanding towards future directions.

Keywords: Iron, Homeostasis, Mammals

Consequences of conditional ferritin h gene deletion on cellular iron homeostasis and iron absorption in mice

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Ferritin H with its ferroxidase activity is essential for iron deposition into ferritin. We have established Fthlox/lox mice in which the ferritin H allele can be conditionally deleted upon crossing with mice transgenic for tissue-specific and/or inducible Cre. Ferritin H-deleted mouse embryonic fibroblasts lost their iron storage capacity and showed rapid cell death after exposure to iron salt in the medium. This was reversed by wild-type ferritin H but not a mutant ferritin H lacking ferroxidase activity. Cell death was preceded by an increase in cytoplasmic free iron, reactive oxygen species, and mitochondrial depolarization. Further deletion of ferritin H in various tissues confirmed that loss of iron storage is usually accompanied by severe cell damage, particularly in iron-loaded mice. Recently, we have investigated the role of ferritin H in the control of intestinal iron absorption. Although the control of iron absorption requires hepcidin investigations in dogs and rats indicated that intestinal ferritin might also control of intestinal iron. Mice with the intestinal ferritin H gene deletion showed increased serum iron levels and transferrin saturation as compared with control mice. They had accumulated iron at 12 weeks in the liver, and to more pronounced levels at 36 weeks in liver and spleen. Interestingly, this accumulation was more significant in females than males. The ferritin H deleted mice showed induced liver hepcidin mRNA levels and reduced duodenal expression of DMT1 and Dcytb mRNA, while hephaestin and ferroportin mRNA levels were unaffected. In spite of these feedback controls, intestinal ferroportin protein and ⁵⁹Fe-absorption were increased more than two-fold on average in the deleted mice. This was accompanied by IRP2 inactivation and increased ferritin L protein expression, suggesting an increased intracellular free iron-pool in the intestinal cells and the likely possibility that ferroportin mRNA translation was IRP-dependently derepressed. There was a marked increase of genes induced by oxidative without visible morphological changes in the mucosa. Thus hepcidin-mediated regulation alone is insufficient to restrict iron absorption in mice and intestinal ferritin H is also required, presumably to limit iron efflux.

Keyword: Iron, Regulation, Ferritin Knock-Out

Hepcidin regulating brain iron metabolism

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Brain iron homeostasis is maintained by a balance of both iron uptake and release, and accumulating evidence has revealed that brain iron concentrations increase with aging. Hepcidin, an iron regulatory hormone produced by hepatocytes in response to inflammatory stimuli, iron, and hypoxia, has been shown to be the long-sought hormone responsible for the regulation of body iron balance and recycling in mammals. Our results show that hepcidin is widely expressed in the murine brain. In cerebral cortex, hippocampus and striatum, hepcidin mRNA levels increased with aging. Injection of hepcidin into the lateral cerebral ventricle resulted in decreased Fpn1 protein levels in cerebral cortex, hippocampus and striatum. Additionally, treatment of primary cultured neurons with hepcidin caused decreased neuronal iron release and Fpn1 protein levels. LPS treatment increases the endogenous hepcidin expression, which regulated the FPN1 level and ferritin level. These data provide evidence that hepcidin may be involved in the regulation of brain iron metabolism. Neuroinflammation plays an aggravating role in Parkinson's disease (PD). Mounting evidence suggests that iron is involved in the mechanisms underlined in many neurodegenerative diseases. However, it remains unknown whether the brain iron dysregulation induced by inflammation contributes to the PD pathogenesis. In this study we also discovered that hepcidin enhanced the neurotoxicity after LPS treatment in the MPTP mouse model of PD. Indeed, LPS treatment induced significant increase of hepcidin by stimulating both IL-6 expression and STAT3 activation in mouse brain. Intra-cellular increase of hepcidin caused iron accumulation by down-regulating the ferroportin1 level which enhanced MPP⁺-induced cell death in SH-SY5Y cells and MPTP-induced dopaminergic neurodegeneration in vivo. Conversely, knockdown of hepcidin attenuated PD-related dopaminergic neurodegeneration to turn back of dopaminergic cell loss acquired with MPTP alone. Overall, our results indicate that hepcidin links neuroinflammation to iron dysregulation, and contributes to an enhancement of the dopaminergic neurodegeneration in the MPTP mouse model of PD.

Keyword: Hepcidin, Iron, Parkinson's disease

Roles of DMT1 and ZIP14 in iron uptake by the liver

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The transmembrane metal-ion transporters DMT1 (Divalent Metal Transporter 1) and ZIP14 (ZRT/IRT-like Protein 14) have been shown to mediate the uptake of iron into mammalian cells. Both proteins have been implicated in the cellular assimilation of iron from transferrin and the uptake of non-transferrin-bound iron (NTBI), which appears in the plasma during iron overload. Here we aimed to: (1) investigate the regulation of DMT1 and ZIP14 by iron in the liver; (2) determine if DMT1 is required for iron accumulation by the liver; (3) test the hypothesis that hepatocyte DMT1 mediates the uptake of NTBI and the assimilation of iron from transferrin. To investigate the iron-dependent regulation of DMT1 and ZIP14, we studied iron-deficient (FeD), iron-adequate (FeA), and iron-overloaded (FeO) rats. Western blot analysis revealed that hepatic ZIP14 levels were unaffected by iron status, whereas DMT1 levels were elevated in FeD and lower in FeO animals relative to FeA controls. To investigate if DMT1 is required for normal hepatic iron uptake and uptake during iron overload, we studied mice lacking DMT1 specifically in hepatocytes (*Dmt1^{liv/liv}*), as well as these mice crossed with models of genetic iron overload, i.e., *Hfe^{-/-}* and hypotransferrinemic (*Hpx*) mice. We found that *Dmt1^{liv/liv}* mice had normal hepatic non-heme iron concentrations and that the double-mutant *Dmt1^{liv/liv}:Hfe^{-/-}* and *Dmt1^{liv/liv}:Hpx* mice accumulated similar amounts of hepatic iron as did their respective *Hfe^{-/-}* and *Hpx* controls. To determine if hepatocyte DMT1 is required for the uptake of NTBI and the assimilation of iron from transferrin, we injected into *Dmt1^{liv/liv}* mice ⁵⁹Fe-labeled NTBI or transferrin and measured ⁵⁹Fe uptake by the liver. We found that *Dmt1^{liv/liv}* mice efficiently took up NTBI, but had a 40% reduction in the assimilation of iron from transferrin. Collectively these data indicate that, although hepatocyte DMT1 appears to be required for the efficient assimilation of iron from transferrin, it is not required for hepatic iron accumulation under normal and iron overload conditions or for NTBI uptake. Our data also suggest that ZIP14 is the predominant mechanism of NTBI uptake, as ZIP14 continues to be expressed during iron overload, whereas DMT1 is markedly downregulated. Future studies with *Zip14^{-/-}* mice will directly test the role of ZIP14 in iron uptake by the liver.

Keywords: Transferrin, Non-transferrin-bound Iron, Iron Overload

Copper and the compensatory response to iron deficiency

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Iron and copper interactions have been recognized for more than 150 years and early studies on the interplay between these trace minerals dates back to the early 19th century. Recent investigations have demonstrated that genes related to copper homeostasis are induced in the intestine of iron deficient rodents. Moreover serum and liver copper levels increase during iron deficiency in many mammalian species including humans. These observations suggest that copper dependent processes in part mediate the compensatory response to iron deficiency. In the proximal intestine, where dietary iron is absorbed, increased expression of the Menkes copper ATPase (Atp7a) and metallothionein (Mt) genes was shown. Atp7a encodes a copper exporter and Mt is known to bind copper; their induction suggests that enterocytes accumulate copper during iron deficiency (which has indeed been shown). Molecular analysis of the Atp7a promoter determined that this induction is transcriptionally mediated by a hypoxia responsive transcription factor (HIF2 α). Interestingly, this places Atp7a in a group of genes induced by iron deficiency (including Dmt1, Fpn1 etc.), many of which have proven roles in intestinal iron homeostasis. Additional points of interaction between iron and copper include two multi-copper ferroxidases, hephaestin (Heph) which is a membrane bound protein found in enterocytes, and ceruloplasmin (Cp), which is a circulating protein of hepatic origin. Recent studies have provided evidence that Cp production responds directly to liver copper levels in a positive direction. It was hypothesized that increased copper in hepatocytes leads directly to increased metallation of the Cp protein resulting in higher levels of the holo form of the enzyme being produced and secreted. Moreover, a novel cytosolic version of Heph has been identified and was shown to increase in enterocytes derived from iron deficient rats. It is tempting to speculate that increased expression of Atp7a in the duodenum plays a role in increasing liver copper levels during iron deficiency which then leads to increased production of the active form of the Cp enzyme, which in turn maximizes iron release from storage sites to maintain erythropoiesis. Recent studies support this supposition, but further experimentation is required before strong conclusions can be drawn.

Keywords: Iron, Atp7a, Ceruloplasmin

Study metal homeostasis in the *Drosophila* model

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Metal homeostasis at the organismal level is not well understood. *Drosophila* as an excellent model organism has been successfully used in a number of studies, including development and human disease modeling. Here we aim to understand how metal homeostasis occurs and how metals might relate to CNS diseases in a *Drosophila* setting. For the first purpose, we started by systematically analyzing how zinc transporters, Zips and Znts function in zinc metabolism in *Drosophila*. *Drosophila* contains 8 Zips and 6 Znts. We are particularly interested in how zinc is absorbed in the gut. Several zinc transporters, including Zip1, Zip2 and Znt1, were found to coordinate in the zinc absorption in the gut. Towards the second direction, we try to relate various dimensions of metal metabolism to CNS disorders, in particular common human neurodegenerative diseases modeled in *Drosophila*. Indeed, some aspects of metal homeostasis play important roles in the development of neurodegenerative diseases. In summary, our work indicates that *Drosophila* can complement nicely the current major research platform, the rodent system, to gain significant insights in trace metal studies.

Keywords: Zinc, *Drosophila*, Neurodegeneration

Lipoprotein lipase: a new target of iron regulation

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The Belgrade rats display an iron-loading anemia phenotype that not only resembles patients with Divalent Metal Transporter-1 (DMT1) missense mutations, but also thalassemic patients with transfusional iron overload. Serum triglyceride levels associated with VLDL were significantly increased in 12-week old Belgrade rats (*b/b*) compared with heterozygote littermates (*+/b*) (325.5 ± 33.3 vs 145.3 ± 10.7 mg/dL, $p=0.001$; $n=6-9$). Increased synthesis of triglycerides does not appear to account for the dyslipidemia since the expression of lipogenic genes, including fatty acid synthase (FAS) and acetyl CoA carboxylase (ACC), was not up-regulated. Moreover, triglyceride secretion kinetics were unchanged after injection with Triton WR1339, a lipoprotein lipase inhibitor. In contrast, the ApoB-100/ApoE lipoprotein ratio in plasma VLDL fraction of *b/b* rats was doubled that of *+/b* rats, suggesting that *b/b* rats have slower plasma VLDL removal. Clearance of VLDL remnant into liver does not appear to be affected since *b/b* LDL receptor levels were similar to *+/b* controls. Although protein levels of lipoprotein lipase (LPL) associated with adipose and skeletal muscle were similar in *b/b* and *+/b* rats, a significant reduction in serum lipoprotein lipase (LPL) activity in Belgrade rats was observed. After heparin injection, LPL activity was determined to be 1.0×10^{-4} mM/min for *b/b* rats compared with 1.7×10^{-7} mM/min in *+/b* rats ($p=0.03$; $n=4-7$). Insulin signaling was assessed by determining the amount of phosphorylated Akt in peripheral tissues after portal vein injection of insulin; levels of phospho-Akt were similar in *b/b* and *+/b* rats. In addition, glucose and insulin tolerance tests did not indicate insulin resistance, suggesting other factors modulated the apparent reduction in LPL activity. Control serum from *+/b* rats was supplemented with ferric ammonium citrate (FAC) to levels of iron comparable to serum from *b/b* rats. Addition of FAC inhibited LPL activity in a dose-dependent manner. This novel finding suggests iron loading interferes with lipolytic activity necessary for triglyceride delivery, promoting dyslipidemia in the Belgrade rat and possibly in patients with iron overloaded disorder.

Keywords: Belgrade Rat, DMT1, Serum Iron, Triglyceride, Lipoprotein Lipase

A novel mammalian zinc transporter, ZIP11 regulated by zinc through transcription and mRNA stability

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Sophisticated regulatory systems must exist to maintain zinc homeostasis in the animals and in the cells to keep body health. Movement of zinc into and out of cells and subcellular organelles is mediated by zinc transporters. Many zinc transporters facilitate zinc uptake in the cells and their expressions are regulated by zinc. They play the critical roles in the occurrence and development of cancer and diabetes, and have relationship with inflammation. But the functions of a new gene, ZIP11 which is the sole member in the *gufA* subfamily of the ZIP-family are not yet been identified. The current study investigated the regulation of the ZIP11 gene by zinc and the mechanisms underlying changes in ZIP11 mRNA abundance. Meanwhile, we studied whether ZIP11 took part in zinc trafficking in the cells. Our results showed that the highest expression level of ZIP11 mRNA was found in mouse stomach, testis and cecum. The mRNA level of ZIP11 is regulated by the zinc content of the body using zinc-deficiency mouse model. Actinomycin D was used to prove that the mRNA level of ZIP11 regulated by zinc had no relation to the mRNA stability. We identify 5 MRE sequences upstream of the first exon of ZIP11, which are involved in response to elevated extracellular zinc concentration by luciferase reporter assay, and found that MRE2, MRE3 played major roles in positive regulation of ZIP11 promoter activity, and MRE5 played minor. In contrast, MRE4 had an opposite effect, while MRE1 had no effect on the promoter activity. These changes became more significant when MTF-1 was cotransfected with ZIP11 promoter. It implied that zinc regulated ZIP11 expression by binding the MRE sequence of ZIP11 promoter via MTF-1. In addition, detection of cellular MT level, staining of zinc with fluorescence probe, cellular zinc content, and cell viability assay after transfection of ZIP11 in HEK293 cells fully validated that ZIP11 was a zinc importer. These observations suggest that the novel gene, ZIP11 appears to function in zinc uptake cells, and its mRNA abundance is regulated by zinc binding to the MRE sequence of ZIP11 promoter via MTF-1.

Keywords: ZIP11/SLC39A11, Zinc Transporter, MRE

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Recent advances in chromium nutrition of animals

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Chromium (Cr) functions in the trivalent form to enhance insulin sensitivity. Until recently it has been assumed that practical diets for domestic animals contain sufficient Cr to meet animal requirements. However, over the past 15 years considerable research has indicated that swine, poultry, and cattle diets may contain inadequate amounts of bioavailable Cr to maximize animal health and productivity. Chromium supplementation to swine and cattle diets has increased insulin sensitivity following intravenous administration of glucose. In swine increasing dietary Cr has increased litter size in sows and reduced carcass fat in growing and finishing pigs. Supplementing high producing dairy cows with Cr has increased feed intake and milk production, especially in early lactation. Stress increases urinary losses of Cr, and studies in poultry and cattle have indicated that Cr supplementation to diets can alleviate some of the adverse effects of stress on animal productivity and health. Studies conducted in several different countries have reported that Cr supplementation improved growth and feed efficiency in broilers exposed to heat stress conditions. Chromium supplementation of calves stressed, via weaning and transporting, has reduced incidence of respiratory diseases in some studies. A number of studies in cattle and poultry have demonstrated that Cr can increase cell-mediated and humoral immune responses. Research has also indicated that Cr can reduce production of proinflammatory cytokines by activated immune cells.

Keywords: Chromium, Cattle, Poultry

Functional genomics of selenoproteins in pigs and chickens

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Exciting progress has been made in functional genomics of selenoproteins of rodents, but such research is scarce in pigs and chickens that are excellent models for human physiology. We first identified 25 porcine and 14 avian selenoproteins using in silico cloning followed by PCR. Using corn and soy produced in the Se-deficient area of Sichuan, China, we composed a Se-deficient basal diet (BD, 14 µg Se/kg) and conducted long-term feeding trials of pigs and broiler chicks. In the pig experiment, we determined effects of dietary Se deficiency (BD), adequacy (0.3 mg Se/kg as Se-enriched yeast), and excess (3.0 mg Se/kg) on gene expression of all 25 selenoproteins in various tissues using quantitative real-time Q-PCR. Responses of porcine selenoprotein gene expression to dietary Se concentrations exhibited three patterns. In the broiler experiments, day-old broiler chicks (n = 60/group) were fed the BD un-supplemented with Se or vitamin E, or the BD + rac- α -tocopheryl acetate at 50 mg/kg, Se (as sodium selenite) at 0.3 mg/kg, or both of these nutrients for 6 weeks. Classical Se/vitamin E deficiency diseases including exudative diathesis and pancreatic atrophy were replicated by feeding the current practical Se-deficient diet and the incidences were related to selenogenome expression in liver and muscle of chicks. Notably, expression of four selenoprotein genes was altered by dietary vitamin E concentrations. Lastly, we have induced moderate obesity and insulin resistance in pigs by feeding them with a high-fat diet and found that the induced-metabolic disorder enhanced or decreased gene expression of 17 selenoproteins in various tissues of pigs. Overall, our findings provide basic information on Se functional genomics and reveal novel metabolic roles of selenoproteins in metabolism of pigs and chickens that serve as major food-producers and relevant models of human disease.

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Keywords: Selenoproteins, Pigs, Chickens, Genomics

Distribution of total selenium species within the tissues and products of food producing animals

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Selenium (Se) supplements used in the diets of food producing animals typically come in two primary forms; inorganic (sodium selenite [Na₂SeO₃] [NaSe]) and organic (selenoyeast [SY]). Augmenting the diets of food producing animals with supplementary Se results in commensurate increases in the Se content of milk and tissues, and that when comparing comparable doses of NaSe and SY, responses of SY supplemented animals are markedly greater than those of NaSe. This difference has often been attributed to differences in the uptake and assimilation of the different selenium forms. Selenomethionine (SeMet), the predominant form of Se found in most SY supplements, can be ultimately utilised for either selenoprotein synthesis, or deposited/stored non-specifically within body proteins, whereas the fate of NaSe is either utilisation for selenoprotein synthesis or methylation and excretion. Within the studies that have compared NaSe and SY the deposition of SeMet has been postulated but little data has actually been presented on the actual deposition of selenized amino acids within the tissues and milk of food producing animals. Speciation analytical techniques have permitted the quantification of not only total Se but also identification and quantification of a number of selenium fractions. Studies using comparable doses of NaSe and SY in a range of livestock species confirm that the differences seen between sources in total Se accumulation within milk and tissue protein are primarily a consequence of SeMet incorporation. In addition, Se deposition (total Se and Se fractions) differs between tissue types (visceral [offal] and muscle) and is further modulated within tissue type by Se source. Furthermore, speciation data provides an insight into the effects that genotype and age have on the efficiency of organic Se capture; older unimproved genotypes tend not to accumulate SeMet to the same extent as improved genotypes and accumulation of SeMet in older animals is less pronounced than that of younger ones. Further advances in speciation analyses may provide additional information that could be used to more effectively target the use of Se supplements that may ultimately result in the production of functional foods with health promoting properties.

Keywords: Selenium, Speciation, Animal Food Products

Impacts of dietary supranutritional selenium on growth and vascularity of key nutrient transferring

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Dietary supranutritional levels of Se (HSe) occur in areas with elevated environmental Se or through supplementation above requirement but below toxicity. Maternal nutrition is a primary factor impacting growth and development of key nutrient transferring tissues (intestines, placenta, and mammary gland) involved in nutrient acquisition and delivery to offspring. Growth, development, vascularization, and function of these tissues are essential processes underlying nutrient uptake and expenditure, fetal development, immunological competence, neonatal survival, postnatal growth, and metabolic regulation. Tissue vascularization is crucial for nutrient transport across tissues; thus angiogenesis, or the formation of blood vessels, is critical for proper function. HSe fed throughout gestation in sheep has either increased ($P \leq 0.08$) or had no effect on lamb body weight near term. Maternal dietary HSe can alter growth and/or vascular measurements in intestinal, placental, and mammary tissues; with increased ($P \leq 0.05$) intestinal mass, crypt cell proliferation, and angiogenic factor mRNA expression associated with the VEGF and endothelial NO systems in some but not all studies. Placental cotyledonary tissues from first parity ewes fed HSe throughout gestation have greater ($P \leq 0.08$) DNA (mg/g), increase cellular proliferation, and elevated mRNA expression of VEGF receptor 1 compared with those fed adequate Se. Offspring (180 d old) from ewes fed HSe have demonstrated increased intestinal mass, increased visceral adiposity, decreased intestinal DNA, and increased capillary area density in intestinal villi. Interestingly, in these weaned and growing offspring from HSe fed ewes, digestion coefficients were reduced ($P \leq 0.07$) when compared with offspring from ewes fed adequate Se. Feeding ewes HSe during gestation resulted in increased mammary gland mass, capillary area density, capillary surface density, total colostrum yield, and increased milk yield for the first 20 d of lactation. Data are taken to indicate that dietary supranutritional Se can impact key nutrient transferring tissues at both the cellular and functional level.

Keyword: Maternal Nutrition, Selenium, Vascularization

Variation in mineral content of the food supply: lessons learned from studies of selenium

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Biofortification of plant foods with mineral elements has been attempted in many areas of the world with varying degrees of success. Molecular techniques as well as conventional selective breeding have been utilized to increase the iron and zinc content of multiple crops; especially for foods targeted toward food-insecure regions. The country of Finland has for twenty years used enriched fertilizer as a means of enhancing the selenium content of plant and animal foods. Studies of enhanced selenium content of animal and plant foods consumed in North America illustrate the complexities of biofortification. Both amount and chemical form of selenium in a food is affected by many factors including plant species, geographical location, year and farming system. Additionally, the selenium content of a plant has been shown to interfere with production of other phytochemicals. Nutritional databases often do not show potential variability, which may give a false picture of the food and nutrient supply.

Keywords: Food Composition, Selenium, Biofortification

Study on the effect of threonine chelated iron in piglets

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Iron (Fe) has many physiology functions, the required Iron for pigs were met from feed or supplements of inorganic Iron, organic Iron or amino acid chelated Iron. The objective of the present investigation was to evaluate the utilization of threonine-chelated Iron in weaned piglet diet. A total of 192 weaning pigs of 29d-old with the average body weight of 7.84 ± 1.11 kg were selected and allotted at random into four groups in 24 pens (8 piglets for each pen and 6 pens for each group), and fed one of the four diets (basal diet with 75mg/kg, 100 mg/kg, 125 mg / kg of threonine chelated Iron or 100 mg / kg of ferrous sulfate (FeSO_4)) for 27d. The results showed that dietary Iron source had significant effects on performance of weaned piglets ($P < 0.05$). Compared with inorganic iron, the feed conversion ratio of piglets fed diet containing threonine-chelated Iron significantly reduced ($P < 0.01$) and the average daily gain of piglets fed diet containing 100mg/kg or 125mg/kg threonine-chelated Iron increased by 15.15% and 6.06%. Adding threonine-chelated Iron also improve serum Fe^{2+} concentration, enhanced immune function, compared with inorganic Iron. Adding 100mg/kg threonine chelated. Iron increased serum IgG levels (0.62 vs 0.75 g/L, $P < 0.05$) and serum Fe^{2+} concentration (48.00 vs 65.58 $\mu\text{mol/L}$, $P < 0.01$). Dietary Iron source had no significant effect on serum ferritin and serum transferrin concentration and total iron binding capacity ($p > 0.05$), but it had significant effects on serum transferrin saturation ($p < 0.05$). Compared with inorganic iron, adding 100mg/kg or 150mg/kg threonine chelated Iron significantly increased Serum transferrin saturation ($P < 0.01$). Based on the above results, dietary threonine-chelated Iron supplementation (100-150 mg/kg) could effectively improve performance of weaned pigs by enhanced immune function, serum Fe^{2+} concentration and increased Serum transferrin saturation.

Keywords: Threonine-chelated Iron, Performance, Piglets

Effects of Cr⁶⁺ stress on the non-specific immunity of *Scylla paramamosain*

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A experiment was conducted to determine the effects of different concentrations of water-borne Cr⁶⁺ (0.5mg/L, 1.0mg/L, 2.0mg/L, 4.0mg/L, 8.0mg/L) stress and nature seawater (don't add Cr⁶⁺, as the control) on the immune parameters[total haemocyte count (THC), Phenoloxidase, Lysozyme, Ca²⁺-ATPase and Na⁺,K⁺-ATPase, superoxide dimutase (SOD), acid phosphatase (ACP), alkaline phosphatase (AKP)] of mud crab *Scylla paramamosain*. The results showed that THC decreased significantly after exposure to Cr⁶⁺ for 1d (P<0.05), and showed time-dose-effect relationship. The THC was restored gradually to the THC of the control group after 9d Cr⁶⁺ exposure (P> 0.05). Phenoloxidase activity was suppressed in hemolymph when exposed to different concentrations of Cr⁶⁺ for 1d (P<0.05), but the variation of PO activity was not related to Cr⁶⁺ concentration. Lysozyme activity was significantly elevated in hemolymph by 4.0 mg/L and 8.0 mg/L Cr⁶⁺. The activation depended on exposure time of Cr⁶⁺ (time-effect relationship), which suggested a decrease in activation with prolongation of exposure time. The antibacterial activity was significantly inhibited in hemolymph of (P<0.05), and showed the time-dose-effect relationship. The activities of Ca²⁺-ATPase and Na⁺,K⁺-ATPase were significant decreased by Cr⁶⁺ exposure in gills after 1d (P<0.05). The activities of Ca²⁺-ATPase and Na⁺,K⁺-ATPase were stimulated by Cr⁶⁺ increasing with time. Superoxide dimutase (SOD) activity was increased by Cr⁶⁺ exposure in gills, hepatopancreas and muscle (P<0.05). Acid phosphatase activities in gills, hepatopancreas, muscle of *Scylla paramamosain* were not significantly effected by Cr⁶⁺ exposure (P>0.05), while the alkaline phosphatase activity in gills, hepatopancreas, muscle of *Scylla paramamosain* activated by Cr⁶⁺ exposure. The effect of water-borne Cr⁶⁺ exposure on gill and hepatopancreas microstructure of *S. paramamosain* put up the dose-time effect. Some changes were observed in histopathological microstructure of gill and hepatopancreas after 9d.). In conclusion, the effects of Cr⁶⁺ stress on the non-specific immunity of *S. paramamosain* was significant.

Keyword: Chromium (Cr⁶⁺), *Scylla Paramamosain*, Immune Parameter

Mineral clearance from plasma and liver following injection with a trace mineral complex is affected by cattle breed

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Limited information is available concerning the influence of cattle breed on the clearance rate of trace minerals. The objective of this study was to examine the effects of injection with a new formulation of injectable mineral on liver and plasma concentrations of copper (Cu), manganese (Mn), selenium (Se), and zinc (Zn) in Angus and Simmental cattle. Ten Angus and ten Simmental steers were blocked by breed and initial BW (332 ± 33 kg) and injected with either Multimin[®]90 (MM) or sterilized saline (CON) at a dose of 1 mL/45 kg BW. Multimin[®]90 contains 60 mg Zn/mL, 10 mg Mn/mL, 15 mg Cu/mL (as disodium EDTA complexes), and 5 mg Se/mL (as sodium selenite). Steers received a corn-silage based diet and inorganic sources of Zn, Mn, Cu, and Se were supplemented at NRC recommended levels. Jugular blood was collected immediately prior to injection and at 8, 10 h and 1, 8, 15 days post-injection. Liver biopsies were collected 3 d prior to injection and on d 1, 8 and 15 post-injection. Plasma concentrations of Zn, Mn, and Se were greater ($P = 0.01$), and Cu tended to be greater ($P = 0.12$) over the 15 d post-injection period in MM steers vs. CON steers. Regardless of treatment, Simmental cattle had lower plasma concentrations of Cu, Zn, and Se ($P \leq 0.05$) compared with Angus cattle. Liver concentrations of Cu, Se, and Zn were greater ($P = 0.05$) in MM steers compared with CON steers in the post-injection period. Liver Mn concentrations tended to be greater ($P = 0.06$) in MM steers compared with CON steers in the days post-injection. Interestingly, Simmental cattle exhibited greater ($P = 0.01$) liver Mn concentrations in the days following injection compared with Angus cattle (7.0 and 6.0 mg/kg Mn), regardless of treatment. It is unclear if this breed difference is biologically relevant; however, these data may suggest that differences in liver excretion of Mn exist between the two breeds. Overall, this study identified breed differences among Angus and Simmental cattle in the clearance rate of an injectable TM, suggesting that cattle of different breeds may benefit from specialized mineral supplementation programs. Future research may explore potential breed differences in expression of genes encoding proteins involved in mineral metabolism.

Keywords: Cattle, Breeds, Minerals

Selenium status of livestock in the Tibetan autonomous region of China

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Livestock production is the predominant industry in the Tibetan Autonomous Region (TAR) of China. A national Chinese survey in 1979–1982 found low selenium content (<0.02 ppm DM) in forages and feed supplements over large areas of TAR. It is likely that livestock in many counties of TAR across three main production systems could be at risk from selenium deficiency resulting in poor production and health and increased mortalities. We conducted two surveys of the mineral status of Tibetan yaks and dairy herds and sheep flocks in a total of 8 counties that are laterally distributed across 3 different livestock production systems: pastoral, cropping and agro-pastoral. The first survey was during 2003 and 2004 in the late autumn/early winter and late winter/early spring respectively, when livestock are unable to graze and are maintained on stored roughage and supplements fed near villages and households. The second survey was during 2009 in the summer and early autumn which is the peak growing period for pastures. We found that yaks and dairy cattle were at risk from Se deficiency with blood Se (BSe) values < 0.25 µmol/L. The lowest county mean BSe concentrations in yaks in the pastoral system were 0.08 µmol/L (first survey) and 0.13 µmol/L (second survey) and in the agro-pastoral system 0.22 µmol/L (first survey) and 0.25 µmol/L (second survey). Dairy cattle in a crop-based county near Lhasa had a mean BSe of 0.23 µmol/L in summer. The lowest herd mean BSe concentrations were 0.09 µmol Se/L for dairy cattle in one river-valley village in central Tibet and 0.10 µmol Se/L for yaks in a pastoral location in northern Tibet. Sheep were usually found to have BSe concentrations > 0.5 µmol/L and were considered not at risk from selenium deficiency. However, there is some dispute that the deficiency threshold for sheep should be higher at 0.9 µmol Se/L. Se status of livestock was dependent on location, with significant variation between county locations and between villages and households within counties. Moreover, it was difficult to interpret the overall impact of the selenium status on livestock production and health because of confounding factors such as the poor feedbase limiting protein and energy supply, inadequate veterinary programs, and poorly conceived agronomic programs.

Keyword: Selenium, Livestock, Tibet

Copper status of livestock in the Tibetan autonomous region of China

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Livestock production is the predominant industry in the Tibetan Autonomous Region (TAR) of China. An earlier mineral survey conducted in 7 counties during the late autumn/early winter and late winter/early spring of 2003-2004 found pastures and many feed supplements were inadequate in copper (<5 mg Cu/kg DM) for livestock. These findings also varied according to geographic location within the counties. However, copper deficiency diseases are difficult to diagnose in grazing livestock on the basis of copper concentrations in soil, pasture and plasma. Notwithstanding this, plasma copper concentrations of < 9 µmol Cu/L, observed in the sheep, dairy cattle and yaks surveyed, can indicate primary chronic copper deficiency (CCD). The possibility of induced CCD can also be inferred from the low copper to molybdenum ratios (i.e. <3:1) measured in feedstuffs, as well as the presence of other copper antagonists such as high iron and sulfur concentrations in the pastures. Tibetan livestock could be at risk from both primary and induced copper deficiency resulting in impaired growth, poor neural, reproductive and immune function, and reduced general health.

In 2009, we conducted additional surveys to extend our findings into the warmer and wetter growing period of summer and early autumn. The same 7 counties from the earlier 2003-2004 survey plus another county were re-visited, being representative of pastoral, cropping and agro-pastoral livestock production systems. Yaks and dairy cattle were sampled from a total of 5 and 15 towns respectively in summer, of which town mean plasma copper of <9 µmol/L were found in 4 and 10 of these towns, respectively. In contrast, copper deficiency was less of a problem in sheep, with the overall mean total plasma copper concentration of 11 µmol Cu/L, pooled for season. Moreover, significant variation in copper status between and within counties was evident in all livestock species surveyed. In some instances normal plasma copper concentrations (i.e. > 9 µmol Cu/L) were associated with a high proportion of TCA-insoluble copper. These results support earlier findings from the 2003-4 survey that copper-induced deficiencies may occur in Tibetan livestock. The importance of potential copper antagonists must also be considered.

Keywords: Copper, Livestock, Tibet

Symposium 13(M)

Title: Genomics of Selenocysteine and Selenoproteins

Sponsor: TEMA-14

Location: Conference Room 2

Cysteine/selenocysteine replacement in selenoproteins: a novel pathway for cysteine biosynthesis and its consequences on selenoprotein function

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Cysteine (Cys) is normally incorporated into proteins in response to its genetic codewords, UGC and UGU. However, we have found that NIH 3T3 cells, when grown in the presence of thiophosphate, insert Cys in response to the selenocysteine (Sec) codeword, UGA, in thioredoxin reductase 1 (TR1). This Cys residue was synthesized by Sec synthase (SecS) on tRNA^{[Ser]Sec}. The incorporation of Cys in place of Sec was dependent on the Sec insertion sequence element in the 3'UTR of TR1 mRNA. Furthermore, selenophosphate synthetase 2 that normally synthesizes the active selenium donor, selenophosphate, was found to also catalyze thiophosphate formation in the presence of ATP and sulfide which, in turn, reacted with phosphoseryl-tRNA^{[Ser]Sec} to generate Cys-tRNA^{[Ser]Sec} in the presence of SecS. Cys was also found to occur *in vivo* at UGA codewords in mouse liver TRs. Cys/Sec replacement in liver was regulated by dietary selenium wherein Cys occurred at 10% of the Sec levels in TR 1 of mice maintained on a diet with normal levels of selenium and at 50% in liver TR1 of mice on a selenium deficient diet. The data demonstrate a unique Sec machinery-based mechanism for *de novo* biosynthesis of Cys and its incorporation into protein in response to UGA Sec codewords. These results also suggest new biological functions for thiophosphate and sulfide in mammals. We are currently examining the levels of Cys/Sec replacement, and/or the occurrence of other amino acids, in TR1 and glutathione peroxidases 1 and 4 in mammalian cells grown in the presence of various antibiotics and in cancer cells.

Keyword: Cysteine, Selenocysteine, Thioredoxin Reductase 1

Biogenesis and translation of selenoprotein mRNAs

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The amino acid selenocysteine is the major biological form of selenium. It is specifically incorporated into the active site of selenoproteins, a family of oxidation-reduction enzymes involved in a variety of important functions, such as reduction of reactive oxygen species, thyroid hormone maturation, sperm maturation and muscle development. Selenocysteine sets apart from the other amino acids because of its peculiar biosynthesis pathway and incorporation mechanism into selenoproteins in response to a reprogrammed UGA codon. A complex machinery is involved in selenoprotein synthesis whose mechanism of action is far from being understood. Among the molecular components of the machinery, of prime importance are the SECIS element, an RNA stem-loop lying in the 3' untranslated region of selenoprotein mRNAs, and the SECIS-binding protein SBP2. We have established that the RNA binding domain of SBP2 is composed of two distinct modules, one of which providing selectivity to SECIS elements and binding specificity to the ribosomal 60S subunit. We also discovered that the assembly and maturation pathway of selenoprotein mRNAs into messenger ribonucleoprotein particles is idiosyncratic. It shares molecular complexes, protein chaperones and structural features with small nuclear RNPs (snRNAs) and small nucleolar RNPs (snoRNAs) involved in pre-mRNA splicing and ribosomal RNA maturation, respectively. These similarities, combined to the occurrence of SECIS RNA-like motifs in sn(o)RNAs, suggest a common evolutionary origin of some of the building blocks constituting the selenoprotein synthesis machinery and sn(o)RNPs.

Keywords: Selenoprotien, 3' Untranslated Region, UGA codon

Functional genomic studies of selenoprotein function

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Selenium (Se) exerts many of its biological functions through its incorporation as selenocysteine into selenoproteins. Genomic approaches using transcriptomics, siRNA gene silencing or single nucleotide polymorphism (SNP) analysis are providing new insights into selenoprotein function and biochemical pathways affected by Se intake. Since marginally low Se intake may modulate colorectal cancer (CRC) risk, we are using these approaches to investigate roles of Se and selenoproteins in the colon. Reporter gene, protein-RNA binding and over-expression studies suggest that rs713041, a SNP present in a region of the glutathione peroxidase 4 gene (GPX4) corresponding to the 3' untranslated region (3'UTR), influences 3'UTR function and interferes with the selenoprotein hierarchy in Caco-2 cells. rs713041 also affects the response of lymphocyte glutathione peroxidase 1 and 4 activity to Se supplementation in healthy volunteers. Additionally, two SNPs in the selenoprotein P gene (SEPP1), one in the coding region (rs3877899) causing an amino-acid change and one in the 3'UTR (rs7579) affect the pattern of plasma isoforms of human SePP. Additionally, both rs3877899 and rs7579 were found to affect various blood markers of Se status. Genetic association studies suggest that SNPs in SELS, GPX4, and SEPP1, and interactions with other variants, influence risk of CRC. Gene microarray studies in mice indicate that expression of GPx1, SelW, SelH, SeP15 and SelM are particularly sensitive to Se intake (Kipp et al, 2009 Mol Nutr Food Res. 53:1561-72). Additionally bioinformatic analysis indicates that a variety of pathways are affected by moderate changes in Se intake: Wnt signaling, translation, mTOR signaling, NFκB signaling, and Nrf2-regulated pathways. siRNA gene silencing and reporter studies indicate that SelH knock-down affects Nrf2 signaling and that Se supply affects NFκB signaling response to TNFα in Caco-2 cells. Our studies emphasize the potentially important roles of selenoproteins SePP, SelS and SelH in colonic cell function. *Funding from Food Standards Agency, NuGO, Wellcome Trust, Newcastle Healthcare Charity and World Cancer Research Fund is gratefully acknowledged.*

Keywords: Selenium, SNP, Colon

Selenoprotein engineering

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Selenium is naturally incorporated into proteins, in the form of selenocysteine and selenomethionine. Due to the potent nucleophilicity of selenium anion, selenocysteine is ubiquitous in many important human proteins, such as deiodinase, peroxidase and protein disulfide isomerase. Therefore, deficiency of selenium is often associated with human disease, and dietary supplement of selenium can improve health and longevity. Despite biologists' strong interest in selenium proteins, it has been difficult to obtain selenium proteins, severely limiting our ability to investigate their structure, mechanism and implications in human health. This difficulty is largely due to the different protein translation mechanism of selenocysteine between prokaryotes and eukaryotes. Recently, we have devised genetic engineering and biosynthetic routes to facilitate the site-specific incorporation of phenylselenocysteine in *E. coli* (Jiangyun Wang et al. *Angew. Chem. Int. Ed.* 2007, 46, 6849–6851), and made significant progress to genetically encode selenocysteine, and other interesting selenium-containing amino acids. Our progress in this area will be presented in this conference.

Keyword: Selenocysteine, Unnatural Amino Acid, Genetic Codon Engineering

Selenoprotein W, a selenoprotein in search of a function

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Since selenium (Se) status influenced the levels of selenoprotein W (SeW) in animal tissues, the levels of SeW were determined in tissues from Chinese living in deficient, normal and excess Se area of China. SeWs were lowest in tissues from people living in deficient areas, intermediate in those living in adequate areas and highest in those living in high Se areas. SeW sequences have been determined in chickens, zebrafish, frog, sheep, cattle, horse, dog, pig, rat, mouse, humans, monkeys and orangutan. Rodent SeWs contain four cysteines but only two in this selenoprotein from all other species of animals. Cysteine at the 9th position and selenocysteine at the 13th position are present in all 13 species of animals. The homology of the coding nucleotide sequences and deduced amino acid sequences of SeW varied from 55 to 60% between chicken and other animal SeWs from mammals to aquatic invertebrates. However, when chicken, zebrafish and frog were not included the homology of SeWs was much higher (81 to 98%) among the other animals. Many functions have been proposed but the primary one has yet to be definitely determined.

Keywords: Selenoprotein W, Species Differences, Biological Function

Selenium-dependent skewing of macrophage phenotypes and its consequences in a cancer model

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Selenium (Se) in the form of selenoproteins, imparts many health benefits and anti-inflammatory properties. In the present study, we investigated the anti-inflammatory activity of Se using a LPS and IL4 treated murine bone marrow-derived macrophage model. Supplementation with Se (100-250 nM) of IL4 treated macrophages significantly increased the expression of alternatively activated macrophage (M2) markers, Arg-I and Mrc-1. Se treatment also increased the enzymatic activity of Arg-I and surface expression of Mrc-1. Conversely, expression of classically activated macrophage (M1) markers, TNFa, and IL1b, were significantly decreased in LPS treated macrophages that were cultured in 100 nM Se and IL4, suggesting a synergistic effect of Se and IL4. Furthermore, studies with inhibitors of two transcription factors, PPAR γ and STAT6, which are pivotal for the activity of Se and IL4, respectively, completely ablated the Se dependent expression of M2 markers. Similar results were also obtained with pharmacological inhibitors of hematopoietic prostaglandin D2 synthase enzymes, suggesting Se supplementation of macrophages produces endogenous activators from the arachidonic acid pathway to mediate PPAR γ -dependent switch from M1 to M2 phenotype in the presence of IL4. Furthermore, treatment of leukemia stem cells from two diverse models of leukemia showed that switching of macrophage phenotype is critical from the apoptosis of these cancer stem cells. These data show that selenium status is a critical regulator of macrophage activation, which is pivotal to activate pathways of anticarcinogenic mechanisms in cancer stem cells as well as effect wound healing and resolution of inflammation. *NIH DK077152*

Keywords: Prostaglandins, Macrophages, Cancer Stem Cells

Inhibition of selenocysteine tRNA^{[Ser]Sec} aminoacylation provides evidence that aminoacylation is required for regulatory methylation of this tRNA

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Selenium is incorporated into protein as selenocysteine (Sec), the 21st amino acid in the genetic code. There are two isoforms of Sec tRNA^{[Ser]Sec} that differ by a single methyl group, Um34, at the wobble position. The non-Um34 isoform supports the synthesis of a subclass of selenoproteins, designated housekeeping, while the Um34 isoform supports the expression of another subclass, designated stress-related selenoproteins. We investigated the relationship between tRNA^{[Ser]Sec} aminoacylation and Um34 synthesis which is the last step in the maturation of this tRNA. Mutation of the discriminator base at position 73 in tRNA^{[Ser]Sec} dramatically reduced aminoacylation with serine, as did an inhibitor of seryl-tRNA synthetase, SB-217452. Although both the mutation and the inhibitor prevented Um34 synthesis, neither precluded the synthesis of any other of the known base modifications on tRNA^{[Ser]Sec} following microinjection and incubation of the mutant tRNA^{[Ser]Sec} transcript, or the wild type transcript along with inhibitor, in *Xenopus* oocytes. The data demonstrate that Sec tRNA^{[Ser]Sec} must be aminoacylated for Um34 addition. The fact that selenium is required for Um34 methylation suggests that Sec must be attached to its tRNA for Um34 methylation. This would explain why selenium is essential for the function of Um34 methylase and provides further insights into the hierarchy of selenoprotein expression.

Keyword: Selenocysteine, tRNA Methylation, Um34

Iron status modulates tRNA thiouridine biosynthesis and its modification in rat skeletal muscle and L6 myotubecell

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Transfer RNA (tRNA) modifications play an important role in decoding of mRNA to ribosome. A lot of modified nucleosides are found in wobble positions, especially uridine. tRNA^{Lys}(UUU), tRNA^{Glu}(UUC) and tRNA^{Gln}(UUG) are modified to 5-methoxycarbonylmethyl-2-thiouridine (mcm5s2U), required for the proper decoding of NNR codons. IscS/Nfs1p and IscU is required for the post-transcriptional modification of thiouridine in tRNAs in yeast, however, such processes are still unknown in mammals. Mitochondrial IscS protein level was specifically decreased in iron-deficient rat skeletal muscle. Therefore, we investigated biosynthesis and thio-modification of tRNAs in modified iron status. Weanling male Wistar-strain rats were divided into control control (35 mg Fe/ kg diet, C) or an iron-deficient group (< 6 mg Fe/kg diet, ID) , or the pair-fed control group (PF group; D group intake normal iron) . At 6 weeks, rats were killed and hind leg skeletal muscle sampled. Also rat L6 myotube cells were cultured with or without the iron chelator deferoxamine. Using 2 different iron deficiency models, we firstly demonstrated iron deficiency decreased the thio-modification in cytosolic tRNA^{Lys}(UUU) and tRNA^{Glu}(UUC), but not in mitochondrial tRNA^{Lys}(UUU) and tRNA^{Glu}(UUC). The modified nucleotide profile analyzed by HPLC also demonstrated the mcm5s2U content in DFO-treated L6 myotube was decreased to 48% of without DFO-treated cell. In addition, dietary iron deficiency decreased the expression of cytosolic tRNA^{Lys}(UUU) and tRNA^{Glu}(UUC), however, there was not affected on DFO-treated L6 myotube cell. On other hand, dietary iron deficiency decreased mitochondrial IscS protein level in skeletal muscle to 74% of those of the control, while mitochondrial IscU was increased about 50% in iron-deficient rat skeletal muscle. In summary, our study is the first using in vivo and in vitro model to demonstrate that the thio-modification of tRNA is modulated by iron deficiency, and suggests that the iron-sulfur cluster machinery may be involved in regulation of cytosolic tRNA thio-modification in skeletal muscle.

Keywords: Iron, Transfer RNA, Thiouridine-modification

Application of proteomic techniques for the discovery of zinc status biomarkers

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There is no reliable biomarker for the determination of zinc status. Although plasma protein is a rich source for biomarker discovery, low-abundance proteins with greater diagnostic potential, are often masked by the presence of the high-abundance plasma proteins. The aim of this study was to develop a reliable plasma sample preparation method and apply 2-DE proteomic analysis, using plasma from zinc deficient rats, to find novel biomarkers of zinc status. 50 rats were randomly divided into 5 groups and fed for 2 weeks with a semi-synthetic diet of different Zn content: acute zinc deficiency (<1mg Zn/kg), zinc deficiency (3mg Zn/kg) and zinc adequacy (35mg Zn/kg), along with pair-fed groups. Seppro rat spin columns were initially used to remove the seven most abundant proteins from plasma and molecular filtration was used for concentration and desalting. Different protein loading amounts, two sizes of 2-DE gels and two staining procedures were also compared. 200 µg of protein loaded on 17cm 2-DE gels stained with coomassie provided a better visualization. Gel images from both flow-through (depleted) fractions and bound proteins of plasma from 20 rats, and also 4 quality control samples, were analysed using Samespots software. There were 553 spots in depleted gels and 582 spots in bound gels. Three proteins were up-regulated and 5 proteins down-regulated by acute zinc deficiency. The statistical significance of the results was limited because of the low reproducibility of the Seppro columns. Single-use ProteinExtract Albumin/IgG removal kits were then used to remove the abundant plasma proteins, and they gave better recovery of depleted protein and stable reproducibility (CV=7.1%). 300µg of both depleted and bound plasma protein from 50 rats and 6 quality controls were analysed on 2-DE gels and the identity of 35 significantly changed proteins was obtained by trypsinisation and LC/MS/MS. Enzyme-linked immunosorbent assay (ELISA) and western blot analysis are being used to validate results from 2-DE gel analysis. *This project was funded by the Scottish Rural and Environment Science and Analytical Services, the National Research Foundation of Korea (Grand No. NRF 220-2008-1-F00013) and LIRANS strategic research fund.*

Keywords: Zinc, 2-D gel, Plasma

Molecular cloning, chromosomal localization and expression profiling of porcine selenoprotein M gene

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Selenoprotein M may regulate a myriad of biological processes through its redox function. In pigs, neither the nucleotide sequence nor the amino acid sequence of the protein is known. Furthermore, patterns of tissue expression and regulation by dietary selenium (Se) have not been examined. We determined the full coding sequence (CDS) and the chromosomal location of the porcine gene, *SELM*, and described its expression profile *in vivo* under different dietary Se concentrations. The cDNA sequence of porcine *SELM* from the start codon to the poly(A) tail was cloned by reverse transcription PCR. The CDS contained 429 bases with a typical mammalian selenocysteine insertion sequence of form 2 (F2) located in the 3'-untranslated region. The gene was mapped to chromosome 14q21, where porcine *SELM* and its neighboring genes exhibited a similar organization to human homologues on chromosome 22q12.2. The expression pattern of *SELM* mRNA in muscle, thyroid, cerebral cortex, pituitary, testis, liver, and kidney was analyzed with real-time quantitative PCR in young male pigs fed a Se-deficient corn-soybean meal basal diet supplemented with 0.0, 0.3, or 3.0 mg Se/kg in the form of Se-rich yeast. Though the *SELM* mRNA abundance in each of the 7 tissues was not affected by the dietary Se concentrations, it was significantly higher in thyroid ($P < 0.01$) than in cerebral cortex, pituitary, testis, liver, and kidney at all of the 3 dietary Se concentrations.

Keywords: Selenoprotein M, Chromosome Location, Expression, Thyroid, Pig

Symposium 14(N)

Title: Trace Element Toxicology and Geochemistry

Sponsor: TEMA-14

Location: Conference Room 3

MeHg exposure pathway to inhabitants in Guizhou, China

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Me-Hg is highly toxic, and the nervous system is its principal target tissue for humans. Although the general population is primarily exposed to Me-Hg through contaminated fish and marine mammals, in Hg mining areas a long history of mining activities can produce serious Hg pollution to the local environment. In a study of 98 persons from the Wanshan Hg mining area, hair Me-Hg levels indicated Me-Hg exposure. Rice, the staple food of the local inhabitants also showed high total Hg (T-Hg) and Me-Hg levels. The geometric mean concentration of T-Hg and mean concentration of Me-Hg in rice samples collected from 3 villages in Wanshan Hg mining area were 36.2 , and 8.5 $\mu\text{g}/\text{kg}$, respectively, which were significantly elevated compared to the rice samples collected a reference area, where the mean T-Hg and Me-Hg concentrations were 7.0 and 2.5 $\mu\text{g}/\text{kg}$, respectively. Pork meat, vegetable, and drinking water samples collected in Wanshan Hg mining area contained highly elevated T-Hg, but very low levels of Me-Hg. The relationships between the estimated rice Me-Hg intake and hair Me-Hg levels confirmed rice with high Me-Hg levels indeed was the main route of Me-Hg exposure for the local residents in the Wanshan Hg mining area. From our study, we can conclude that the main human exposure to Me-Hg via food consumption is not restricted to fish, but in some cases in mining areas of China to frequent rice meals. We then used Guizhou province a region seriously contaminated with Hg in China. In four case study regions with severe pollution from Hg mining and smelting (Wanshan), traditional zinc smelting (Weining), heavy coal based industry (Qingzhen) and a village in a remote Nature Reserve (Leigong). The probable daily intake (PDI) of MeHg for adult population was considerably higher in Wanshan than the other three places. The PDI of MeHg for residents in the three other regions were all well below 0.1 $\mu\text{g}/\text{kg}$ bw/day . In all four regions, rice consumption accounted for 94–96% of the PDI of MeHg. The major finding from our study is that rice consumption is by far the most important MeHg exposure route, however, most of the populations have low PDI of MeHg.

Keywords: Methylmercury, Exposure, Rice

Influence of aluminum on the transcriptional regulation of gene expression

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Aluminum is the most abundant metal and the third abundant element in the earth's crust. However, aluminum is not an essential element for man and animals but causes harmful effects. Therefore, living bodies are not able to escape the toxicity of aluminum in the environment. The rate of excretion of aluminum in the urine was assumed to have a limiting value [1]. Therefore, an excess intake of aluminum indicated that aluminum content in the body remained high for several days after the absorption of aluminum from the intestine. It is widely known that accumulation of aluminum in the body has been linked to disease conditions [2-4]. The toxic effects of aluminum to neuronal cells were examined to show apoptotic cell death via endoplasmic reticulum stress, implicating an influence of aluminum on the gene expression [5, 6]. Also, it was shown that astrocyte-neuron interaction was important in the process of toxic effects in the central nervous system [7]. In addition, renin was the only positively identified up-regulated gene in kidneys determined by DNA sequencing [1]. The up-regulation of renin was confirmed by RT-PCR and Western blotting experiments in the dose dependent treatments and the time course observation in mice. The up-regulation of the renin expression by aluminum is a strong indication of the influence of aluminum on the renin-angiotensin-aldosterone-system, resulting in the induction of essential hyper-tension. The role of the transcriptional network is widely recognized to be important in the regulation of gene expression. The interaction of the transcription factors may explain the wide variety of regulation of genes. Molecular mechanism of the influence of aluminum on gene expression will be presented.

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Keywords: Aluminum, Transcription Factor, Gene Expression

Environmental biogeochemistry of high arsenic groundwater

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Long-term intake of arsenic-contaminated groundwater has caused endemic arsenic poisoning in parts of China. A case study has been made for more than ten years at Datong Basin of northern China. The high arsenic and fluoride groundwaters from Datong basin are mostly soda waters with Na/(Cl+SO₄) (meq) ratio greater than unit, arsenic and fluoride up to 1547 µg/L and 10.4 mg/L respectively, and with pH between 7.6 and 9.1. The high pH condition of soda water favors arsenic desorption from oxyhydroxide surfaces, thereby increasing the concentration of As in the aqueous phase. Microcosm experiments were conducted to understand the mechanism of microbially mediated mobilization of Fe and As from aquifer sediments. An arsenic-resistant strain (16S rRNA 99.9% similar to *Arthrobacter*, family Micrococcaceae) isolated from aquifer sediments of a borehole specifically drilled for this study at Datong basin was used as inoculated strain, and glucose and sodium acetate as carbon sources for the experiments. The results of the microcosm experiments revealed the important role of microbial activities on Fe and As mobilization and also their strong geochemical affinity. The difference in magnitude of Fe and As release may reflect the effect of carbon source on the growth pattern and composition of microbial communities. Biomarker and hydrochemical characteristics of geogenic arsenic-contaminated aquifers were also analyzed to understand the impact of natural organic matter (NOM) biodegradation on arsenic enrichment in groundwater. This indicates that the mobilization of arsenic within aquifer system is related to the reductive dissolution of Fe-oxyhydroxides and/or the competitive adsorption of HCO³⁻. Microbial reduction and oxidation of Fe-oxyhydroxides and native organic matter could occur within the aquifer system. All the sediments contain petroleum-sourced hydrocarbons, which may have undergone biodegradation, as suggest by the dominance of C₂₅-C₃₁ n-alkanes, C₂₉ sterane and the distribution pattern of hopanes. The presence of unresolved complex mixtures (UCMs) in all samples also indicates the effect of biodegradation.

Keywords: Biogeochemistry, Arsenic Groundwater, Datong Basin

Effect of selenium-enriched broccoli extract and various selenocompounds on arsenic-induced toxicity

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Accumulation of arsenic (As) in ground water and plants poses a health risk to both humans and animals. Selenium (Se) is a trace element essential for animal and human growth, and may exert its protective effect on As-induced toxicity through modulations of cell proliferation, cell cycle progression, activities of antioxidative-related enzymes and gene expression of other related proteins. The objective of this study was to investigate the possible mechanism involved in the Se effect on As-induced toxicity. Selenium-enriched broccoli extract (SeB) and several selenocompounds (sodium selenite, sodium selenate, selenomethionine, selenomethylselenocysteine) were used to investigate the potential effect of Se on arsenic trioxide (As₂O₃)-induced cytotoxicity in primary culture of porcine aortic endothelial cells (PECs). PECs were pretreated with 1 μM of Se for 24 hr prior to 20 μM As₂O₃ treatment up to 24 hr. Cell viability, cytotoxicity, cell cycle progression, apoptotic effect, related enzyme activities and gene expression pattern were investigated. The results from trypan blue exclusion and MTT assay indicated that Se treatment at 1 μM did not induce cytotoxicity in PECs, and Se pretreatment reduced the cytotoxicity induced by 20 μM As₂O₃. Se treatment did not affect cell cycle progression, but the apoptosis was reduced by SeB in As₂O₃-treated PECs at 8 hr. Pretreatment of Se did not affect the activities of glutathione-S-transferase (GST) and superoxide dismutase (SOD) in As₂O₃-induced PECs. However, cellular glutathione peroxidase (cGPX) activity was increased after Se pretreatment in As₂O₃-induced PECs. The mRNA level of selenoprotein W (SeW) was increased by Se pretreatment, but the mRNA levels of MDR1 and MRP2 were increased only by SeB pretreatment in As₂O₃-induced PECs. The results in this study indicated that SeB may protect PECs from As₂O₃-induced cytotoxicity through reduction in apoptotic event, increase in cGPX activity, and modulation in gene expression of SeW and multidrug resistance transporters.

Keywords: Se-enriched Broccoli Extract, Arsenic Trioxide, Porcine Aortic Endothelial Cells

Heavy metals contamination and human risk assessment in the vicinity of abandoned gold mine site in Korea

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Korea has a long history of gold mining and the most extensive activities occurred during the early and middle 20th century, and most of Au mines have been abandoned during 1970s – 1990s without any environmental treatments of the mine sites. In this paper the Songcheon(SC) gold mine was selected in order 1) to investigate the contamination levels and dispersion patterns of arsenic and heavy metals(Cd, Cu, Pb, Zn and Hg) in the vicinity of the mine site, 2) to estimate the bioaccessible fractions of the metals in soils and plants by using the SBET(Simple Bioavailability Extraction Test) and the EHS(Extraction of Heavy metals in Stomach and small intestine) test, and 3) to assess the risk of health effects on the residents around the mine areas. Samples of tailing, soil, crop plant and water were collected around the mine site and analyzed for As, Cd, Cu, Pb, Zn and Hg by ICP-AES and ICP-MS. Contamination levels of As and heavy metals were plotted around the mine site, and the pollution index (PI) of multi-elements in soil was proposed in this study. The average of human-bioaccessible fraction in soil and crop plants was estimated. The main contamination sources of As, Cd, Cu, Pb, and Zn in study area are from tailings and their effluents according to ore and gangue mineralogy. The contamination level of Hg is almost negligible except for some mine tailings. The suggested pathways of contaminants were from mine tailings – agricultural soil/groundwater- to finally human. From the results of the SBET and the EHS test, the hazard index (HI) value of the SC is 37.5 and 16, respectively, and particularly hazard quotient (HQ) value of As of the mine is 26.3 and 15, respectively. The cancer risk for As of SC mine is estimated as 4.6 E-03(SBET by drinking water pathway) and 2.7 E-03 (EHS test), which exceed the acceptable risk (1 in 100,000) for regulatory purposes.

Keyword: Heavy Metals, Gold Mine, Human-Bioaccessibility, Risk Assessment

Potential health risk of multielemental exposure through foodstuffs from Wanshan mercury mining area, China and effect of selenium supplementation in local residents

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The town of Wanshan in Northeastern Guizhou was one of the largest mercury mining areas in China since the Qin Dynasty (ca 220 BC). Large-scale mining and smelting activities officially ceased in 2001, and new regulations restrict mercury emissions. Owing to the long history of mercury-related activities, local residents in Wanshan, Guizhou, China, have suffered from long-term mercury exposure. Multielemental concentrations were determined by inductively coupled plasma-mass spectrometry (ICP-MS). The target hazard quotient (THQ) and hazard index (HI) were calculated to evaluate the potential human risk from individual heavy metals. The average contents of Hg, Pb, Cd, Mn, and Se in most frequently consumed foodstuffs were: 31, 248, 121, 1035, and 32 µg/kg respectively. Among them, Cd and Hg were the most important contributors to heavy metal contamination. Eight of 10 vegetables were contaminated heavy metals but the sampled rice, pork, radish and potato were below the safe level of the Chinese food hygienic limits of toxic heavy metals. In this study, the average dietary intakes of Hg, Pb, Cd, Mn, Se by an adult man of 60 kg living in Wanshan were: 27, 167, 86, 1061, 42 µg/day. The HIs for multielement dietary intake were 3.11, with the relative contributions of Hg, Pb, Cd, Mn and Se as 22.3%, 24.3%, 45.0%, 3.9% and 4.4, which indicates potential health risk. Vegetables were the main source of heavy metal dietary intake, and rice the secondary contributor. Thus 103 volunteers from the Wanshan area were recruited 53 were supplemented with 100 µg of Se daily as selenium-enriched yeast for 3 months while 50 volunteers received placebo. Significantly increased urinary mercury excretion was observed and urinary malondialdehyde concentrations 8-hydroxy-2'-deoxyguanosine concentration decreased significantly after Se supplementation. This 3-month selenium supplementation trial indicates that daily supplementation of 100 µg of selenium in the form of selenium-enriched yeast can help the urinary excretion of mercury and decrease oxidative damage to lipids and DNA in long-term mercury exposed people.

Keywords: Selenium, Yeast, Mercury, Excretion

Aluminium contamination in parenteral iron therapies: is patient exposure a problem?

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Parenteral iron therapy is used in the treatment of severe iron deficiency anaemia, mostly in patients with end stage renal failure, but also in patients poor iron absorption. Parenteral iron therapy involves the iiv delivery of a high concentration of sugar complexed iron, of the order of 20 to 100 mg ml⁻¹, in doses of 2 to 4 ml via dilution in a vehicle such as saline. However, if clinical circumstances demand it, a greater dose may be administered (up to 15–20 mg of iron/kg of body weight). Here we have shown that in four parenteral iron agents, available via prescription in the UK, iron is delivered with minor mineral contaminants, particularly aluminium. An inductively coupled plasma mass spectrometry (ICP-MS) screening analysis was undertaken for ferric carboxymaltose, iron(III) dextran complex, iron(III) isomaltoside and iron(III)-hydroxide sucrose complex. Interestingly, As, Tl, Mn and Br were observed in all four agents at approximate levels of 0.1, 0.3, 10 and 30 µg ml⁻¹ respectively. Aluminium levels ranged from 0.3 to 42 µg ml⁻¹. Subsequently, ICP – optical emission spectrometry (ICP-OES) confirmed the following range of aluminium concentration: ferric carboxymaltose (n = 2 different batches) = 0.51 and 1.54 µg ml⁻¹; iron(III) dextran complex (n = 2 different batches) = 0.32 and 41.65 µg ml⁻¹; iron(III) isomaltoside = 4.82 µg ml⁻¹; iron(III)-hydroxide sucrose complex = 14.65 µg ml⁻¹. The U.S. food and drug administration (FDA) has indicated in a warning letter (NDA 08-809) that patients with impaired kidney function will accumulate toxic levels of aluminium when receiving 4 - 5 µg Al/kg of body weight/day with tissue loading possible at lower levels. The data we present indicate that administration of iron(III) dextran complex or iron(III)-hydroxide sucrose complex could deliver 2.2 and 2.0 µg Al/kg of body weight/infusion respectively (assuming a 4 ml iron(III) dextran complex infusion (at 41.65 µg ml⁻¹ Al concentration) or a 10 ml iron(III)-hydroxide sucrose complex infusion is administered, i.e. a 200 mg iron dose for both as described in manufacturer guidelines). Such levels are only slightly lower than those noted by the FDA and although patients would not receive daily infusions they may be as frequent as 3 per week. This aluminium is also co-delivered with a high dose of iron that will saturate transferrin, suggesting free circulation.

Keywords: Aluminium, Iron, Toxicity

High aluminum intake affects on the immune response toward Th2 in neonatal SD rats

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Aluminum (Al) is commonly used as an adjuvant to induce allergy-type responses in animal asthma models. Certain infant formulas contain high concentrations of Al while high Al intake increased serum and tissues Al in animal studies. Therefore, concerns have been raised that high dietary Al effects the immune system of neonates and that those animals with higher plasma and/or tissues Al levels are more susceptible to specific antigens. An animal model with intragastric injection of Al was used in the first study to mimic extra high levels of Al in infant formula. Three-days old Sprague-Dawely pups were divided into 3 groups, including intragastric injection of 0.9% saline (control), 1.3 µg Al/g b.wt/day (Low Al, LAI) and 13 µg Al/g b.wt /day (High Al, HAI). Each animal was injected twice a day for 2 weeks, then killed at 18-days. In the second study, 2 groups of 3-days old Sprague-Dawely pups were intragastrically injected with 0.9% saline (control) or 13 µg Al/g b.wt/day (HAI) y twice a day for 15 days. In order to amplify the general immunity and examine on specific immunity, animals were OVA/TiterMax Gold adjuvant-immunized at 6-days of age, then killed at 19-days. The results showed that the Al levels in serum, liver, spleen and/or kidney of HAI group were significantly higher than control and/or LAI group in both studies. On the systemic immunity, the level of IgG was significantly lower in HAI group than that in the control in both studies while IgA was increased in immunized rat of HAI animals only in the second study. The secretion of IFN-γ was significantly decreased in HAI group of study I while only the secretion of IL-10 was significantly increased in study II. Based on the Th1/Th2 ratio, there was a tendency toward Th2 in HAI group. In intestinal immunity of study II, the cell proliferation of MLN lymphocyte was significantly higher in HAI group compared to control group. The level of IgA in intestinal homogenized fluid was significantly decreased in HAI group. In conclusion, the immune response has not been toward Th2 in LAI group in which Al concentration was similar as high Al content in infant formula. However, the experimental duration in this study is comparatively shorter than children with formula. Therefore, further study is needed to see if a longer feeding period with lower Al level would result in the similar immune response as HAI group in this study.

Keyword: Aluminum, Neonates, Th1/Th2 ratio

Characterization on beef-cattle farm systems according to toxic and trace metal levels

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Animal production on intensive systems, designed for high productivity, involve mineral supplementation that can be associated with toxicities. In contrast, in organic farms livestock feed is locally produced and the use of minerals is restricted, favoring mineral deficiency cases. The extent to which environmental inputs of toxic metals affect exposure of livestock may also vary with farming practice and the magnitude to which such practices are interdependent with the land. The aim of the present study was to identify factors that are likely to exert mineral unbalances with a potential adverse effect on animal health under different beef-cattle farms across NW Spain (including intensive, conventional and organic management practices). Farm husbandry practices like the use of a high proportion of forage and low or no mineral supplementation can lead to trace metal deficiencies. Calves from organic farms tend to show Co, Cu and Se concentrations within the deficient-marginal levels. In contrast, calves from intensive systems (lesser from conventional farms) tend to show hepatic Cu above the adequate levels. Grazing in organic systems may have a beneficial effect on the status of other elements, such as Fe, even though dietary Fe concentrations were not exceptionally high. This most likely reflects ingestion and assimilation of Fe from soil. For toxic metals, the tissue ratio of toxic metal accumulation and the intra-farm variation of toxic element concentrations reflect animal adaptation to cope with different farm types and the effect of standardization practices management across farm types. The proportion of concentrate in the ration demonstrated a relationship of renal As and Cd and hepatic Hg residues in calves and those in diet related to obtain more nutrition through forage that can be contaminated with soil or to a direct ingestion of soil when grazing and are dependent of certain farm practices management.

Keywords: Metals, Beef-cattle, Farm Systems

The effect of zinc on lead expelling, copper and iron in lead toxicity mice

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We aimed to observe the effect of zinc on lead expelling, blood and femur copper and iron in lead toxicity mice. Mice administered with 0.55g/L lead acetate solution in drinking water for 30 days were used as lead poisoned group, and the mice of a zinc supplemented group was simultaneously administered with zinc sulfate by gavages. A positive drug control group was setup by simultaneous CaNa₂-EDTA injection. Blood and femur lead levels of mice in the zinc supplemented group decreased significantly with their blood iron and zinc levels higher than that of the lead poisoned group; the femur zinc, iron and zinc/copper were much higher than those in CaNa₂-EDTA group. Zinc sulfate could enhance lead expelling in lead poisoned mice as effectively as CaNa₂-EDTA treatment.

Keywords: Zinc, Lead Expelling, Trace Element, Mouse

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Development of food fortification in China

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As a developing country, China is facing a nutrition double burden both micronutrient deficiency and energy over nutrition exist widely in urban and rural regions. The nutrition situation of double burden requires systematic strategy which requires establishing a partnership mechanism among government, private sectors and civil society to eliminate both micronutrient deficiencies and over intakes of food energy. Chinese Dietary Guideline, as target of diet nutrition and general approach, should play a fundamental role for both over and under nutrition control and prevention. The guide requires to keep food diversity, keep physical activities, eat more vegetables and fruits eat less salt and cooking oil etc. Campaigns and communication activities have been launched out by government, academies, mass media as well as other health related departments. The awareness of nutrition and obesity of residents is getting increased in recent years, but as developed country, the public education is somewhat not strong enough to support a rapid lifting of nutrition and health knowledge. Thus to promote dietary guideline knowledge is long term and persisting program. Food fortification, as assumed a sustainable and low cost method for nutrition deficiency control, especially micronutrient deficiencies, has been accepted a government orientation method, such as iodine salt, iron fortified soy sauce, multi-nutrient fortified wheat flour and rice, cooking oil and complementary food supplements. Though only iodine salt so far is the only national mandatory fortification project, other governmental recommended projects as well as other voluntarily food fortification projects developed quickly and nutrient supplements also developed fast in the market such as married women are required to take folic acid pills for prevention of neuro-tube defect. Yingyang Bao as infant complementary food supplement has been used as earth quake disaster area and other poor regions, the preliminary observation showed significant results for the malnutrition control and prevention. Food fortification in China is still on the initial stage in term of mass or universal food fortification except iodine salt project. It is believed that mass food fortification as measures in control and prevention micronutrient deficiency defined as a public health issue will develop in the future in China.

Keywords: Food Fortification, Micronutrient Deficiency, Iron fortified Soy Sauce

Effects of bioactive polyphenolic compounds on iron and zinc absorption

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Tea and red wine are sources of polyphenolic compounds known for their many beneficial effects on health, mainly from antioxidant properties and chelation of metals such iron and zinc. of these compounds. However, this chelation may decrease absorption of iron, and possibly other trace metals from the diet. We examined the effect of epigallocatechin-3-gallate (EGCG), green tea extract (GT) and grape seed extract (GSE) on the absorption of ⁵⁵Fe and ⁶⁵Zn in human intestinal Caco-2 cells grown on microporous membrane inserts. An ⁵⁵Fe study was conducted by 0.46 – 46 mg/L of EGCG, GT and GSE. Polyphenols inhibited the transepithelial transport of non-heme ⁵⁵Fe in a dose-dependent manner. However, apical iron uptake was significantly increased by addition of polyphenolic compounds. The addition of ascorbic acid offset the inhibitory effects of polyphenols on iron transport. The polyphenol-mediated apical iron uptake was significantly inhibited by membrane impermeable Fe²⁺ chelators, but at 4°C, the apical iron uptake was still significantly higher than at 37°C. These results suggest that polyphenols enhance the apical iron uptake partially by reducing the conversion of ferric to ferrous ions and possibly by increasing the uptake of polyphenol-iron complexes via the energy-independent pathway. Similarly, bioactive polyphenolic compounds also significantly inhibited heme-⁵⁵Fe absorption in a dose-dependent manner. Ascorbic acid was able to offset the inhibitory effects of polyphenolic compounds when polyphenols were added at the lower concentrations (≤ 4.6 mg/L). The transfer of iron across the basolateral membrane of the enterocyte was extremely low in the presence of polyphenolic compounds, indicating that basolateral exit via ferroportin-1 was impaired-possibly through formation of a nontransportable polyphenol-iron complex. Expression of proteins involved in iron transport and metabolism was not changed by EGCG, GT and GSE. In contrast, only GSE significantly reduced zinc absorption but not EGCG and GT. The decreased zinc transport was associated with the reduced apical zinc uptake. The effect of GSE on zinc absorption is very different from that on iron absorption. While GSE decreased zinc absorption by reducing the apical zinc uptake, the polyphenolic compounds inhibited iron absorption by enhancing the apical iron uptake. The inhibition of zinc absorption may be due to the presence of procyanidins in GSE, which bind zinc with high affinity, and block the transport of zinc across the apical membrane of the enterocyte.

Keywords: Epigallocatechin-3-gallate, Green Tea Extract, Grape Seed Extract, ⁵⁵Fe, ⁶⁵Zn

Study on iron bioavailability from a representative diet in Chinese urban women of childbearing age

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The objectives of the study were to determine dietary iron bioavailability of different sources by using a double label stable isotope technique in a typical representative Chinese urban diet. Thirty healthy childbearing age women were recruited from a military medical college. They were randomly divided into 3 groups with 10 subjects in each group. About 30mg ⁵⁷Fe were administered in the form of ferrous sulfate, reduced iron powder and reduced iron powder plus Na₂EDTA. The stable isotopes were divided into 15 meals in 5 days. Thirty minutes after supper of the fifty day of experiment, about 1 mg of ⁵⁸Fe was given intravenously. Fourteen days later, blood sample were collected to analyze the isotope ratios with TIMS. Fecal samples were collected daily before 8 AM. After wet digestion, iron content was analyzed by AAS. Iron content in Food samples was also analyzed by AAS. The mean(±SD) iron intake from the representative Chinese diet was 12.2±1.1mg/d, which is lower than the AI level of DRIs (20mg/d). In the ferrous sulfate group, reduced iron powder group and reduced iron powder plus Na₂EDTA group, the apparent absorption were 12.6%, 8.0%, and 4.9% (P>0.05). The fractional utilizations in the above-mentioned three groups were 5.8%, 2.1%, and 2.4% (P<0.05). In conclusion, the ferrous sulfate group showed the best bioavailability in the representative Chinese diet. The addition of Na₂EDTA did not increase the bioavailability of reduced iron powder in fortified wheat flour.

Keywords: Iron Bioavailability, Isotope Technique, Representative Diet

Sodium iron EDTA as a food fortificant: implications for iron homeostasis and tissue iron distribution

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Sodium iron ethylenediaminetetraacetate (NaFeEDTA) has considerable promise as an iron fortificant because it is less affected by iron absorption inhibitors than most other forms of food grade iron. A major advantage is that EDTA binds iron with higher affinity than many absorption inhibitors but this may alter the regulation of iron absorption and/or the metabolism of the iron once it is absorbed. The EDTA-bound iron may enter the body as an intact complex and thus the normal down regulation of iron absorption in iron adequate individuals may not occur, possibly leading to iron overload. We compared the regulation of iron absorption from NaFeEDTA and FeSO₄ in normal and iron loaded rats. Animals were fed diets containing either 35 mg/kg iron or 30,000 mg/kg iron for 29 days to achieve normal or iron loaded status. Iron absorption was assessed by feeding a meal containing either FeSO₄ or NaFeEDTA labeled with ⁵⁹Fe and monitoring whole body retention of the radioactive iron over a period of 9 days. Iron absorption by the normal iron status rats was 65% and 49% for FeSO₄ and NaFeEDTA, respectively, but decreased to 13% and 10% in the iron loaded rats, indicating that rats are able to down regulate iron absorption from NaFeEDTA just as effectively as they down regulate absorption from FeSO₄. We also compared the tissue distribution of iron in rats given iron either orally with food or by subcutaneous injection as either FeSO₄ or NaFeEDTA. Estimated total body nonheme iron levels were similar in rats fed NaFeEDTA or FeSO₄, but the tissue distribution was different: it was 53% lower in the liver and 86% higher in the kidneys among rats fed NaFeEDTA than among those fed FeSO₄. In contrast, total body nonheme iron was 3.2-fold higher in rats injected with FeSO₄ than in rats injected with NaFeEDTA. We conclude that iron is dissociated from EDTA prior to or during intestinal absorption and therefore enters the body via the normal DMT-1/Ferroportin pathway. The differences in tissue distribution between orally administered iron from FeSO₄ and NaFeEDTA may be due to absorbed EDTA that re-combines with iron in the plasma. Further studies on the effects of prolonged exposure to dietary NaFeEDTA on kidney iron accumulation are warranted.

Keywords: Iron, EDTA, Fortification

Assessment of zinc bioavailability in Chinese representative diet

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We investigated zinc content in representative Chinese diets, and determined fractional absorption of exogenous zinc in women of childbearing age by using a double-label stable isotope technique. We measured isotopic enrichment in feces and urine after oral and intravenous administration of stable isotopes of zinc (⁶⁷Zn and ⁷⁰Zn) to determine fractional absorption (FA). Twenty young women, students of a medical college in Shijiazhuang City were recruited. Foods were labeled extrinsically with 4 mg ⁶⁷Zn (consumed simultaneously with vegetable soup) at the second day of the test period. Shortly after consuming the labeled meal, each subject was given an intravenous injection of 2mg ⁷⁰Zn. Subsequently, fecal and 12-h urine samples were collected for 10 and 3 days, respectively, ashed, and passed through ion-exchange columns to separate zinc from other elements before analyzed for isotope ratios by thermal ionization mass spectrometry (TIMS). Total zinc contents of the samples were measured by atom absorption spectrometry (AAS). Apparent zinc absorption was calculated as the difference between isotope dose and fecal excretion. True absorption of zinc was determined by eliminating the disturbing effect of the endogenous secretion. Balance study was also conducted to measure the apparent absorption of total zinc. From 32h onwards the enrichment of ⁶⁷Zn and ⁷⁰Zn in urine declined proportionately so that the fractional absorption (FA) of zinc could be determined as follows: FA=enrichment (oral/iv). Mean (SD) calculated dietary zinc intake was 10.22(0.80) mg/d. Mean dietary Fe/Zn weight ratio was 1.1(0.1). Mean phytic acid intake was 301(29.3) mg/d. 2. Apparent and true absorption of ⁶⁷Zn were 36.2(9.7)% and 38.2(10.1)%,. Mean FA determinations from urine was 35.6(12.9)%. Apparent absorption of total zinc determined by balance technique was 29.9(10.1)%. The total amount of the net zinc absorbed was 3.92(1.15)mg. True absorption of ⁶⁷Zn was great than the apparent absorption determined by balance technique. 3. The phytate: zinc molar ratio in the diet was approximately 3:1. Phytic acid by Ca/zinc molar ratio in the diet was 45:1. No inhibitory effect of phytic acid on zinc absorption was found.

Keywords: Stable Isotopes, Rare Earth Element, Adult Women

Biotechnological approaches for micronutrient enrichment for food applications

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Micronutrient deficiencies are causing serious health concerns world wide and especially in developing countries like India. Iron deficiency anaemia is rampant in India and hence an urgent need to enhance bio available iron through dietary means. Similarly the problem of Iodine which was widespread was tackled to large extent through public distribution of iodized salt. Vitamin A deficiency related blindness is also of concern. Meeting Vitamin B₁₂ and Gamma linolenic acid (GLA) requirements is also a problem since the Indian population is by and large vegetarian. To address some of these issues we have carried out studies on the biotechnological production of algae with enriched micronutrients such as Iron and Zinc. The aspects of bio magnification were exploited to *in situ* enrich Iron and Zinc in *Spirulina* – an edible algal form. The extent of increase in Iron was to nearly 3 fold higher than in control (~50 mg per100g biomass), similarly the enhancement of Zinc in *Spirulina* was demonstrated. We found that seaweeds are also good source of Iron. Several *Spirulina* and seaweed based products were prepared with increased content of Iron and other micronutrients. The bioavailability was also high in the iron fortified *Spirulina*. Our recent study has demonstrated increase of Iron content in eggplant by cloning ferritin gene from *Arabidopsis*. Recently we have confirmed the presence of true form of Vitamin B₁₂ in *Spirulina*. Cloning of delta -6 desaturase gene from *Spirulina* into Soybean resulted in production of GLA otherwise not present in soybean. This opens up a possibility of production of GLA through a vegetable route. We have developed large scale cultivation methodology for production of biomass of *Dunaliella* for Beta carotene and *Haematococcus* for the production of ketocarotenoid- Astaxanthin. This includes safety studies on the consumption of biomass. Betacarotene rich *Dunaliella* has recently received approval by US-FDA for consumption. Thus there is possibility of biotechnologically enrich sources of micronutrients for nutritional outreach to needy population. These aspects would be discussed in detail.

Keywords: Zinc, Iron, Food

Investigating the uptake of nanoparticulate dietary iron

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Despite many years of research into strategies to fight iron deficiency anaemia, this remains one of the greatest global health risks affecting nearly one billion people worldwide. The disorder is associated with increased morbidity and reduced cognitive development in childhood and with poor outcomes in pregnancy. Standard treatment is mostly based on ferrous iron salts, which are cheap and reasonably well absorbed but cause significant gastrointestinal disturbances. We have developed a nanoparticulate (2–10 nm diameter) ferric iron oxide that is doped with dietary ligands and aims to mimic natural dietary iron. This compound shows a favourable gastro-intestinal disaggregation and dissolution profile, indicative of potential good cellular uptake. We are investigating the cellular uptake route of iron from this nanoparticulate source and comparing it to the uptake of soluble ferric and ferrous iron using a Caco-2 cell model. We found that nanoparticulate iron is efficiently taken up by these cells. Firstly, we have investigated the kinetics of cellular ferritin formation, as a marker of cellular utilisation of iron, using the different iron sources. Results suggested that two different uptake mechanisms for nanoparticulate and soluble iron may be of relevance. We hypothesize that the predominant uptake route for nanoparticulate iron is through endocytosis followed by lysosomal dissolution after which the released iron joins a common cellular iron pool. This was investigated further using specific inhibitors connected with endocytic uptake. Here, chlorpromazine, an inhibitor of clathrin mediated endocytosis, showed ~ 60 % inhibition of uptake for nanoparticulate iron whereas uptake of the soluble iron forms remained unaffected. Similarly, monensin, a compound known to alter functions that depend on acidification of lysosomes, did significantly lower ferritin formation for nanoparticulate iron but not soluble. This again is suggesting different uptake routes and furthermore a desirable slow release of iron when given in the nanoparticulate form as opposed to the soluble iron. Future work will look into the absorption of nanoparticulate iron in the DMT-1 (soluble ferrous iron transporter) knockout mouse model to further support our hypothesis. *This PhD project was kindly funded by the U.K. Medical Research Council and the Rank Prize Fund.*

Keywords: Iron, Nanoparticulate, Cellular Uptake, Ferritin

Iodine-fortified milk improves iodine status in toddlers

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Inadequate iodine intakes during the second year of life may result in impaired development. In New Zealand, mandatory iodine fortification of bread has recently been implemented for controlling and preventing iodine deficiency. However, New Zealand toddlers are unlikely to achieve their dietary iodine requirements through consumption of this bread. Therefore, the aim of this study was to evaluate the efficacy of iodine-fortified toddler milk for improving biochemical iodine status in healthy 12-20-month-old New Zealand children. In a 20-week double-blind randomised placebo-controlled intervention trial, 135 children (mean age 16.8 months, 54.1% boys) were assigned to one of two groups: Fortified Milk (n=45), or Placebo (n=90). The groups replaced their regular cow milk with either an iodine-fortified powdered cow milk (138.5 µg iodine/100 g powder), or a non-fortified powdered cow milk (40.5 µg iodine/100 g powder), depending on group assignment. The milks were reconstituted with water before consumption (17 g powder to 100 mL water). Adherence and milk powder intakes were assessed by 7-day weighed records collected at baseline, and weeks 2, 7, 11, 15, and 19. Casual urine samples were collected at baseline and 20 weeks for determination of urinary iodine concentration (UIC). At baseline, median UIC (25th and 75th percentiles) did not differ between the groups (P>0.05) and was 43 (28, 62) µg/L in the Fortified Milk group and 55 (30, 91) µg/L in the Placebo group, which was indicative of iodine deficiency in this population (i.e., UIC<100 µg/L). During the intervention, mean (95% CI) intakes of study milk powder did not differ between the groups (P>0.05) and were 74.6 (64.5, 84.8) g/day in the Fortified Milk group and 66.5 (59.3, 73.7) g/day in the Placebo group. These milk powder intakes provided mean iodine intakes of 103.3 (92.5, 114.0) µg/day in the Fortified Milk group and 26.7 (19.1, 34.4) µg/day in the Placebo group (P<0.01). Over 20 weeks, median UIC increased to 91 (45, 176) µg/L in the Fortified Milk group (P<0.01), but did not change in the Placebo group (49 [26, 67] µg/L; P>0.05). In the Fortified Milk group, the proportion of children with UIC<50 µg/L decreased from 66% at baseline to 29% at 20 weeks, and those with UIC<100 µg/L decreased from 86% at baseline to 53% at 20 weeks (P<0.01). The proportion of children with low UIC did not change in the Placebo group as a result of the intervention (42% at baseline vs. 50% at 20 weeks with UIC<50 µg/L, and 82% at baseline vs. 93% at 20 weeks with UIC<100 µg/L; P>0.05). Thus, replacement of usual milk with iodine-fortified toddler milk can result in iodine intakes that substantially improve the biochemical iodine status of New Zealand toddlers. This strategy avoids radical changes in toddlers' dietary habits.

Keywords: Iodine, Toddlers, Fortification, Food-based Strategy

Simple Strategies to Assess Fe Fortificants in Commercial Product Formulations

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Micronutrient malnutrition currently affects billions of people's lives around the world, causing many adverse effects on human health, not all of which are clinically evident. Iron deficiency anemia is the biggest nutritional deficiency worldwide, prevalent in both developing and industrialized countries and primary affecting women, infants and young children. Potential solutions include dietary diversification and food fortification, the latter being generally accepted as the more cost-effective solution. Beyond fortification, increasing the bioavailability of iron in food is perhaps a more sustainable method of preventing micronutrient deficiencies. Development of new food products with relevant levels of iron fortification constitutes a challenging process since the highest bioavailable forms of iron are chemically reactive and often create detrimental side effects in the food matrix. By contrast, inert iron compounds are chemically stable in the food matrix but have low bioavailability in humans due to their low solubility in the gastrointestinal tract during digestion. As a result, food manufacturers constantly seek iron sources with adequate stability and bioavailability. Whereas stability of minerals in the food matrix is a straightforward process and is often part of the routine analysis of the food, bioavailability studies of minerals require in-vivo measurements, but human studies are time-consuming and expensive, complicated to perform and often yield variable results. Several in-vitro methods have been proposed as preliminary screening tools for assessing nutrient bioavailability. The design of such in-vitro systems is difficult since they are intended to simulate the in-vivo environment, which requires a good knowledge of gastrointestinal physiology conditions. Factors such as pH, ionic strength, enzyme concentrations, transit time, etc; make this task a real challenge. In this work, we explored the applicability of simple in-vitro tests as a means to examine the enhancing effect of some commercial chelated iron compounds such as NaFeEDTA as a fortificant in different food matrices and study the challenges to obtain accurate data in model systems as well as food matrices.

Keyword: Iron, In-vitro Test, NaFeEDTA

Bioaccessibility of iron and zinc from green leafy vegetable based foods

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Iron and zinc deficiencies are the major global public health problems affecting mainly children and women of child bearing age. In India the majority of the population is dependent on plant based foods wherein the bioavailability of micronutrients iron and zinc, is poor. Therefore, there is a need for developing cost effective food based strategy to combat these deficiencies. Green Leafy Vegetables (GLVs) form an essential part of the Indian diets. They are sources of micronutrients including carotenoids (Vitamin A), iron, calcium, ascorbic acid, riboflavin and folic acid. Two commonly consumed GLVs fenugreek (*Trigonella foenum-graecum*) and Shepu or dill (*Anethum graveolens*) were selected for the study. Food preparations viz, fenugreek bhaji (Curry) and shepu dal vada, a deep fried product with pulses, were prepared in the traditional way. Iron and zinc bioaccessibility was determined using an in vitro procedure involving equilibrium dialysis during simulated gastrointestinal digestion. Organic acids are known to enhance micronutrient bioavailability. Hence to know the influence of organic acid containing foods like raw mango powder (*Mangifera indica*), tamarind (*Tamrindus indica*), lime juice (*Citrus aurantifolia*) and tomato (*Solanum lycopersicum*) on zinc and iron bioaccessibility, the acidulants were added at organoleptically acceptable levels. The results indicate that iron and zinc bioaccessibility of fenugreek curry increased on addition of acidulants. The per cent increase in bioaccessible iron was highest with the addition of lime juice (193%), followed by raw mango powder (149%), tomato (50%) and least increase was recorded in tamarind added bhaji (15%). While in case of zinc bioaccessibility, the per cent increase was highest in bhaji with raw mango powder (14.63%) followed by tamarind (5.69%), tomato (3.25%) and lime (1.62%). The iron and zinc bioaccessibility of Shepu dal vada indicated that acidulants influenced differently. The per cent increase in bioaccessible iron was highest with the addition of tomato (20.31%) followed by tamarind (7.81%), while addition of raw mango powder and lime juice exerted a negative influence on bioaccessible iron (9.37 and 3.12%, respectively). In conclusion, addition of acidulants to the traditional green leafy vegetable based products can improve bioaccessibility of iron and zinc.

Keywords: Iron, Zinc, Bioavailability

Symposium 16(P)

Title: State-of-the-Art Instruments and Methodology

Sponsor: TEMA-14

Location: Conference Room 5

X-ray fluorescence microscopy: a new and versatile view of trace metals in biological systems

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A hard X-ray micro-nanoprobe operating at the Australian Synchrotron provides versatile X-ray fluorescence microscopy (XFM). X-ray probes are used for elemental and chemical microanalysis across length scales ranging from millimeter through micron resolution studies to the ultimate resolution of 60 nanometers. XFM is ideally suited to quantitatively map trace elements within whole biological specimens and environmental samples. The elemental sensitivity of the fluorescence probe provides valuable information for investigations in a variety of biological applications, and the highly penetrating nature of hard x-rays enables measurement of whole cells or tissue sections. Examples of biological and environmental systems that have been investigated with XFM range from entire human heart section, through tissue sections of mice brains, sections of cereal grains and single cells and neurons. Recent advances in x-ray fluorescence detection schemes now enable 3D information or fluorescence tomography in realistic time periods. Chemical speciation (valence) mapping in high definition is also possible and some recent examples will be presented.

Keywords: X-Ray Fluorescence Microscopy, Microanalysis, Chemical Speciation, X-Ray Microprobe

Fluorescent imaging of biological zinc at in vitro and in vivo condition

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Zinc is the second most abundant trace metal element following iron. Zn(II) plays vital roles in cellular metabolism, gene expression, apoptosis, neurotransmission, and so forth. It is also associated with physical growth retardation and neurological disorders such as cerebral ischemia and Alzheimer's disease. The spatial and temporal tracking of in vivo Zn(II) is challenging but essential to address these issues. Intact in vivo Zn imaging, which provides information on Zn²⁺ homeostasis and requires a combination of suitable animal models and fluorescent sensors, is highly demanded. Success fluorescence imaging of cellular Zn(II) can be realized using fluorescent sensors. We have been engaged in the development of Zn(II) sensors that can be excited by visible light and have variable Zn(II) binding affinity. These require largely the rational design and optimization of fluorophores and chelators. Recent progresses made in our group will be summarized.

Keywords: Zinc, Fluorescence, Imaging

From selenols to selenium nanoparticles: mapping Se metabolic pathway in yeast using mass and X-ray spectroscopy

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Saccharomyces cerevisiae and many other microorganisms have the remarkable ability to accumulate large quantities of metallic/metalloid elements. This ability has been exploited for the production of yeast based mineral supplements which have been used for decades. However, the efficacy/toxicity of trace element is depends on its chemical form (i.e. speciation). Using high resolution mass spectrometry the selenium analogs of the key metabolites of the sulfur amino acid pathway has been identified in selenium enriched yeast. Employing the developed analytical method the stress response of *Saccharomyces cerevisiae* to Se-Met, Se (IV) and Se (VI) was studied metabolites identified. Here we report the presence of nanometer sized metallic deposits in yeast cells grown in the presence of either, Se, Au, or Pt identified using a combination of synchrotron based micro X-ray fluorescence and hard x-ray microscopy and nano secondary ion-, electrospray- and inductively coupled plasma-mass spectrometry.

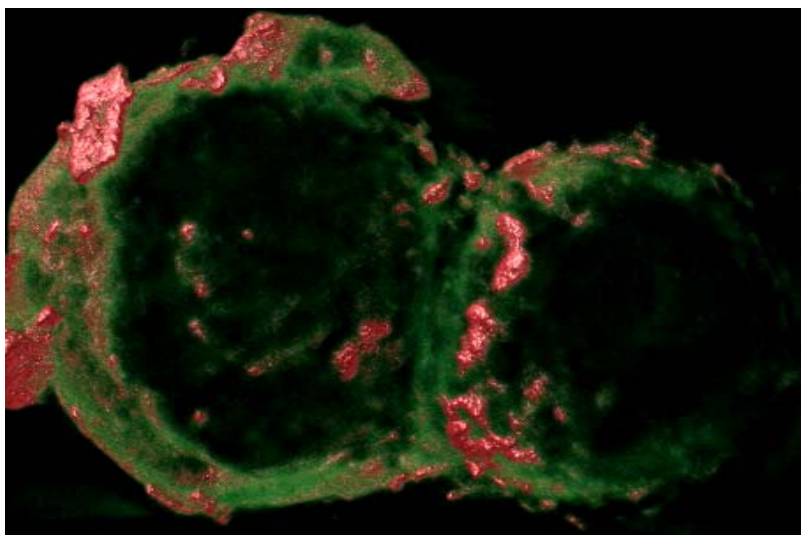


Figure 1: X-ray tomography of a selenized yeast cell cluster

Keywords: Selenols, Selenium Nanoparticles, Yeast, Mass, X-ray Spectroscopy

Quantitative LC-MS/MS techniques for characterizing selenocysteine abundance change in the hepatic GPX1 protein of SOD1 knockout mice

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Superoxide dismutase (SOD) and glutathione peroxidase (GPX1), are important antioxidant enzymes in humans. We showed a 40% loss of specific activity in GPX1 purified from SOD1^{-/-} mouse liver homogenate compared to that of the wild-type mice. To explore mechanisms for GPX1 activity loss, a quantitative GeLC-MS/MS analysis for IP pull-down GPX1 extracts from mouse liver tissue was performed. After liver homogenates of both SOD1^{-/-} and wild-type mice were pre-cleared and incubated with anti-GPX1 antibody and the protein G agarose beads, the precipitates were subjected to SDS-PAGE for separating the GPX1 protein band that was excised and digested in situ. The in-gel-extracted tryptic peptides were reconstituted for nanoLC-MS/MS analysis. The identified peptides covered over 90% GPX1 protein sequence for both genotype samples. Notably, the 47th residue in the tryptic peptide (residues 37-52) of GPX1 exhibited two forms: native selenocysteine and the Se-lost dehydroalanine. Using extracted ion chromatogram from IDA analysis and multiple reaction monitoring analyses, we found the ratio between the SOD1^{-/-} and the wild-type for selenocysteine and the dehydroalanine substitute was 0.65 and 1.3, respectively. There are no differences found for all other identified peptides in the hepatic GPX1 protein between SOD1^{-/-} and the wild-type. In conclusion, the relative abundance change of the selenocysteine residue into the dehydroalanine form in the hepatic GPX1 protein of the SOD1^{-/-} mice is remarkably consistent with its ~40% decrease in GPX1 activity providing direct evidence of SeCys mediating the SOD-GPX1 kinetic mechanism. Likely, the physiological level of SOD1 activity plays an important role in maintaining the integrity of selenocysteine in the hepatic GPX1 protein in vivo. We suspect that the elevated Sec to DHA in the active site of GPX1 may trigger a conformational change causing dissociation of the active tetramer to inactive dimer.

Keywords: Selenocysteine, SOD1, GPX1, Nano LC-MS/MS

Application of omic techniques for the discovery of zinc status biomarkers

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Zinc plays an essential role in maintaining health status. Zinc deficiency exists not only widely in developing countries, but also in developed countries. Zinc deficiency has been recognised as a major health risk factor in the world. Lack of reliable biomarker of assessment zinc nutritional status prevent the earlier diagnosis, treatment in order to improve the zinc nutritional status in individual and as well as in public population. Zinc deficiency in human has been investigated for nearly half a century; however, there is no reliable biomarker in assessment zinc nutritional status so far. Traditional research methods focus on the measurement zinc concentration or zinc related metabolic biomarkers in biofluid, especially, blood in variety experimental/physiological conditions. Recently, quickly developed genomic, proteomics and metabolomic techniques have been applied into zinc biomarker discovery and bring hope for finding the zinc biomarker. We report our research on 1) using DNA microarray to screen the zinc related gene expression by using zinc deficiency zebra fish model; 2) using 2-D gel electrophoresis to screen the biomarkers in zinc deficiency rat model; 3) highlight the potential of zinc biomarker discovery by using high profile metabolomics techniques which we are doing.

Keywords: Zinc, Gene Expression, Metabolomics, Plasma

Bioelementology as integrative approach in trace element research

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Despite the biological role of chemical elements coming under intensive study in the last decades, the “*lack of multidisciplinary approach has been the Achilles heel of biological trace element research*” (V. Iyengar, 1989). The desire to integrate the "organic" and "inorganic" approach in studying the biological role of chemical elements is observed in a number of fundamental works. Since 2003 we put forward and develop the concept of bioelements and bioelementology as an integrative scientific direction. Bioelement is the elemental functioning unit of living matter, which is a biologically active complex of chemical elements as atoms, ions and nanoparticles with organic compounds of exogenous (primary) or biogenous (secondary) origin. Bioelements include any chemical structures found in living nature, but which do not have a set of fundamental properties of living things: metabolism, variability, reproduction and heredity. The assembly of bioelements can be called “bioelementome”. We propose to subdivide bioelements into simple (atoms, ions, among them structural elements C, H, N, O, P, S, Si, Ca, electrolytic K, Na, Ca, Cl, Mg, enzymatic Mg, Fe, Zn, Cu, Mn, Co, Cr, Mo, Se, Sn, F, I, Ni, V, B, and water as the universal solvent), and complicated ones, consisting of the above-mentioned 68 molecules (8 of them are nucleosides, which compose DNA and RNA, 20 are natural amino acids necessary for protein synthesis, at least 32 glycans, 8 types of lipids). Also, bioelements can be subdivided into primary, i.e. those which could exist before the origin of life, and secondary, i.e. those which have formed as production of living organisms. On our opinion, the progress in trace element research will be due to interdisciplinary approach such as bioelementology. It needs change in educational programs for high school students of biological, chemical and physical specialties, creation of special programs for biotechnologists, medical researchers, ecologists and pharmacists. And this will demand united efforts of scientists and specialists from adjacent fields. Integration of scientific researches without division into separate parts, studied by only one of the “omics”, though this will demand deeper and more global planning of scientific investigations on the basis of the multidisciplinary concept.

Keywords: Bioelementology, Bioelements, Trace Elements

Speciation of selenium in selenium-enriched cereal from higher selenium area by LC-UV-HG-AFS

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Selenium is one of the essential elements and food is the main source of selenium for humans. The bio-availability of selenium is strongly linked to its chemical form, thus more information is needed not just the determination of total selenium in food. The method for speciation analysis of four selenium species (selenite (Se⁴⁺), selenocystine (SeCys), methyl-selenocysteine (Methyl-SeCys) and selenomethionine (SeMet)) has been performed by on-line coupling of liquid chromatography (LC), UV decomposition, hydride generation (HG), and atomic-fluorescence spectrometry (AFS). For solid samples, a soft extraction step was required before determination. Different kinds of enzymes and series of concentration of these enzymes were chosen for the soft extraction step. The extraction time and the influence of ultrasound on the soft extraction were also considered. We found ultrasound before the zymolysis of solid samples could improve the extraction ratio of selenium and the optimization step of the soft extraction is (0.2g solid sample): 1. add 0.2ml Proteinase K (500 mg/L) and shake for 18h at 50°C; 2. add 0.2ml Proteinase K (500 mg/L) and shake for 6h at 50°C; 3. add 0.4ml Proteinase XIV (500 mg/L) and shake for 6h at 37°C. The speciation of selenium in selenium-enriched cereal (rice, corn, wheat and soybean) from higher selenium areas was determined using the optimization method. The extraction ratio for selenium was from 62% to 97% and SeMet was the main form of selenium in cereal which contributed 81% to 100% selenium of the total selenium.

Keywords: Speciation of Selenium, Cereal, High Selenium Area

Selenium content in raw, cooked and in vitro bioaccessible fractions of Se-enriched rice

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In the Nawanshahr-Hoshiarpur region of Punjab, India, more than 1000 hectares of agricultural land is significantly affected by high levels of selenium (Se) and its concentrations in food grains was highest ever recorded in grains for human consumption. The present study was carried out to examine the levels of Se in rice as raw, cooked and in vitro bioaccessible fractions. Se content as estimated using neutron activation analysis (NAA) was 58.25 ± 5.9 microg g⁻¹ in raw rice and 52.52 ± 1.7 microg g⁻¹ in boiled rice prepared through conventional cooking. The rice was further subjected to in vitro gastric (GA) and gastro-intestinal (GI) digestion. Approximately 52 % (30.66 ± 2.8 microg g⁻¹) and 65 % (38.01 ± 3.5 microg g⁻¹) of total selenium found in rice was observed to be bioaccessible after GA and GI digestion. Reference material [Wheat Flour (Durum) NIST 8436] as well as internal standard (ICP Spex elemental standard) were analysed as controls during Se estimations. Rice being one of the staple diets of the population, regular consumption of locally produced rice may lead the population of the study area to an excessive intake of selenium, whereas the same crop produce can be a promising raw material for naturally enriched products to be used to supplement human diet in low selenium areas.

Keywords: Selenium, Bioaccessibility, Rice

Comparative analysis of gallium in human hair and blood

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Gallium (Ga) is a relatively rare non-essential trace metal that has found uses in diagnostic radiology, and as an antineoplastic agent, and for the control of cancer-related hypercalcemia. We studied the distribution of gallium in the hair and whole blood of 96 occupationally non-exposed subjects (38 men, 58 women). The study was conducted following the declaration of Helsinki on the ethics of the human subject research. Gallium analysis was performed by ICP-MS at the CBM, Moscow, Russia, an ISO certified analytical laboratory. International certified standards for hair and whole blood analysis were used for the control. Median gallium concentration in the hair was 0.026 µg/g (men: 0.020 µg/g, women: 0.039 µg/g) whereas median concentration of gallium in the blood was 0.003 µg/g⁻¹ (the same for both men and women). More women than men have their hair gallium above the median ($P < 0.01$ by chi-square) whereas there were no statistically significant differences between men and women recorded in the whole blood. The results showed the importance of assessing gallium in hair. Hair appears to be a more sensitive indicator tissue for assessing gallium metabolism the whole blood. The reason for observed difference of greater gallium accumulation in men than women remains to be elucidated.

Keyword: Gallium, Hair and Blood, Gender Difference

Poster Presentation

PT01-PT68

Location: Corridor of Large Auditorium, 7th Floor of Main Building

Corridor of Conference Room, 8th Floor of Main Building

A novel nanobiomaterial for time-controlled tissue delivery of copper enhances vascular responses in a mouse model of limb ischemia

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The angiogenic effect of copper (Cu) makes it of clinical significance. Cu can promote vascularization, thus its role in the manipulation of cancer therapy and degenerative diseases such as heart disease has been tested in experimental animal studies. Cu is also of toxicological significance and larger amounts can cause oxidative stress. Therefore, a controlled delivery system for Cu would be a desirable tool for clinical application of Cu. For this purpose, the present study was undertaken to develop a time-controlled nanobiomaterial for the tissue delivery of Cu. A short peptide named NM (composed of His, Arg, and Gly residues) with Cu²⁺ binding sites was synthesized. The data obtained showed that the NM can bind to Cu²⁺ and form a stable hydrogel-like nanobiomaterial (Cu-NM) fabricated with nanofibers. The Cu-NM can slowly release Cu²⁺ *in vitro*. To determine the therapeutic effect of Cu-NM on vascular regeneration, a mouse model of hindlimb ischemia was established using male BALB/c mice (10-12 weeks). Ischemia was induced by a complete ligation and excision of the right femoral artery and its branches. Three days after femoral artery ligation, some mice were injected 50 µl of Cu-NM (containing 80 µM Cu²⁺) at two sites in the adductor muscle of the right hindlimb of mice every 2 days for 3 times. Other mice were injected 50 µl of Cu solution (80 µM CuSO₄) or 50 µl of H₂O as controls. Compared with H₂O -treated controls, Cu-NM treatment significantly increased the perfusion, determined by Laser Doppler Perfusion Imaging (Moor instruments), and decreased tissue necrosis, determined by histopathological analysis. Furthermore, Cu-NM significantly increased the vasculature density in the ligation-affected areas. Interestingly, CuSO₄-treated mice showed more serious necrosis and less vasculature density than the H₂O -treated controls. The data obtained demonstrated that the designed Cu-binding nanobiomaterial could stably retain Cu²⁺ in the action site and slowly deliver Cu²⁺ in a time-dependent fashion, avoiding the severe side effects of Cu²⁺ at high concentration *in vivo*, and promote vascularization and regression of the ischemic limb.

Keywords: Copper, Nanobiomaterial, Limb Ischemia

Bioavailability of iron from malted finger millet (*Eleusine coracana*) based supplementary food

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Anemia is the most common nutritional problem in the world and more so in India with millions, especially the young being affected. Although many factors are responsible for the onset of iron deficiency, the most likely cause of this nutritional problem in developing countries like India is the poor bioavailability of dietary iron from predominantly plant food diets. Finger millet (*Eleusine coracana*), one of the staple crops of India, is a rich source for many nutrients, with many functional and health beneficial properties. Traditionally finger millet malt is used as supplementary food for children. Also, diarrhea remains the second leading cause of death among children under five globally. Probiotic bacteria are considered to have a role in immunomodulation and also aid in absorption of nutrients. In view of these, the objective of this study was to determine iron bioavailability of finger millet malt and the identify factors influencing the iron bioavailability. Porridge made from each of the samples; 1) Unseived native finger millet flour 2) sieved finger millet malt and 3) sieved composite mix consisting of malted finger millet, green gram and wheat in the ratio of 2:1:1 were used in this study. Phytic acid and polyphenols were measured by anion exchange and Folin Ciocalteu Reagent method, respectively. An *in vitro* method using Caco-2 cell culture was employed to assess iron bioavailability. Malting decreased polyphenol content by 50% with no effect on phytate in the composite malt mix compared with native finger millet flour and malt. The iron bioavailability from composite malt (217.37 ng ferritin/mg protein) was lower than finger millet malt alone (448.25ng ferritin/mg protein) but better than unmalted flour (138.25 ng ferritin/mg protein). Influence of adding *Lactobacillus acidophilus* to the composite malt mix on iron bioavailability was also investigated. The results indicate that probiotic bacteria along with polyphenol oxidase, added to further decrease polyphenols, significantly increased iron solubility by nearly 80%. In conclusion, malting reduced inhibitors of iron absorption and addition of probiotic bacteria *Lactobacillus acidophilus* and mushroom tyrosinase can increase iron solubility, which may be important to improve iron absorption.

Keywords: Finger Millet, Iron Bioavailability, *Lactobacillus Acidophilus*, Mushroom Tyrosinase

Changes in mineral status of internal forces conscripts induced by use of an arginine preparation

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Effect of arginine on mineral status was studied in a group of 17 soldiers aged 19 to 27 years. They were surveyed before and after 2 mo. course administration of L-arginine in dosage 0.15 g/day and subjected to quantitative determination of chemical elements in blood serum. The multielement analysis (Cr, Cu, Fe, K, Li, Mg, Na, P, Pb, Se, Sn, V, Zn) was performed by ICP-AES/ICP-MS using instruments Optima 2000 DV and Elan 9000 (Perkin Elmer Corp., USA) in the test laboratory of ANO "Centre for Biotic Medicine" (Moscow, Russia). Along the arginine application course there was detected an increase in serum concentration of macro elements Ca (86.5 ± 2.0 to 99.7 ± 5.4), Na (2653 ± 23 to 3201 ± 91), and trace elements Cr (0.158 ± 0.013 to 0.227 ± 0.013) and V (0.042 ± 0.0026 to 0.0675 ± 0.0048); a decrease in concentration of essential and conditionally essential elements: K (715 ± 68 to 456 ± 59), Fe (4.11 ± 0.73 to 1.69 ± 0.26), Cu (0.956 ± 0.057 to 0.778 ± 0.038), Se (0.126 ± 0.006 to 0.104 ± 0.007), Li (0.0752 ± 0.0055 to 0.0496 ± 0.0045). Also, there was an increase in the level of Pb (0.0004 ± 0.0001 to 0.0036 ± 0.0015). All these changes were significant at $p < 0.05$. Thus the results showed a moderate indirect effect of arginine on mineral metabolism. Increased Pb can be explained by activated elimination of this toxic trace element from the depots (bone tissue, reticuloendothelial system), since arginine can be involved in such processes, particularly in regulation of functions of the hematopoietic system and reticuloendothelium. A decrease of the Fe/Pb, Cu/Pb and Se/Pb ratios on the background of a slight increase in Ca concentration may be also regarded as a reflection of interelement antagonism with the accumulation of essential hematotropic elements Fe, Cu in erythrocytes and the displacement of Pb deposited there. The reduction of K/Na ratio in the blood serum was possibly due to K accumulation in blood cells and transition of Na ions to serum (extracellular fluid). Thus, arginine may play the role of a bioligand, affecting redistribution of electrolytes and hematotropic trace elements between blood cells and serum.

Keywords: Arginine Supplementation, Mineral Metabolism, Blood Serum

Comparative genomics analyses reveal complexity of trace element dependence in biology

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Trace elements are needed in small quantities but are essential for all living organisms. A growing number of trace element-dependent proteins (user proteins) and pathways have been characterized, which highlight importance of these elements for life. On the other hand, little is known about the evolutionary dynamics of the dependence of user proteins on trace elements. Here, we carried out comparative genomics analyses to study metal dependence of metal-binding protein families as well as selenium dependence of selenoprotein families. Many zinc protein families evolved representatives that lack this metal, whereas selenocysteine in proteins is dynamically exchanged with cysteine. Loss of copper ligands has also been observed in members of several cuproprotein families, which was mostly accompanied by changes in function of these proteins. Several other elements, such as molybdenum and nickel, have a limited number of user protein families but they are strictly dependent on these metals. Thus, comparative genomics of trace elements provides a foundation for investigating fundamental properties, functions and evolutionary dynamics of trace element dependence in proteins and organisms.

Keywords: Trace Elements, Comparative Genomics, Dependence

Copper chelator tetraethylenepentamine reduces deferoximine-induced hypoxia-inducible factor-1 accumulation and vascular endothelial growth factor expression

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Copper is required for the transcriptional activity of hypoxia-inducible factor-1 (HIF-1), but the mechanism of action has not been understood. The stability of HIF-1 α is a critical regulatory mechanism for HIF-1 transcriptional activity and factor inhibiting HIF-1 (FIH) in the nucleus plays a crucial role in the stability of HIF-1 α . Iron chelator, deferoxamine (DFO), by removing the cofactor iron for FIH can stabilize HIF-1 α to increase the transcriptional activity of HIF-1. The present study was undertaken to determine the effect of copper deprivation on DFO-induced HIF-1 transcriptional activation to test the hypothesis that copper may affect HIF transcriptional activity through its interaction with FIH. Human umbilical vein endothelial cells were treated with DFO at a final concentration of 100 μ M in cultures for 4 hours in the concomitant presence or absence of 50 μ M copper chelator, tetraethylenepentamine (TEPA). At the end of the treatment, cellular proteins were isolated for western blot analysis of HIF-1 α . Total RNA was isolated for real-time-RT-PCR analysis of mRNA for vascular endothelial growth factor (VEGF), a protein whose expression is regulated by HIF-1. The results showed that DFO significantly increased the protein level of HIF-1 α and enhanced the expression of VEGF. TEPA significantly reduced DFO-increased HIF-1 α accumulation along with a diminishment of DFO-increased VEGF expression. The data thus demonstrate the removal of copper may suppress the inhibitory effect of DFO on FIH leading to a decreased stability of HIF-1 α even under iron removal condition.

Keywords: Copper, HIF-1 alpha Stability, FIH

Copper is required for cobalt-induced transcriptional activity of hypoxia-inducible factor-1

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Cobalt inhibits prolyl hydroxylases leading to the accumulation of hypoxia-inducible factor-1 α (HIF-1 α) and a concomitant increase in the transcriptional activity of HIF-1. Therefore, cobalt has been under the development as a drug to activate HIF-1 under some disease conditions. However, it has been shown that ischemic or hypoxia conditions in vivo resulted in the HIF-1 α accumulation with the loss of copper (Cu), under which condition the activation of HIF-1 would not occur unless Cu was supplemented. The present study was undertaken to test the hypothesis that Cu is also required for the activation of HIF-1 transcriptional activity induced by cobalt. Human umbilical vein endothelial cells subjected to the treatment with 50 μ mol CoCl₂ for 4 hrs resulted in an accumulation of HIF-1 α , determined by western blot analysis, and an increase in the level of mRNA for vascular endothelial growth factor (VEGF), determined by a real-time RT-PCR analysis. Cu chelator, tetraethylenepentamine (TEPA), at 25 μ mol did not affect the accumulation of HIF-1 α but blocked the increase in the VEGF mRNA level, an effect that could be reversed by an addition of excess Cu. The present study thus demonstrated that Cu was required for cobalt-activated transcriptional activity of HIF-1, although Cu did not affect cobalt-induced accumulation of HIF-1 α in the cells.

Keywords: Cobalt, Copper, HIF-1

Copper nanoparticles as modulators of apoptosis and structural changes in tissues

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Research on copper nanoparticles influence on apoptosis and structural changes of liver, spleen, kidney tissues as well as cerebral cortex under copper multiple introductions into organism of animals are presented. Male Wistar rats (150-180g), were injected im. weekly with an aqueous suspension of copper nanoparticles (2.0 mg/kg animal weight). Test samples were taken 3 hours, 1 day, 3 and 7 days after each injection. Caspase-3 expression was assessed to reveal readiness to apoptosis. Immunohistochemical researches were carried out with monoclonal antibodies on paraffin sections. Immunopositive cells were counted among 1000 and expressed in ‰. Copper nanoparticles distribute in organs and tissues of animals and cause specific structural changes. The increase of copper nanoparticles to toxic thresholds results in dystrophy and necrosis. This process is reversible at one-fold introduction into liver by repeated introduction copper nanoparticles appear in vascular part of periportal hepatocytes and Kaunsilmen's bodies. Accurate expression enhancement of Caspase 3 in microgliocytes (brain macrophages) has been registered seven days after one-fold intramuscular introduction of copper nanoparticles (dose–2 mg/kg of animal body weight), in liver cells - three and seven days after three-fold intramuscular introduction of copper nanoparticles (total dose was 6 mg/kg of animal body weight), in proximal kidney tubules - three hours, one, three and seven days after three-fold intramuscular introduction of copper nanoparticles (with total dose 6 mg/kg of animal body weight), in spleen cells three hours, one, three and seven days after 12-fold intramuscular introduction (with total dose 24 mg/kg of animal body weight). The most significant morphometric changes of spleen white pulp occur in 7 days after repeated introduction. Lymphoid follicles increase after the second introduction as result of germinal center enhancement and mantle, marginal layers enhancement where the processes of cell differentiation and outcome into red pulp occur. Received data enables us to propose using index of cells readiness to apoptosis defined by Caspase-3 expression.

Keywords: Copper, Nanoparticles, Apoptosis

Copper stimulates proliferation of human umbilical vein endothelial cells in a vascular endothelial growth factor-independent pathway

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Studies in vivo have shown that dietary copper (Cu) supplementation reverses pressure overload-induced cardiac hypertrophy in a mouse model, which is vascular endothelial growth factor (VEGF)-dependent and correlates with enhanced angiogenesis. Because Cu stimulation of endothelial cell proliferation and differentiation would play a critical role in angiogenesis, the present study was undertaken to examine the effect of Cu on proliferation of human umbilical vein endothelial cells (HUVECs) in cultures. The HUVECs were treated with Cu sulfate at a final concentration of 5 μ M Cu element in cultures or with a Cu chelator, tetraethylenepentamine (TEPA) at a final concentration of 25 μ M in cultures. Cell proliferation and Cu effect on cell cycle were determined. In addition, the effect of Cu on VEGF and endothelial nitric oxide synthase (eNOS) mRNA levels was determined, and anti-VEGF antibody and siRNA targeting eNOS were applied to determine the role of VEGF or eNOS in Cu effect on cell proliferation. Cu significantly stimulated and TEPA significantly inhibited cell proliferation, and the TEPA effect was blocked by excess Cu. Cu increased the number of cells in the S phase and correspondently decreased the number in G1 phase. Interestingly, Cu did not increase the level of VEGF mRNA, but significantly increased eNOS mRNA. Furthermore, neutralizing VEGF by anti-VEGF antibody did not suppress Cu-stimulation of cell proliferation. However, siRNA targeting eNOS completely blocked Cu reversal of TEPA inhibition of cell proliferation. The data demonstrate that Cu stimulation of HUVEC cell proliferation is VEGF-independent, but eNOS-dependent.

Keywords: Copper, eNOS, Cell Proliferation

Delaying of insulin signal transduction in skeletal muscle cells by selenium compounds

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Supranutritional selenium (Se) intake and high serum Se levels have been associated epidemiologically with increased risk for type 2 diabetes. We hypothesized that a surplus of dietary Se compounds and/or abundantly expressed antioxidant selenoenzymes may impair the sensitivity of target tissues for insulin. Therefore, we compared the capability of inorganic and organic Se compounds (sodium selenite, sodium selenate, L-selenomethionine, methylseleninic acid (MSA)) to interfere with insulin signaling in rat differentiated L6 myotubes, an in-vitro cell culture model for skeletal muscle cells. All tested Se compounds stimulated expression and/or activity of the cellular selenoproteins glutathione peroxidase 1 (GPx1) and selenoprotein W (SelW), with selenite and MSA being the most efficient Se donors. When applied at doses of 1 μ M, only selenite and MSA delayed insulin-induced phosphorylation of protein kinase B (Akt) and attenuated insulin-induced phosphorylation of forkhead box class O transcription factors FoxO1a and FoxO3. Insulin-stimulated glucose uptake was lowered by selenite and MSA as well, whereas high concentrations of L-selenomethionine (100 μ M) increased glucose uptake. Moreover, at doses of 1 μ M, only selenite and MSA had a significant inhibitory effect on generation of intracellular reactive oxygen species (ROS). Taken together, the results suggest that the Se(IV) compounds selenite and MSA may impair the insulin sensitivity of myocytes by influencing cellular redox homeostasis. Keeping in mind these results as well as recent epidemiological and mechanistic insights, a more careful handling of dietary selenium supplements appears to be advisable.

Keywords: Selenium, Akt, FoxO, GPx, Diabetes, ROS

Development and utilization of mineral elements to enhance the quality of distinctive agriculture

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Panzhihua is rich in mineral resources with reserves of ten billion tons of 76 minerals had been found there. It is also famous for a subtropical distinctive agricultural, and ninety percent of fruit and vegetables produced are sold to all over China. Microelements we need derived from food, but many people can't get enough elements from food, in the period that transgenic plants, chemical fertilizers are widely used. The animal and plant entire life cycle is much shorter than before so to find another way to supply elements is of great significance, and related research is carried out in the Panzhihua area. Spectrographic analysis of chemical composition indicate mines containing 30 kinds of various chemical elements of which more than 10 essential elements for human being occur in Panzhihua. So, research into element distribution, soil enrichment, biotransformation, the impact on human health, had been listed as important questions for study. This measure will enhance the quality of agriculture as the "gold standard". Through assemble monitor buffer of cytology, guava grow in different district of Panzhihua, is benefit for cell heredity, immunization and proliferation, due to element in soil, air, fruitage. We must hang featured agricultural production bases and develop specific essential element for body together. We must try to research and develop safe agriculture and biological industry that is high yield, fine quality, ecological and safe. We will achieve agricultural products fine quality, nutrition, functional only if we do it. In the process of research, we will combine food and nutrition structure optimization and prevention of nutritional diseases together. Try our best to set up technological safeguards system for food safety and healthy lifestyle. Lead science diet, achieve "food diversity, nutritive equilibrium, knowledge diet, meal scientifically, delicious way to wellness", realize the goal that life expectancy increasing one year in the time of twelve five year ending.

Keywords: Panzhihua, Mineral Resources, Microelement Exploitation

Distribution and speciation of arsenic in mice after subchronic exposure to sodium arsenite

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The adverse impact of chronic arsenic exposure via drinking water is worldwide public health problem. Arsenic exposure is associated with increased risk of developing cancer of the skin, lung, liver and kidney and non-cancer effects such as cardiovascular disease, immune suppression and neurotoxicity. The toxicity of arsenic varies with its chemical speciation. We have studied the toxicity, accumulation, distribution and metabolism of arsenic through the determination of total arsenic concentration and arsenic speciation in C57BL/6N 8-week male mice either control or arsenic-exposed. The arsenic-exposed group was treated at the concentration of 10 mg/L sodium arsenite for six months through oral administration while the control group were treated with deionized water. Livers, kidneys, lungs, brains, hearts, spleens, muscles, and blood samples were collected for analysis by inductively coupled plasma-mass spectrometry (ICP-MS). Standard reference material DORM-2 and DOLT-3 were used, and the average recovery rates were 97.93% and 92.57%, respectively. Total arsenic concentration of the arsenic-exposed group increased particularly in kidneys and lungs. In serum and blood cells, only small amounts of arsenic were found. Arsenic treatment also decreased chromium in kidneys ($P < 0.03$) and serum ($P < 0.05$) and copper in heart ($P < 0.05$). Four arsenic species which including arsenous acid (As^{III}), arsenic acid (As^{V}), methylarsonic acid (MMA), dimethylarsinic acid (DMA) were studied in liver, kidney and heart.

Keywords: Arsenic Exposure, Arsenic Speciation, Mice, Trace Element

Effect of calcium salts on the bioavailability of non-heme iron in humans

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Calcium has been described as an inhibitor of iron absorption in the intestine. However, it is unclear how different calcium salts alter the bioavailability of this micronutrient. We have determined the effect of different calcium salts in non-heme iron bioavailability in humans. Over a period of 28 days, in 4 different days, 13 healthy women ingested 5 mg of iron as FeSO₄ (⁵⁵Fe- or ⁵⁹Fe-labeled) with 800 mg of a calcium salt: calcium gluconate, calcium chloride, calcium citrate or calcium carbonate, with calcium chloride as a control. On day 14 and 28 blood samples were obtained to determine bioavailability and iron nutritional status. Results: The geometric means (and range ± 1SD) of iron absorption was 17.8 % (9.6 to 32.8 %) for calcium chloride, 13.5 % (5.9 - 30.8 %) calcium gluconate, 11.9 % (5.9 to 24.2 %) calcium citrate and 16.5 % (7.9 to 34.4 %) for calcium carbonate. Repeated measures ANOVA F = 3.79, p < 0.02, post hoc Dunnett p < 0.05 for calcium citrate v/s control. Non-heme iron bioavailability only decreased in the presence of 800 mg of calcium as calcium citrate, the most commonly used calcium salt in food fortification.

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Keywords: Iron, Calcium, Anemia, Supplementation

Effects of sub-chronic aluminium exposure on learning and memory functions and antioxidative capacity in rats

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We observed the effects of sub-chronic aluminum exposure on the learning and memory functions and antioxidative capacity in rats and explored the mechanism of aluminum neurotoxicity. Forty male Wistar rats were randomized into four groups of 10 animals each. Aluminum chloride (AlCl₃) at a low (75 mg/kg bw), medium (150mg/kg bw) and high(300mg/kg bw) dose was applied to male Wistar rats by gavage once a day for 7 wk. The rats in the control group were given Al-free water by gavage throughout the experiment. Changes in the body weights of the rats were observed every two days and food intakes were calculated everyday. At the end of the experiment, passive avoidance tests were used to assess short-term memory. Cholinesterase (AChE) in the brain, superoxide dismutase (SOD) and malondialdehyde (MDA) in the brain and serum were determined. Compared with control group, the body weight of the high dose group decreased significantly ($P<0.05$). Sub-chronic aluminum exposure caused some changes in the step-through latency of passive avoidance, but these results were not statistically significant. Compared with the control group, the activities of SOD and AChE in the brain were significantly decreased, while MDA levels were significantly increased in Al exposure groups ($P<0.05$). The body weight and AChE activity in the brain were decreased and lipid peroxidation was enhanced after sub-chronic aluminum exposure but learning and memory functions were not changed.

Keywords: Aluminum Exposure, Learning and Memory Function, Antioxidant

Effects of supplemental zinc in broiler diets on carcass traits and meat quality

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Zinc (Zn) is an essential trace element, and plays important roles in various biological activities in animals. Some research showed that zinc could improve carcass traits of steers. The limited studies regarding the effect of zinc on carcass traits of poultry only measured skin and part of carcass traits. The objective of the experiment was to investigate the effect of dietary supplemental Zn on growth performance, carcass traits and meat quality of broilers. A total of 468 commercial 1-d-old Arbor Acres male broilers were randomly allotted by BW to 1 of 13 treatments (6 replicate cages of 6 chicks per cage) in a completely randomized design involving a 4 × 3 factorial arrangement of treatments (4 sources of Zn × 3 levels of supplemental Zn plus the Control with no supplemental Zn). Birds were fed the Zn-unsupplemented basal diet (the control) and the basal diet supplemented with 60, 120 or 180 mg Zn/kg as Zn sulfate (ZnSO₄·7H₂O), Zn amino acid A (Zn-AAC) with a chelation strength of 6.5 formation quotient (Qf) (11.93% Zn), Zn proteinate B (Zn-ProB) with a chelation strength of 30.7 Qf (13.27% Zn), or Zn proteinate A (Zn-ProA) with a strong chelation strength of 944.0 Qf (18.61% Zn) for 42 days. The results showed that birds fed diets supplemented with Zn had higher ADFI (P<0.10), ADG (P<0.05) and percentage of eviscerated yield (P<0.10) than birds fed the control diet. Supplemental Zn significantly increased (P<0.05) the b* value in breast muscle and pH Values in thigh muscle, decreased (P<0.10) shear force in thigh muscle, and decreased (P<0.10) drip loss in breast and thigh muscle. The DM and intramuscular fat (IMF) contents of the breast muscle in broilers fed diets with supplemental Zn were higher (P<0.10) than that of the control. There were no significant differences (P>0.10) in all the parameters among the three Zn level treatments. Results from this study indicate that Zn could promote growth and improve production performance of broilers independent of Zn source.

Keywords: Zinc, Meat Quality, Broiler

Efficacy of dietary selenium sources and vitamin E on growth and carcass characteristics of finishing pigs

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The experiment was conducted to investigate the effects of dietary supplementation with different selenium source (sodium selenite and seleno-methionine) and vitamin E on performance and meat quality of finishing pigs. Sixty-four crossbred (Duroc× Landrace× Largewhite) pigs (initial BW 69 ± 3.1 kg) were randomly allotted to four treatments according to a randomized complete block design (Four pigs×4 pens for one treatment). Pigs were fed corn-soy-bean meal-based diets supplemented with 0.30 mg/kg Se from sodium selenite (SS)(control), 0.30 mg/kg Se from sodium selenite and 100IU vitamin E (SE), 0.15 and 0.30 mg/kg Se from seleno-methionine (SM1 and SM2), respectively. One pig per pen was slaughtered, and carcass measurements were collected, loin quality was evaluated for pH, drip loss, and lightness, Anti-oxidation enzyme activity of longissimus dorsi muscle were measured. No performance or carcass measurement benefit resulted from either Se source or vitamin E during 40 days ($P>0.05$). Compared with inorganic Se-added treatments, water loss of loin was significantly decreased in organic Se-added treatments ($P<0.05$). Meat color redness (a) value was significantly increased in organic Se-added treatments in comparison with the control ($P<0.05$), and also 0.30 mg/kg Se (Se-Met) supplementation significantly decreased meat color yellowness (b) value ($P<0.05$). Superoxide dismutase (SOD) activity of longissimus dorsi muscle was significantly increased in Se—Met treatment compared with the control ($P<0.05$). Pigs dietary added 100IU/kg vitamin E significantly increased SOD activity of muscle in comparison with the control treatment ($P<0.05$), no significant differences were observed. These results indicate that diets supplemented with 0.15~0.30mg/kg Se (Se—Met) can significantly improve meat water loss and meat color of finishing pigs.

Keywords: Finishing Pigs, Selenomethionine, Meat Quality

Epigenetic effects of zinc deficiency on learning and memory ability in rats aged 0~2 years' old

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The molecular mechanism linking zinc deficiency on the impairment of learning and memory ability is not fully understood. Zinc is a component of the active site of enzymes that epigenetically modify DNA and histone. Recent evidence indicates that DNA methylation and histone acetylation are rapidly and dynamically regulated in nervous system and they are also important for synaptic plasticity and memory formation. Therefore, the effects of zinc deficiency on the epigenetics-related enzymes (DNA methyltransferases, DNMT and histone deacetylase, HDAC) expression and the methylation patterns of brain-derived neurotrophic factor (BDNF) gene which plays important roles in the development of the nervous system has been examined in this study. Six female Wistar rats were randomly divided into pair-fed group (PF; 30mg Zn /kg, n=3) and zinc-deficient group (ZD; 1mg Zn /kg, n=3) after parturition. PF rats consumed the same intakes as that of the corresponding ZD partner on the previous day. Ten offspring (5 males and 5 females) of each group were selected when they were weaned and fed the same diet as their mother. All 20 rats were killed when they were 2-month-old. The hippocampus and prefrontal cortex were removed for further analysis. In RT-PCR analysis, mRNA levels of DNMT1, HDAC2 and HDAC3 of hippocampus and DNMT1 of prefrontal cortex in ZD rats were elevated whereas the mRNA levels of BDNF gene of hippocampus and prefrontal cortex were decreased compared with those in PF rats. The early-life zinc deficiency produced a significant increase in methylated BDNF exon IX DNA and a corresponding decrease in unmethylated BDNF exon IX DNA in comparison with zinc adequate subjects. These results suggest that zinc deficiency in rats aged 0~2 years'old influences the modification of DNA methylation and histone acetylation, which would, in turn, impair learning and memory ability together.

Keywords: Epigenetic, Zinc Deficiency, Learning and Memory, Rats

Essentiality of selenium and thioredoxin reductase in *C. elegans*

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C. elegans expresses only a single selenoprotein, thioredoxin reductase-1 (trxr-1), and expresses the necessary proteins and tRNA needed to synthesize and incorporate selenocysteine, suggesting that *C. elegans* would be a good model organism for studying eukaryotic selenium (Se) metabolism, as thioredoxin reductase has been proposed as important in mammalian Se reduction and metabolism. The *C. elegans* genome also encodes a cysteine paralog, thioredoxin reductase-2 (trxr-2); mammalian orthologs of trxr-1 and trxr-2 as well as thioredoxin are all essential for embryogenesis in mice. We have characterized the effect of 0-5 mM Se as selenite on growth and reproduction in the wildtype (WT) strain (N2-Bristol) using a defined axenic media containing negligible Se. Twelve-day growth studies show a sigmoidal response curve with reduced growth at >0.1 mM Se, 50% growth reduction at 0.2 mM Se, and inability to reproduce at >1 mM Se. Importantly, no growth defect is observed in *C. elegans* cultured in 0 mM Se. SDS-Page analysis of *C. elegans* cultured axenically with [⁷⁵Se]selenite results solely in a ⁷⁵Se doublet with a major band at 72 kDa. Trxr specific activity in WT is ~17% of the activity found in Se-adequate mouse liver. To further investigate the essentiality of Se-dependent trxr-1 and its family members, we obtained two trxr-1 deletions strains (RB1961 and FX03462) and one trxr-2 deletion strain (RB1764). Strains were outcrossed to N2 males 3 times, and genotypes confirmed by sequencing. Agreeing with our growth data, trxr-1 mutant strains are viable and grow to similar densities as WT congenic strains. Growth of the trxr-2 mutant is also unaffected. To further determine if thioredoxin reductase is essential for *C. elegans*, we crossed the single mutants and found that the trxr-1/trxr-2 double mutant is also viable with no growth defects. Trxr-2 mutants readily incorporate ⁷⁵Se into thioredoxin reductase, but trxr-1 mutants and the double mutant lack ⁷⁵Se proteins. These studies indicate that thioredoxin reductase is not essential for growth and survival in *C. elegans*, and suggest that additional reductases readily metabolize Se in *C. elegans*. (Funded in part by UW WIS04909 and WIS01435)

Keywords: *C. elegans* ⁷⁵Se Proteins, Thioredoxin Reductase

Estimation of dietary selenium intakes of Taiwanese by a self-constructed food selenium content data

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Selenium (Se) is one of the essential trace elements for humans. The dietary sources of Se include organ meats, seafoods (0.4 ~ 1.5 µg/g), meats (0.1~ 0.4 µg/g), grains and their products (<0.1 ~ > 0.8 µg/g), dairy products (<0.1~ 0.3 µg/g), vegetables and fruits (<0.1 µg/g). The selenium contents of food vary depending on the selenium content in soil. Because the food selenium content data are not available in the Food Nutrient Content Database published by the Department of Health (DOH) in Taiwan, we analyzed the Se contents of about 100 food items from the major Se food sources to perform an estimate on the minimum dietary selenium intakes of Taiwanese and analysis about the relationship between food protein content and Se content. The Se contents of the major food sources are non-fat dried milk powder (7.6 µg/100 g), grains and cereals (9.7 ±16 µg/100 g), beef (30±7.8 µg/100 g), poultry (34.1 ±2.6 µg/100 g), pork (35.2±6.8 µg/100 g), fresh water fish (36.4 ±8.5 µg/100 g), eggs (46.7 ±15 µg/100 g), seafoods (57.7 ±28.6 µg/100 g) and ocean fish (118.3 ±103.3 µg/100 g). We also found that the Se content of various portions of pork was negatively correlated with their fat content and positively correlated with their protein contents. We further used the food consumption data from the series of The Nutrition and Health Survey in Taiwan (NAHSITs 1993 ~1996, 1999~2000, 2001 ~2002) to evaluate the dietary Se intakes of Taiwanese adults, elderly and school-age children. The dietary selenium intakes are about 74 µg/day for schoolchildren, 84 µg/day and 59 µg/day for adult males and females, 76 µg/day and 55 µg/day for elderly men and women, respectively. These dietary Se intakes all meet the Recommended Dietary Allowances of 40 ~55 µg/day established by DOH of Taiwan.

Keywords: Selenium, Taiwan, Food

Food iron bioavailability of the mixed Canadian diets

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Iron deficiency is one of the major worldwide health concerns. Heme iron, found in meat, fish and poultry (MFP) is highly absorbable in contrast to non-heme iron found in other foods. Recommendations for dietary iron assume 18% iron bioavailability in local mixed diet. Our objective was to estimate food iron bioavailability of the mixed Canadian diet, using ~35,000 food intake records from the 2004 Canadian Community Health Survey (CCHS 2.2-Nutrition). Heme values extracted from the literature were mapped into the Canadian Nutrient File database. Iron in food with no MFP source was considered to be non-heme iron. By assuming 250mg iron stores for women and 500 mg for men, appropriate absorption factors were applied to heme and non-heme iron based on the co-consumption of the amount of enhancers and MFP using the Monson algorithm for the food iron bioavailability. Total bioavailable iron was the sum of absorbable heme iron and non-heme iron. Usual intake distributions of iron and bioavailable iron were estimated using SIDE software using the full probability approach. Median total iron, total bioavailable iron, and food iron bioavailability for men 19 or above were 15.6 mg/d \pm 0.6, 1.1 mg/d \pm 0.02, 7.3% \pm 0.07, and 11.9 mg/d \pm 0.1, 1.1 mg/d \pm 0.02, 9% \pm 0.08 for women aged 19 or above. For females aged 14-18, 19-30 and 31-50, when status was assessed using total iron, the prevalence of inadequate intakes were 11.9%, 16.8% and 18.3%; while the prevalence of inadequate iron intakes were 68.1%, 74.6%, 70% when assessed by total bioavailable iron. For Canadians aged 19 or above, 45% of the dietary iron was from grain products, 24% from meat and alternatives, 18% from vegetables and fruits, 3% from milk and alternatives and 11% from other foods. These results indicate that the iron bioavailability of the typical Canadian diet, on average, ranged from 6% to 9%, which is significantly lower than the 18% that was used for the establishment of the DRIs. Results also showed the main food sources of iron for Canadians were mainly from lower bioavailable non-heme sources than from highly bioavailable meat (heme) sources.

Keywords: Iron Bioavailability, Absorbable Iron, Monson Model

Hair tungsten (wolfram) is increased in human depression

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Tungsten (W) is a non-essential element of a low order of toxicity. The tungsten (W) ion antagonises the normal metabolic action of the molybdate ion, and therefore can inhibit molybdate-dependent enzymes. We studied the distribution of tungsten (W) in the hair and whole blood of occupationally non-exposed depressed (n=48; 15 men, 33 women) and control (n=48; 28 men, 25 women) subjects. Depression was diagnosed by the certified psychiatrist following the DSM-IV criteria. The study was conducted following the declaration of Helsinki on the ethics of the human subject research. Tungsten (W) analysis was performed by ICP-MS at the CBM, Moscow, Russia, an ISO certified analytical laboratory. International certified standards for hair and whole blood analysis were used for the control. There were no difference in tungsten (W) hair and whole blood concentration between men and women. Median tungsten (W) concentration was increased in the hair of depressed subjects (depressed 0.020 $\mu\text{g/gE}^{-1}$, control 0.007 $\mu\text{g/gE}^{-1}$), and median concentration of tungsten (W) in the blood was also increased in the depressed subjects (depression 0.0031 $\mu\text{g/gE}^{-1}$, control 0.000385 $\mu\text{g/gE}^{-1}$). The difference was statistically significant by the chi-square test ($p < 0.01$ for the hair and $p < 0.05$ for the whole blood). Hair appears to be a more sensitive indicator tissue for assessing tungsten (W) metabolism than whole blood. The reason for observed difference of greater tungsten (W) accumulation in the hair and whole blood of depressed than in the normal subjects remains to be elucidated.

Keywords: Tungsten, Hair and Blood, Depression

Hepatic oxidative damage induced by moderate Cu supplementation in cattle

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Copper (Cu) is an essential metal associated with several enzymes that acts as an electron transfer intermediate in redox reactions. However, redox properties, when in excess also generate free radicals that can be seriously deleterious to cells. Hepatic toxicity, caused by Cu overload, is hypothesized to result from redox properties of Cu and is the formation of reactive oxygen species. We evaluated at a histopathological level the effect of the commonly used Cu supplementation (15 mg/kg DM) in intensively reared cattle on (i) the induction of oxidative damage—as inducible nitric oxide synthase (iNOS), nitrotyrosine (NITT), malondialdehyde (MDA) and 8-oxoguanine (8-oxo)—that (ii) could increase apoptotic cell death—determined by cytochrome c (cyto-c), and terminal deoxynucleotidyl transferase dUTP nick end labelling (TUNEL). Liver samples from Cu-supplemented (15 mg Cu sulphate/kg DM, n=5) and non-supplemented calves (n=5) were collected at slaughter and processed for analysis. Cell counts were carried out in 0.39 mm² areas around central veins and portal triads (0.78 mm² for each animal) in 6 µm liver sections which allowed statistical analysis. An analysis of variance (ANOVA) was used to check the influence of the region within the liver (central veins versus portal triads) and Cu supplementation (Cu-supplemented versus non-supplemented) on positive cells of the different staining distribution. iNOS and NITT positive (+) cells significantly increased, mainly around the central veins in the animals from the Cu supplemented group, while no differences were appreciated for the rest of the oxidative stress and apoptosis markers. Thus, under the conditions of this study, which are the conditions of the cattle raised in intensive systems in many European countries, routinely Cu supplementation increased the risk of the animals to undergo subclinical Cu toxicity, with a significant and important increase of oxidative damage measured by iNOS and NITT. These increases could be considered as the initial pathological changes in the liver of Cu exposed cattle before further damage in lipids, DNA and finally apoptosis.

Keywords: Copper, Subclinical Toxicity, Oxidative Stress

Identification of selenoproteins from amphioxus genomes via bioinformatics method

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With genome sequencing in a huge amount of biological data are available for the prediction of selenoproteins in various species. However, it is still difficult to identify the open reading frame (ORF) of eukaryotic selenoprotein genes, because the TGA codon for a selenocysteine (Sec) residue is also a stop codon. Although the identification of selenoproteins from genomes through bioinformatics methods has been conducted in many species, only a few results have been reported on the ancient invertebrate selenoproteins, eg, *Ciona intestinalis*. A gene assembly algorithm SelGenAmic has been constructed and presented in this study for identifying selenoprotein genes from eukaryotic genomes. A method based on this algorithm was developed to build an optimal TGA-containing-ORF for each TGA in a genome, followed by protein similarity analysis through conserved sequence alignments to screen out selenoprotein genes from these ORFs. This method improved the sensitivity of detecting selenoproteins from a genome due to the design that all TGAs in the genome were investigated for its possibility of decoding as a Sec residue. Using this method, 35 selenoprotein genes belong to 23 protein families were identified from the genome of *Branchiostoma floridae*, which is a representative of the invertebrate subphylum Cephalochordata. Among them a selenoprotein W gene was found to have two Sec residues while no similar phenomenon was found in SelWs of other species. Additionally, the methionine-S-sulfoxide reductase A (MsrA) was firstly identified as a selenoprotein in the metazoan *Branchiostoma floridae*, while selenoprotein MsrAs had only been found in bacteria and green algae before. Interestingly selenoproteins such as selenoprotein U and selenoprotein J which had not been found in mammalian were found in amphioxus, and a selenoprotein P which only has the N terminal region containing one Sec residue was also found in the study. This selenoprotein P was the most primeval member found up to the present in the SelP family. Application of this method to *Branchiostoma floridae* proves its successes in identifying Sec-decoding TGA from large-scale eukaryotic genome sequences, which fills the gap in our knowledge on ancient Cephalochordata selenoproteins.

Keywords: Selenoprotein, Bioinformatics, Branchiostoma Floridae

Impact of macro- and trace elements in reproductive health: data of multielement ejaculate investigation in subfertile males

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It is known, that some TE deficiencies and intoxications can play a negative role in fertility. We investigated 168 subfertile 19–49 years old men, living in Moscow region (85 men with astenozoospermia, 17 men with oligoastenozoospermia and 66 men with leucocytospermia). Also there were 91 controls with “normozoospermia” and clinically healthy subjects tested. Collected ejaculate samples were treated by microwave digestion and analysed by ICP-AES/ICP-MS in laboratory of Centre for Biotic Medicine, Moscow. The data demonstrated that the coefficient of spermatozoa motility positively correlated with Cd and negatively correlated with K, Mg, Se, Zn content in ejaculate. Decreased Zn, Se, Mg ejaculate concentration (EC) was found in males with astenozoospermia (Zn, Se, Mg), astenoolygozoospermia (Se) and leucocytospermia (Zn, Se, Mg), which are typical for chronic prostatitis. Also, the lack of Zn, Se, Mg can play the role in pathogenesis of spermatozoa motility derangement. Low Cu EC was associated with low total spermatozoa number; low Fe and K were typical for males with astenozoospermia and astenoolygozoospermia, respectively. It is important to note accumulation of Pb in ejaculate in astenozoospermia. Thus macro- and trace elements imbalances, as suggested by our investigations, have an impact in men’s infertility; multielement analysis of ejaculate can provide the useful information about physiological and ecological (toxicological) reasons of infertility due to the macro- and trace elements metabolism disturbances. Our data demonstrate the perspectives of infertility therapy improvement by macro- and trace elements drugs, nutraceuticals and chelators.

Keywords: Male Subfertility, Ejaculate, Mineral Profile

Investigation of effects of selenium on Ca^{2+} signaling and apoptotic cell death in oxidative stress-induced dorsal root ganglion neurons

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DRG (Dorsal Root Ganglion) sensory neurons have a key role in peripheral nerve diseases such as neuropathic pain and diabetic neuropathy. Ca^{2+} is well known for its role as crucial second messenger in modulating many cellular physiological functions, Ca^{2+} overload is detrimental to cellular function and may present as an important cause of cellular ROS generation and apoptosis. But this topic has not been well known in DRG sensory neurons. The unbalanced cellular mechanism between ROS production and antioxidant system is called as oxidative stress. The aim of this study is to investigate the effects of selenium on lipid peroxidation, GSH, GSH-Px activity, cytosolic Ca^{2+} release, cell viability and apoptosis in DRG neurons. DRG cells were divided into six groups namely control, H_2O_2 , ADPR, Se, Se+ H_2O_2 , Se+ADPR. The doses and times of H_2O_2 , selenium were determined by MTT assay which is used to evaluate cell viability. Cells were incubated with 1 μM H_2O_2 for 2 hours and 200 nM Se for 30 hours. Then, cells were stimulated with 100 μM H_2O_2 or 0.8 mM ADPR (depending on their groups) for evaluating the $[Ca^{2+}]_i$ release. Lipid peroxidation levels were significantly lower in the control, Se, ADPR, Se+ H_2O_2 , Se+ADPR groups than in the H_2O_2 group ($p < 0.001$). GSH-Px activities were significantly higher in the Se and ADPR groups than in the H_2O_2 group ($p < 0.01$). GSH levels were significantly higher in the control, Se, ADPR, Se+ H_2O_2 , Se+ADPR groups than in the H_2O_2 group ($p < 0.05$). Cytosolic Ca^{2+} release was significantly higher in the H_2O_2 group than in the control, Se, ADPR, Se+ H_2O_2 , Se+ADPR groups ($p < 0.001$). Cytosolic Ca^{2+} release was significantly lower in the Se+ H_2O_2 group than in the H_2O_2 ($p < 0.05$). In conclusion, the present study demonstrates that 200 nM selenium induced protective effects on oxidative stress, $[Ca^{2+}]_i$ release and apoptosis in DRG cells.

Keywords: $[Ca^{2+}]_i$ Release, Oxidative Stress, Selenium, Dorsal Root Ganglion Neurons

Iodine content of breads in Canada is highly variable by product type, region and time

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Iodine is an essential trace element nutrient and a component of thyroid hormones. Levels of iodine in foods are highly variable. Naturally occurring iodine in many food sources is low, but can vary due to soil iodine content, agronomic practices, food processing and use of iodized salt. While iodization of table salt is mandatory in Canada, the food processing industry is not required to (but may) use iodized salt. The Canadian Total Diet Study (CTDS) collects food samples at retail from one city per year. These foods are processed as if for home consumption, then combined into food composite samples that are analysed for a variety of endpoints. Food composites from the 2001-2005 and 2008 cycles of the CTDS were prepared by microwave digestion and ICP-MS analysis for total iodine content. In 2009 and 2010, some additional analyses of individual bread products were done. Levels of total iodine in loaf bread or buns and rolls composite samples varied from below the detection limit (<DL, i.e. <29 ng/g) to over 2000 ng/g fresh weight. Geographic differences were noted, with higher values found in some samples from Ontario and Quebec than from other provinces sampled. Follow-on investigation of selected individual bread products revealed large variation within the products comprising a composite, from <DL to several thousand ng/g. Levels of total iodine measured in breads, buns and rolls in Canada in the past decade are highly variable by product type, region and time.

Keywords: Iodine, Breads, Analysis

Iodine status of women from selected rural areas of Sidama Zone, Southern Ethiopia

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This study assessed iodine status, socio-demographic factors and cognitive function of women in Sidama Zone, Southern Ethiopia. A convenience sample of 202 non-pregnant women age 18 and above gave informed consent to participate in this cross-sectional study. Socioeconomic and demographic information was collected by individually-administered questionnaires. Weight, height and mid-upper arm circumference were measured. Thyroid gland enlargement was assessed using palpation and casual urine samples were collected to measure urinary iodine excretion (UIE) and analyzed using the Sandel-Kolthoff reaction. Cognitive functioning was assessed using tests from Raven's Colored Progressive Matrices and Kaufman ABC-II. Mean (SD) age was 30.8 (7.8) y. Mean height was 157.3 (6.0) cm and mid upper arm circumference (MUAC) was 24.8 (2.5) cm. Body mass index (BMI) was < 18.5 for 24.8% of the women and > 25 for only 2%. No woman reported the use of iodized salt. Median UIE was 37.2 µg/L. Participants with UIE <20 µg/L were 22.8% and were classified as severely iodine deficient; 46.5% had UIE from 20 to <50 µg/L or moderate iodine deficiency, and 27.2 % had UIE in the mild deficiency range of 50 to <100 µg/L. Only 3.5% of the women had UIE ≥ 100 µg/L. The visible goiter rate was 1.5% and 14.4% of the women had palpable goiter making a total goiter rate of 15.9%. Scores on cognitive assessments were generally low, but UIE was correlated (<0.05) with short-term memory, visual processing and non-verbal intelligence. Women's education contributed more to the prediction of cognitive test scores than did UIE. Because damage to the brain from iodine deficiency can begin during gestation, it is not surprising that UIE, which reflects only recent iodine intake, was not highly predictive of cognitive scores. We conclude that the widespread occurrence (96.5%) of UIE less than 100 µg/L and a total (palpable + visible) goiter rate of 15.9% in non-pregnant reproductive-age women indicate a very serious public health problem in Sidama Zone of Southern Ethiopia. *Supported by Hawassa University, Oklahoma State University and NIH RO1HD053053 (NICHD & Fogarty International Center)*

Keywords: Iodine Deficiency, Goiter, Ethiopia

Lepidium sativum* L. for iron enrichment of RTE flakes of *Panicum miliare

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Lepidium sativum L. or garden cress seed is a special seed used in special food preparations given to girls at menarche and after delivery in traditional Indian foods. It is rich in iron and also contains several nutraceutical components. *Panicum miliare* or little millet is minor coarse millet with proven health benefits in management of type 2 diabetes, hyperlipidemia and other metabolic disorders. Iron enriched little RTE millet flakes were developed incorporating garden cress seeds for iron enrichment. No additives were used in processing. The flakes were developed by traditional batch processing method by steaming the dehulled millet in a rotary steamer (20 lbs/psi) with intermittent cooling, followed by roller pressing (70 rpm, 0.25 mm gap) along with garden cress seeds (5.0 %), flaking (70 rpm, 0.10 mm gap) and toasting (180- 200⁰ C). The RTE flakes recorded 7.18 per cent increase in iron content (65.83 mg per 100g) over control millet flakes (61.42 mg%). The flakes also recorded high dietary fiber (22.7%), calcium (29.30 mg %) and energy (283 Kcal). Improvement in dialyzable iron content was observed (0.23 mg/100 g) compared to control flakes (0.19 mg/100g). Iron enriched little millet flakes also recorded appreciable amounts of calcium (29.30 mg %), copper (0.37 mg %), zinc (2. 61 mg %) and manganese (0.30 mg %) contents. The flakes were highly acceptable in terms of colour, appearance, taste, texture and over all acceptability. The acceptability index was 73.31 per cent on 9 point hedonic scale. The flakes exhibited a shelf life of more than 6 months. The study indicated the potentials of value added little millet breakfast cereal as a novel food with nutraceutical properties.

Keywords: Iron, Millet, Enrichment

Selenium and antiepileptic drug topiramate modulate Ca²⁺ signaling, oxidative stress and cell viability in PC 12 cells

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Epilepsy is one of the most common and chronic neurological disorder characterized with seizures which occur as a result of biochemical and molecular events. Oxidative stress has been proposed to play crucial role in the pathophysiology of epilepsy and some antiepileptic drugs such as valproic acid induced oxidative stress in human. It has been reported that selenium (Se) supplementation in epileptic patients, regulates antioxidant defense mechanisms and protect cells against neuronal damage. Topiramate (TPM) is effective antiepileptic drug although the mechanism of TPM possible neuroprotective effect is still not well known. We aimed to investigate the effects of TPM and Se on lipid peroxidation, GSH levels, GSH-Px activity, cytosolic Ca²⁺ levels and cell viability in PC 12 neuronal cells.

PC12 cells were divided into eight groups namely control, TPM, Se, hydrogen peroxide (H₂O₂), TPM+H₂O₂, Se+H₂O₂, Se+TPM, Se+TPM+H₂O₂. The therapeutic dosages of H₂O₂, TPM and Se were determined by cell viability (MTT) test. Cells were incubated with 10 µM of TPM for five hours and 500 nM of Se for ten hours. Afterwards cells were treated with 100 µM of H₂O₂ for ten hours before analysis. Lipid peroxidation levels were lower (p<0.05) in control, TPM, Se, Se+TPM, Se+H₂O₂, TPM+H₂O₂, Se+TPM+H₂O₂ groups than in H₂O₂ group. GSH-Px activities were higher (p<0.01) in Se and Se+TPM groups than in H₂O₂ group. GSH levels were higher (p<0.05) in control, TPM, Se, Se+TPM, Se+H₂O₂, TPM+H₂O₂ and Se+TPM+H₂O₂ than in H₂O₂ group. Cytosolic Ca²⁺ levels were also higher (p<0.001) in H₂O₂ group than in control, TPM, Se, Se+TPM, Se+H₂O₂, Se+TPM+H₂O₂ groups. Cytosolic Ca²⁺ levels were also higher (p<0.05) in Se+H₂O₂ group than in Se and Se+TPM groups.

In conclusion, results of current study demonstrated that TPM combination with Se induced protective effect on oxidative stress and cytosolic Ca²⁺ homeostasis in PC 12 cells.

Keywords: Epilepsy, Topiramate, Selenium, Oxidative Stress, Ca²⁺ Signaling, PC12 Neuronal Cells

Male pigs fed a supranutritional selenium diet may develop a predisposition to type 2 diabetes

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Selenium (Se) is an essential trace element with potential health benefits for the prevention of cancer and oxidative stress-related chronic diseases. Recently, epidemiological studies have raised fears that supranutritional Se intake may be a risk factor for type 2 diabetes. Both impaired insulin secretion and insulin resistance of target tissues might be triggered or aggravated by high Se intake. To probe the underlying molecular mechanisms, we compared the expression levels of several selenoproteins, enzymes and transcription factors related to carbohydrate and lipid metabolism in major insulin target tissues of male pigs fed either a Se-adequate (0.17 mg Se/kg) or a Se-supranutritional (0.5 mg Se/kg) diet. After 16 weeks of supplementation, plasma Se concentration had risen in the high Se animals, and this was accompanied by slight increases in fasting plasma concentrations of insulin, cholesterol and triacylglycerols. However, fasting glucose concentrations did not differ between the two groups. Glutathione peroxidase activity was enhanced in skeletal muscle but not in liver or visceral fat of the high Se pigs; there were only marginal differences in mRNA levels of selenoproteins and other antioxidant enzymes in all three tissues. In skeletal muscle of the high Se pigs, pyruvate kinase was down-regulated, whereas the transcription factors FoxO1a and PGC-1 α were up-regulated. In visceral fat of the high Se pigs, mRNA levels of the transcription factor SREBP1 were increased. These changes in transcription factors and enzymes suggest a shift to increased lipid metabolism. We conclude that prolonged Se supplementation may cause disturbances in insulin-regulated carbohydrate and lipid metabolism, but that high Se intake alone is probably not sufficient to induce overt diabetes.

Keywords: Selenium Supplementation, Selenoproteins, Pig, Diabetes, Insulin

Metabolism of platinum after anti-tumor agent oxaliplatin treatment was altered by the ingestion of fucoidan

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Fucoidan is a sulfated fucan polysaccharide with several substitutions, contained in various brown sea algae. Fucoidan extracted from *Cladosiphon okamuranus* (*C. okamuranus*) has a characteristic structure with glucuronic acid and an acetyl group and has various biological activities such as removal of *Helicobacter pylori* from stomach to avoid cancer, anti-infection against enteropathogenic *E.coli* O-157, reducing uric acid contents in blood and also improving the stomach conditions. In addition to these biological activities fucoidan from *C. okamuranus* has beneficial effects in decreasing the severe side effects of anti-tumor drugs of Pt complexes such as persistent nausea, vomiting, tiredness, dizziness, stomach pain and loss of appetite. Since there has been no explanation for these beneficial effects we carried out experiments to observe the metabolism of Pt in mice after anti-tumor agent oxaliplatin treatment with and without fucoidan ingestion. After one day feeding with fucoidan from *C.okamuranus* or from *Sargassum horneri* the Pt containing anti-tumor drug oxaliplatin was injected i.p. to ICR mice (n=5, each group) and the collection of urine and feces in metabolic cages continued for 4 days. The urine and feces were chemically digested by wet-ashing processes with nitric acid and hydrogen peroxide. Pt was analyzed by atomic absorption spectrometry with a graphite furnace. Pt metabolism was compared between the two kinds of fucoidan and without fucoidan in mice. The amounts of Pt excretion in urine were not altered by the ingestion of fucoidan from *C.okamuranus* but decreased in those treated by the fucoidan from *Sargassum horneri*. In contrast Pt excretion into feces was reduced in the presence of fucoidan from *C.okamuranus* but did not alter in the case of fucoidan from *Sargassum horneri*. The reduction of the excretion through the liver may explain the reduction of severe side effects by the Pt anti-tumor agent.

Keywords: Platinum, Anti-cancer Drug, Fucoidan

Methods to estimate trace mineral bioavailability

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Bioavailability is the degree to which an ingested nutrient in a particular source is absorbed in a form that can be utilized in metabolism by the animal. Providing a complete estimate of whole body utilization for trace minerals is problematic, as it is not possible to measure the activity of all the various enzymes, transcription factors and processes that use and/or store these minerals. In most cases, bioavailability can be simplified to the rate that the nutrient in question is released from the ingredient matrix and absorbed. Indeed, commonly-used statistical methods to establish relative bioavailability (RBV) are predicated on the fact that one is comparing identical nutrients (i.e. zinc) from different sources (i.e. zinc sulfate, zinc chelate, etc.), and that the dose responses associated with utilization of the nutrient are themselves identical. In other words, once the nutrients are absorbed, utilization will be the same. Therefore utilization within the body would be identical and does not need to be addressed. Several response variables can be used to estimate the bioavailability of one trace mineral source to that of a second, standard source. These include the deposition or storage of minerals into selected tissues, the enzyme activity, or the expression of mineral responsive genes eg. metallothionein. Each type of response variable has advantages and disadvantages, so ideally multiple variables should be measured. Regardless of the variable(s) tested, care must be taken to ensure that measurements are taken on the dose response curve prior to the plateau. In such cases, common-intercept, multiple linear regression and slope-ratio analysis can be performed to estimate the bioavailability of the test source relative to the standard source. Many experiments have shown that chelated or “organic” trace minerals exhibit greater bioavailability than trace mineral salts. However, it is striking how many experiments indicate no RBV differences between inorganic and organic zinc sources. The supplemental zinc levels in many of these experiments were far above requirement, which can have the effect of minimizing differences between sources. The lack of differences at high levels of supplementation may be due to homeostatic mechanisms at the level of zinc absorption which act to maintain relatively constant level of tissue mineral levels.

Keywords: Trace Minerals, Bioavailability, Zinc

Will selenium increase lentil grain yield and nutritional quality?

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Lentils (*Lens culinaris* L.), amongst the first crops domesticated in the Middle East, have been a food staple for humans since the Neolithic ages. Lentils are an excellent source of protein (25-30%), dietary fiber, and wide range of micronutrients, iron (73-90 mg/kg), zinc (44-54 mg/kg), and selenium (425-673 µg/kg). Lentils are part of daily diets in billions of developing country and vegetarians populations around the world. Plants are not known to require selenium (Se); however, it seems that trace levels of this element can protect plants from oxidative stress. Our preliminary results show that lentils show significant metabolic responses to added Se. This paper will present the potential of added Se as a plant nutrient and its impact on lentil seed yield and nutrient quality. Research on the specific role of Se on physiological, genetic, and environmental variations to retain bioavailable Se forms is in progress. The results from this study could be used to develop high yielding and nutritionally superior lentils as a potential solution to alleviate global Se deficiencies.

Keywords: Selenium, Lentils, Bioavailability

(This abstract is withdrawn by authors)

Micromineral status and nutrient utilisation in Zebu cattle

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Micromineral deficiencies in cattle are omnipresent, both in developing and industrialized regions. Little information is available on the effect of micromineral deficiencies on nutrient use and digestibility, in spite of many deficiency-related symptoms suggesting a relevant role, such as loss of appetite in Zn deficiency and scouring in Cu deficiency. The present study aimed to identify the importance of adequate micromineral provision on nutrient utilisation in zebu cattle in Ethiopia. Eight zebu steers (*Bos indicus*) were randomly divided into two groups. Four animals received micromineral supplementation (Zn, Mn, Cu chelated to glycine MAAC®, MAAC® Se Premix (Novus International, Inc.) and inorganic I and Co) for 4 weeks, the four remaining were controls. The basic diet, identical for all animals, consisted of mixed grasses. Mineral levels were determined in feed, plasma and faecal samples. Apparent nutrient digestibility (DM, ash, protein, fat, NDF, ADF, ADL, minerals) was measured by total collection (3 days), along with concentrations of ceruloplasmin (CP), superoxide dismutase (SOD) and acylcarnitines (ACAR) in plasma as indicators of fermentation and energy substrate use. Faecal nitrogen fractions (FNF) (bacterial, vegetal or animal) and body weight (BW) were also measured. Repeated measures analysis was performed on all data, with baseline data (sampled one week prior to supplementation) as covariate. Feed mineral analysis revealed deficient Cu (5.53-9.60 mg/kg) and Se (0.02-0.09 mg/kg) in combination with high S (0.26-0.39%) and Mo (1.52-3.12 mg/kg) and very high Fe (619-1214 mg/kg) concentrations. Micromineral supplementation increased plasma Cu (0.82 vs. 0.61 mg/l), Zn (1.40 vs. 0.89 mg/l), Mn (0.30 vs. 0.05 mg/l) and Se (0.07 vs. 0.06 mg/l) concentrations (all P<0.05). Faecal Cu, Zn, Mn and Se were also increased (P<0.05), as was faecal Co (P=0.06) concentration in supplemented cattle. Supplementation affected neither apparent nutrient (DM, ash, protein, fat, fibre, mineral) digestibility nor CP, SOD, ACAR, FNF or BW (P>0.05) in this pilot study. Despite clear improvement on micromineral status - notwithstanding high concentrations of Cu and Se antagonists in the diet – supplementation did not impact nutrient digestibility or utilisation in a clear way. Further research should confirm the absence of this relationship.

Keywords: Microminerals, Cattle, Digestibility

Molecular characterization and NF- κ B-regulated transcription of selenoprotein S from the Bama mini-pig

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Selenoprotein S (SelS), a member of selenoprotein family, plays important regulatory function in inflammation and metabolic diseases. SelS expression is up-regulated in response to inflammatory stimulus in many mammal cells, animal models as well as patients. In order to further understand the function of SelS gene, molecular characterization and transcriptional regulation of SelS from a Bama mini-pig were analyzed in the present study. The results showed that pig SelS encoded a protein of 190 amino acids with estimated molecular weight of 21.23 kDa and pI of 9.526. The genomic structure, promoter and deduced amino acid sequence were analyzed and found to share high similarity with those of human SelS. Pig SelS fusion protein was demonstrated to localize in the cytoplasm by fluorescence microscopy. Real-time PCR revealed the ubiquitous expression pattern of pig SelS in diverse tissues, a high level expression was observed in the liver and lung, relatively low expression in other tissues, especially in muscle. Promoter deletion analysis further suggests that an NF- κ B binding site within the SelS promoter is responsible for the up-regulation of SelS transcription.

Keywords: Selenoprotein S, Transcription, NF- κ B

Distribution of V, Zn, Cr, Cu and Se in Panzhihua Sichuan

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Panzhihua is rich in mineral resources. Most essential microelements for human needs have been found there. It's also famous subtropical distinctive agricultural producing, ninety percent of fruit and vegetables sold to all over China. We want to know the distribution of V, Zn, Cr and Cu that are connected with blood sugar in Panzhihua. Soil, leaves and vegetables associated with eight plants were analysed. Of special interest was one plant only grown in Panzhihua, namely the Psidium guajava. We also selected eggplant, pepper, snap bean, cucumber, balsam pear, march melon, potato and tomato and Psidium guajava. We took soil from fifteen to thirty cms depth and vegetables and leaves for analysis by Inductively Coupled Plasma MS to detect V, Zn, Cr and Cu. Analytical Results indicted that showed in Table1. No.1 means trace elements content in vegetables, No.2 means trace elements content in leaves, No.3 means trace elements content in soil.

Table 1 Trace elements content in vegetables (mg/kg)

name	V			Zn			Cr			Cu		
	1	2	3	1	2	3	1	2	3	1	2	3
Eggplant	0.17	0.83	193.5	3.86	4.06	85.6	0.12	0.32	87.0	2.55	1.95	33.9
Pepper	0.15	0.32	198.3	1.74	8.69	109.2	0.08	0.11	67.6	1.03	1.35	26.7
Snap bean	0.14	0.66	195.8	5.03	6.54	73.9	0.09	0.25	49.2	1.05	2.81	17.1
Cucumber	0.08	0.77	197.6	2.60	10.54	73.5	0.06	0.31	49.8	0.69	9.33	15.5
Balsam pear	0.10	0.42	121.5	2.85	11.31	82.8	0.06	0.19	92.1	1.24	1.74	30.1
March melon	0.10	2.00	162.8	2.89	17.45	123.5	0.07	1.05	117.4	0.89	2.74	45.4
Potato	0.06	0.91	115.5	4.50	2.93	32.8	0.06	0.53	110.2	3.79	1.79	20.6
Tomato	0.13	0.61	270.8	0.92	2.31	115.4	0.09	0.55	251.2	0.77	1.00	78.8
Psidium guajava		1.85	190.9		14.93	68.6		0.81	104.6		8.70	23.1
Mean	0.12	0.93	182.97	3.05	8.75	85.03	0.08	0.46	103.23	1.50	3.49	32.36
SD	0.04	0.60	46.42	1.37	5.31	27.94	0.02	0.31	60.80	1.10	3.19	19.71

The soil is rich V, Zn, Cr, Cu. Notably, vanadium is the highest of the four micro elements being higher than copper and zinc. Microelements were much higher in leaves than in fruit. However in fruit, zinc was the highest in leaves. Absorptivity of the four elements from soil to vegetables were Zn>Cu>V>Cr. Hence we can see that V and Cr are not well absorbed by vegetables. Plants mostly absorb soluble vanadium which only occupies one point five percent of vanadium in soil. Vanadium is deemed to be a sensitizer of insulin and has interactions with other microelements, such as copper, zinc and chromium. Fruit grown in Panzhihua has abundant microelements. Psidium guajava has the highest content of vanadium, the local population use it to treat hypertension and glycaemia. Our preliminary research the content in soil, leaf and vegetables provides some interesting information worthy of further study.

Keywords: V, Zn, Cr, Cu, Local Fruit and Vegetables

Prevalence of anemia among schoolchildren in Morocco

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Anemia is a widespread public health problem in developed and developing nations. In developing countries, schoolchildren constitute the population with the next - highest prevalence after pregnant women. This study aimed to determine its prevalence of anemia and its risk factors among preadolescents in North western Morocco. 306 pupils from primary schools were observed and blood samples were taken with their parents consent. We also collected anthropometric data, information about social and demographic characteristics. More than 30% of these children had anemia: prevalence did not differ by sex, but was higher among those living in urban environments. Factors related to food behavior, especially diet diversity, appeared to be important. The prevalence of anemia among schoolchildren is high in the province of Kenitra. Nutrition strategies are needed to alleviate anemia and iron deficiency in schoolchildren.

Keywords: Anemia, Schoolchildren, Morocco

Protective effect of zinc supplementation against aluminium neurotoxicity: possible behavioral, biochemical and histopathological alterations in male rats

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The present study was designed to examine the protective potential of zinc supplementation in ameliorating behavioral, biochemical and histopathological changes induced by aluminium. Animals were exposed orally to aluminium chloride (300 mg/kg bw/day) and through diet administered different doses of zinc, group I (50 mg zinc/kg diet), group II (100 mg zinc/kg die) and group III (200 mg zinc/kg diet). The treatments were given for a period of 9 weeks, and all animals received aluminium chloride after the third week. No significant change on the latency in passive avoidance performance was observed among all animal groups. Significant increases in the number of rearings in group II was observed compared with group I. Compared with group I, the MDA level in the cerebrum was significantly decreased in group II and group III. The activity of AchE in the cerebrum was significantly decreased in group III compared with group I. While the SOD activity and the levels of aluminium and zinc concentrations were not statistically significant among all groups. Compared with group I, the activity of DA and 5-HT had a trend for an increase in group II and group III. Pyknotic nuclei with prominent perineuronal spaces were observed in the hippocampus of rats in group I. Restoration of pyramidal cells was observed in the hippocampus of rats in group II and group III. The results shows that zinc can be used as a neuroprotectant and regulate neurotransmission as well as behavioral functions in aluminium toxic conditions.

Keywords: Al exposure, Zinc, Behavior, Histopathology, Neuroprotection

Regression of abdominal aortic aneurysms by a novel nanobiomaterial for time-controlled delivery of copper in a rabbit model

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Abdominal aortic aneurysm (AAA) is a degenerative disease condition associated with aging and atherosclerosis. Many efforts have been devoted to the development of treatment for this disease, but the surgical removal of AAA is the only option at present. Recent studies have shown that copper (Cu) supplement can reverse cardiac hypertrophy. The present study was undertaken to examine whether Cu can also cause regression of AAA. A rabbit model of AAA was used. AAA was produced by elastase infusion. Four weeks after the infusion, the diameter of perfused segment reaching 150% or greater over the adjacent proximal segment was considered as AAA, determined by ultrasonography. A time-controlled nanobiomaterial for the delivery of Cu, composed of a short peptide (including His, Arg, and Gly residues) with the design of Cu²⁺ binding sites, was used to treat the AAA by directly injecting the stable hydrogel-like Cu-bound nanobiomaterial (Cu-NM) at multiple sites around the AAA tissue. One week after the treatment, the dilation of AAA was significantly reduced in some cases. Analysis in vitro revealed that the Cu-NM could slowly release Cu²⁺. This study thus demonstrates that with a localized Cu delivery, the AAA condition could be improved although the mechanism has not been explored.

Keywords: Copper, Abdominal Aortic Aneurysm, Nanobiomaterial

Selenium-deficiency diseases in chicks are associated with down-regulation of seven common selenoprotein genes in liver and muscle

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Fast-growing broiler chicks are susceptible to Se-deficiency diseases including exudative diathesis (ED). Our objective was to determine if these classical diseases were reproducible by feeding a current practical diet and how the incidences were related to selenome expression in two major tissues liver and muscle. Four groups of day-old broiler chicks (n = 60/group) were fed a corn-soy basal diet (BD, 14 µg Se/kg; produced in the Se-deficient area of Sichuan, China; and not supplemented with Se or vitamin E), or the BD + rac- α -tocopheryl acetate at 50 mg/kg, Se (as sodium selenite) at 0.3 mg/kg, or both of these nutrients for 6 wk. A high incidence of ED and other classical Se-deficiency diseases and mortality of chicks were induced by the BD. The incidences and mortality were completely prevented by supplemental dietary Se, but only partially decreased by supplemental α -tocopherol acetate. Dietary Se resulted in dose-dependent increases (P < 0.05) in GPX activities in plasma, muscle, and liver, but nearly no effect in GPX activities by supplemental α -tocopherol acetate except in wk 2 liver. Dietary Se deficiency decreased (P < 0.05) mRNA levels of 7 common selenoprotein genes (Gpx1, Gpx4, Sepw1, Sepn1, Sepp1, Selo, and Selk) in muscle and liver. While supplementing α -tocopherol acetate enhanced (P < 0.05) only muscle Sepx1 mRNA level, it actually decreased (P < 0.05) hepatic Gpx1, Seli, Txnrd1, and Txnrd2 mRNA levels. In conclusion, dietary Se protected chicks from the Se-deficiency diseases probably by up-regulating selenoprotein genes coding for antioxidant and muscle-protective proteins. The protection of vitamin E was likely mediated via muscle Sepx1 and(or) other independent mechanisms. The inverse relationship between hepatic expression of 4 redox-related selenoprotein genes(Gpx1, Seli, Txnrd1, and Txnrd2) and vitamin E status revealed a novel functional coordination between Se and vitamin E in vivo.

Keywords: Exudative Diathesis, Selenium, Vitamin E, Selenoprotein

Sodium iron EDTA can partly overcome the strong inhibitory effect of polyphenols from brown sorghum on iron absorption in young women and causes less colour changes in sorghum porridges than ferrous sulfate

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Iron deficiency (ID) is the most prevalent micronutrient deficiency worldwide, affecting principally children <5 years of age and women of child bearing age living in the poorer communities of the developing world. Low dietary iron bioavailability from staple cereals such as sorghum might contribute to ID in sorghum-consuming communities in developing countries. Some sorghum varieties contain a considerable amount of polyphenols (PPs) in addition to phytic acid; both well-known inhibitors of non-heme iron absorption. To investigate the influence of PPs from a brown sorghum on human iron absorption in absence of phytic acid and the potential of NaFeEDTA to overcome the inhibitory effect two stable isotope studies were concluded in young women (n=32). The first study investigated the iron absorption from dephytinized sorghum porridges with 17, 73 and 162 mg PPs fortified with FeSO₄. In the second study iron absorption from a porridge containing 162 mg PPs fortified with either NaFeEDTA or FeSO₄ was investigated. Furthermore, color changes in sorghum porridges fortified with different levels of NaFeEDTA and FeSO₄ were measured. Compared to the porridge with 17 mg PPs, the fractional iron absorption decreased from 8.5% to 3.2% (p<0.0001) with 73 mg PPs and to 2.7% with 162 mg PPs (p<0.0001). The difference of fractional iron absorption from porridges with 73 mg and 162 mg PPs was not significant (p=0.25). In the second study fractional absorption from NaFeEDTA was 4.6% which was 1.7 fold higher than the 2.7% from FeSO₄ (p<0.001) but still significantly lower than the 10.7% fractional iron absorption from a FeSO₄-fortified porridge with 17 mg PPs (p<0.0001). NaFeEDTA caused less color changes in sorghum porridges than FeSO₄. These findings suggest that PPs from brown sorghum contribute to low iron bioavailability from sorghum foods and that NaFeEDTA would be the more suitable iron compound than FeSO₄ for sorghum fortification. *This study is part of the INSTAPA project to develop novel staple food-based strategies to improve micronutrient status for better health and development in sub-Saharan Africa, which receives funding from the European Community's Seventh Framework Programme.*

Keywords: Iron Bioavailability, Sorghum, Polyphenols

Effect of the antioxidant ability on formation of selenite cataract in different development stage of rat lens

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Experimental selenite cataract, an important model, has been used for various studies of cataract pathology and pharmacy. It is well known that the injection of sodium selenite to the Wistar rat pups whose eyelids are unopened can induce cataract; however, after eyelids opening, injection of sodium selenite in the same dosage can't induce cataract. The precise mechanism of this difference is unclear by now. In order to reveal the mechanism, mRNA expression of MsrA, MsrB1 and GPx1, GPx activity were detected and MDA content was measured in lens of different age Wistar rats; the ultrastructures of lens endothelial cell (LEC), lens fiber cell (LFC) and ciliary muscle (CM) in different conditions were observed by utilizing transmission electron microscope (TEM). The results showed that following the growth of normal rats, mRNA expression of MsrA and GPx1 as well as GPx activity in lens all were decreased gradually; however, mRNA expression of MsrB1 was increased at first, then decreased with the turning point at the fifth day after eyelid opening. Injection of sodium selenite to the eyelid-unopened Wistar rat pups till the fifth day after eyelid opening, mRNA expression of MsrA, MsrB1 and GPx1, GPx activity all increased significantly, and MDA content increased sharply. TEM photos revealed that when sodium selenite was injected before lens maturation and observed after eyelid opening, some lysosomes appeared, part of mitochondrion crista got broken, endoplasmic reticulum (ER) extended, a lot of vacuoles with many lamellar bodies existed, and cell apoptosis occurred in the LEC; what is more, TEM photos showed that there was an "anthophaein shape" with inhomogeneous electron density in the lens fiber layers, the fluffy structure between fiber layers, and that there were also vacuoles with lamellar bodies in them. When injected after lens maturation, in the LEC layers, there were also many vacuoles but no lamellar body in them, mitochondrion crista extends slightly; apparent crevices and layers dystopy to each other existed in the lens fiber layers. Although there were also many vacuoles, there was no lamellar body in them. These results indicated that at different age paragraph of Wistar rat lens the ability of the antioxidant injury induced by sodium selenite is different, and the function difference of blood-eye barrier also exists; when the Wistar rat pups was injected with sodium selenite before lens maturation, ROS induced by sodium selenite interferes with normal development of lens, results in injury to the LEC due to very weak antioxidant ability, and that MsrB1 may play more important antioxidative role than GPx1 before lens development maturation. * This work was supported by grant from the NSFC (Project No. 30870555)

Keywords: Wistar Rat, Lens, Selenite, Cataract, Blood-Eye Barrier

The strategies of regulation of plant selenium content

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Suppression of cytochrome C oxidase and copper chaperones by phenylephrine in primary cultures of neonatal rat cardiomyocytes: the effects of vascular endothelial growth factor

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Previous studies have shown that treatment of primary cultures of neonatal rat cardiomyocytes with phenylephrine resulted in a suppression of the cytochrome c oxidase (COX) activity, which can be reversed by vascular endothelial growth factor (VEGF). The present study was undertaken to test the hypothesis that phenylephrine suppresses copper chaperones for COX and/or COX component proteins, leading to the suppression of the COX activity. Primary cultures of neonatal rat cardiomyocytes were exposed to 100 nM phenylephrine for 48 hours to induce cell hypertrophy. The hypertrophic cardiomyocytes were collected for western blot analyses of copper chaperone proteins for COX, including COX17, COX11 and Sco2, as well as a nuclear-encoded COX-4 subunit and a mitochondrial-encoded COX-1 subunit of the COX. The data obtained showed that the levels of all of the copper chaperones examined were significantly reduced in the hypertrophic cardiomyocytes. The levels of COX-4 and COX-1 were also significantly decreased. Interestingly, addition of VEGF to the cultures of hypertrophic cardiomyocytes at the end of 48-hours treatment with phenylephrine for 24 hours completely recovered the inhibitory effects of phenylephrine on the copper chaperones and COX proteins, along with the recovery of COX activity. In addition, VEGF treatment also caused the reversal of cardiomyocyte hypertrophy. The results thus demonstrated that phenylephrine-induced COX suppression in hypertrophic cardiomyocytes was related to suppression of copper chaperones for COX and COX proteins, a phenomenon that could be manipulated by VEGF.

Keywords: VEGF, Cytochrome C Oxidase, Copper Chaperone

Tandem use of selenocysteine: adaptation of a selenoprotein glutaredoxin for reduction of selenoprotein methionine sulfoxide reductase

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Several engineered selenocysteine (Sec)-containing glutaredoxins (Grxs) and their enzymatic properties have been reported, but natural selenoprotein Grxs have not been previously characterized. We expressed a bacterial selenoprotein Grx from *Clostridium* sp. (also known as *Alkaliphilus oremlandii*) OhILAs in *Escherichia coli* and characterized this selenoenzyme and its natural Cys homologs in *Clostridium* and *E. coli*. The selenoprotein Grx had a 200-fold higher activity than its Sec-to-Cys mutant form, suggesting that Sec is essential for catalysis by this thiol-disulfide oxidoreductase. Kinetic analysis also showed that the selenoprotein Grx had a 10-fold lower K_m than Cys homologs. Interestingly, this selenoenzyme efficiently reduced a *Clostridium* selenoprotein methionine sulfoxide reductase A (MsrA), suggesting that it is the natural reductant for the protein that is not reducible by thioredoxin, a common reductant for Cys-containing MsrAs. We also found that the selenoprotein Grx could not efficiently reduce a Cys version of *Clostridium* MsrA, whereas natural *Clostridium* and *E. coli* Cys-containing Grxs, which efficiently reduce Cys-containing MsrAs, poorly acted on the selenoprotein MsrA. This specificity for MsrA reduction could explain why Sec is utilized in *Clostridium* Grx and more generally provides a novel example of the use of Sec in biological systems.

Keywords: Selenoprotein, Glutaredoxin, Methionine Sulfoxide Reductase

The iron and selenium status of grazing ewes in Semirom rangelands (Isfahan-Iran)

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The present study reports the iron and selenium status and their variation in grazing ewes in Semirom rangelands (Isfahan- Iran) in spring and summer of 2008. During 4 months, May to September, the Semirom rangelands were grazed by Torki-Ghashghai sheep. According to the plant cover of Semirom, 7 major sites, that were the representative of area and in every site, one nomad sheep herd was selected. Blood samples were taken from the jugular vein of 6-7 non-pregnant and healthy ewes in each herd in 3 different times of grazing season (Early, middle and late time of grazing season) and a total of 137 blood sample was taken finally. Ewes were raised under range conditions without any dietary supplementation. The concentration of iron was detected in serum and selenium (Glutathione peroxidase activity) in whole blood by diagnostic laboratory kits. The results of this study indicated that, Fe and Se concentration in serum (and whole blood for selenium) vary through 3 different times of grazing season ($p < 0.01$) but Fe concentrations in serum (2.139 ± 0.049 mg/L) were significantly lower than critical level, the levels of selenium were in the recommended concentrations in the sheep blood in the first time of grazing season. Fe concentration was 1.677 ± 0.047 mg/L in the middle time and 2.139 ± 0.049 mg/L in the late time of grazing season. Although the levels of selenium agree well with the existing literature data from the early to late time of grazing season increased significantly ($p < 0.01$). Selenium concentration in the whole blood from the early to late time of grazing season of grazing season was 0.189 ± 0.008 , 0.235 ± 0.008 and 0.275 ± 0.009 mg/L. Commonly the Ghashghai nomads spend 8 months of every year in winter quarters and 4 months in summer quarters and the gestation and lactation of lambs take place in winter quarters. According to this study, the deficiency of iron and selenium are not confirmed, therefore the application of these trace element supplements need further investigation.

Keywords: Semirom Rangelands, Sheep, Iron, Selenium

The protective effects of selenium against cadmium-induced apoptosis of LLC-PK1 cells: involvement of reactive oxygen species and mitochondria

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Extensive studies have indicated that the apoptosis pathway appears to be associated with intracellular reactive oxygen species (ROS) production in cadmium-induced nephrotoxicity. However, the precise cellular mechanism remains unclear. The purpose of this study was to determine the relationships between the ROS and cadmium-induced apoptosis, and assess the possible cytoprotective mechanism of selenium. Our study clearly revealed cadmium treatment caused apoptosis in LLC-PK₁ cells, which was partially suppressed by pretreatment with selenium, an antioxidant nutrient. Further studies found that ROS peaked within 12 h in the LLC-PK₁ cells after Cd treatment. In addition, a decrease in mitochondrial membrane potential occurred as early as 3h, and loss in mitochondrial membrane potential became significant at 6h and 12h. During the process, selenium played the same role as *N*-acetyl-L-cysteine (NAC), a free radical scavenger. Pretreatment of cells with selenium partially abolished ROS generation, reversed the reduction of mitochondrial membrane potential and suppressed the activation of caspases involved in cadmium-induced apoptosis. In conclusion, these studies provide a molecular linkage between the ROS and cadmium-induced LLC-PK₁ cells apoptosis, and demonstrated selenium also contributed a potential protection for prevention of cadmium-cytotoxicity via ROS.

Keywords: Cadmium, Apoptosis, Selenium, ROS, Mitochondria

The regulation of initiation of mRNA translation by dietary iron intake in skeletal muscle of rats

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The eukaryotic initiation factors eIF2B, eIF4F and the ribosomal protein S6 kinase (S6K1) play important regulatory roles in the initiation of mRNA translation. Hypoxia can suppress the global mRNA translation through mTOR signaling of activation of phosphorylation of 4EBP1 and S6, the phosphorylation of eIF2 α and the elongation of eEF2. Iron deficiency also induces hypoxia and decline of ATP production in skeletal muscle, however, the mechanism of mRNA translational control in iron-deficient skeletal muscle is still unknown. To investigate dietary iron intake on the regulation of mRNA translation in skeletal muscle, male weanling Wistar rats were divided severe iron deficient diet (ID, < 2 mg Fe/kg diet), an moderate iron deficient (MID, 10 mg Fe/kg diet) groups, and two further groups were pair-fed (IPF) or freely fed a control (C, 35 mg Fe/kg diet) diet for 4 weeks. The diets were prepared by supplementing the AIN93G formula diets with or without ferrous sulfate. At the end of week 4, the final body weight, hemoglobin, serum iron and transferrin saturation was decreased to 13%, 62%, 79% and 82% in severe iron-deficient rats. However, the total iron binding capacity in severe iron-deficient group was 1.1 times of control group, while no difference of hemoglobin and TIBC value existed between the control and pair-fed groups. The expression of p-eIF2 α protein levels significantly increased to 36% in gastrocnemius muscle of severe iron-deficient rats. In contrast, the p-mTOR, p-rpS6 and p-4EBP1 proteins levels were not affected in iron-deficient group. In the moderately iron-deficient group, the hemoglobin was decline to 19% of the control group, while the p-eIF2 α , p-mTOR, p-rpS6 and p-4EBP1 proteins levels were not affected. Together, our data indicate dietary iron intake regulates mRNA translation through the phosphorylation of eIF2 α but not the pathway of mTOR signaling in skeletal muscle of rats.

Keywords: Iron Deficiency, mTOR signaling, eIF2 α

Trace element status and disease occurrence in Swedish organic dairy herds

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Recommendations for trace element supplementation first focused on the prevention of reduced productivity and clinical signs of deficiencies, but the role of trace elements in immunity has been emphasized in recent studies. This issue is most important for the organic movement, which aims for more natural and animal-friendly livestock production, improved immunity and resistance to disease through appropriate nutrition. Since January 2008 the ration for organic herds has been required to be 100% organic (EU Regulation No 889/2008). In organic farms with a high proportion of in-farm produced forage this fact may (adversely) affect the trace element status of animals when the potential role of the concentrate to guarantee the physiological trace metal requirements is constrained. The overall aim of the present study was to investigate the possible effects of 100% organic feed on trace element status in Swedish organic dairy herds. A second aim was to evaluate the potential association of Cu, Se and Zn levels (essential for a well functioning immune system of dairy cows) below the physiological range on the occurrence of clinical mastitis, the predominant disease in dairy cows. Trace element (Cu, Co, Se, Zn, Mn, Mo, I and Fe) concentrations were determined by inductively coupled plasma mass spectrometry (ICP-MS) in 160 serum samples from early-lactating and dry cows collected from 2005 to 2010 in 10 organic and 10 conventional Swedish herds. Multivariable statistical models were performed in Stata version 11 (Stata Corporation, College Station, TX, USA). Results showed that trace elements (below physiological levels) were associated with the change of legislation (in models for Mo, Zn, Co, Se and Fe) and stage of lactation (in models for Fe, Co and Cu), but not with herd type. Preliminary results of the presence of a threshold effect (within or outside safety ranges) of certain trace elements on disease occurrence, with the example of mastitis, by comparing organic and conventional herds will be presented.

Keywords: Organic Feed, Trace Elements, Dairy Cows

Trace elements and meat: does what you eat matter?

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Meat, as a component of the human diet is not only, an important source of toxic metal exposure, but also a valuable source of some essential elements. Therefore it is vital to explore trace element concentrations in different types of muscles. Samples of 4 different types of muscles (diaphragm (DI), cardiac (CA), semitendinous (SE) and pectoral muscle (PE), n=120) from beef calves receiving typical commercial diets were taken and acid digested. The levels of non-essential (As, Cd, Hg, Pb and Sn) and essential (Co, Cr, Fe, Mn, Mo, Ni, Se and Zn) trace elements were analysed by ICP-MS. Post hoc DHS Tukey tests were used to test for differences in trace element concentrations among types of muscles. Spearman correlations were used to evaluate the correlations between non-essential and essential trace elements among the different types of muscle themselves and also with the liver and kidney. For Co, Cu, Fe, Mn, Ni and Se the higher concentrations (up to 2 and 4 times) were found in CA, followed by DI and SE, while PE metal concentrations were significantly lower. For the other essential elements (Cr, Mo and Zn) and the toxic elements (As, Cd and Hg) the lowest levels were found in CA whereas the other muscles showed similar trace element concentrations. This study has demonstrated that in cattle non-essential and essential trace element concentrations significantly varied between muscles. The most active and less fat content muscles (cardiac and diaphragm) showed in general the highest essential and the lowest non-essential trace element accumulation in comparison with the other muscles analyzed (semitendinous and pectoral).

Keywords: Muscles, Food Quality, Cattle

Ultrasound contrast microbubble targeted copper therapy for ischemic myocardial infarction in New Zealand rabbits

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Copper supplementation stimulates myocardial angiogenesis by activating the vascular endothelial growth factor (VEGF) signaling pathways. Copper is required for the transcriptional activity of hypoxia-inducible factor-1, the transcription factor for VEGF expression. The present study was undertaken to determine whether or not copper can stimulate vascularization in established myocardial infarct tissue and induce myocardial regeneration. New Zealand rabbits were used as an experimental model. An open chest and left posterolateral coronary artery occlusion surgery was performed to produce myocardial ischemia. After myocardial infarction developed at four weeks post myocardial ischemia, an ultrasound contrast microbubble targeted Cu therapy twice a week for 3 weeks was applied. The microbubble was constructed by albumin mixed with CuSO₄. One week after the last treatment, echocardiography, hemodynamics, and histology procedures were undertaken to evaluate the effects of the Cu treatment on the infarcted myocardium. The results showed that Cu significantly enhanced myocardial angiogenesis in the infarcted area and reduced the infarcted area. Echocardiography and hemodynamic analyses showed a significant improvement in cardiac function by Cu treatment. In contrast, microbubbles composed of albumin alone did not cause any sign of improvement as measured simultaneously with the Cu-treated animals. These data thus demonstrated that localized copper treatment can stimulate myocardial vascularization along with cardiac structural and functional improvement.

Keywords: Copper, Myocardial Infarction, Microbubble

Use of chelated trace minerals to improve efficacy of osteoarthritis (OA) joint supplements

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The monosodium iodoacetate (MIA) osteoarthritis (OA) rat model is a rapid, reproducible animal model that mimics pain & structural changes associated with human OA. The objective of our trial was to evaluate efficacy of a joint supplement (Natural Eggshell Membrane, NEM) alone or with a blend of chelated trace minerals (Zn, Mn, and Cu chelated by the methionine hydroxy analogue, Ch-MIN), as an anti-inflammatory and/or chondromodulating supplement in a model of (MIA)-induced osteoarthritis (OA). 48 Wistar rats were fed one of 4 dietary treatments (n=12/trt): 1) rat AIN-93M diet, 2) As 1 + 0.6% NEM, 3) As 1 + 0.75% Ch-MIN, and 4) As 1+NEM + Ch-MIN. Treatments were fed for 28 d prior to MIA injection and an additional 14 d post-MIA injection. Intra-articular injections of MIA (1 mg) were administered to male Wistar rats (330 g) in the right or left knee joints at d 0. Changes in hind paw weight distribution (HPWD) and knee swelling between the arthritic and contra-lateral control limb were assessed at d 1, 3, 7 and 14 post-MIA. Serum biomarkers were collected on 24 rats at each time point (d 7 and 14; (n=6/trt/d)). Serum biomarkers included two degradative (CTX-II, COMP) cartilage biomarkers. An improvement in weight bearing ($P < 0.05$) was observed d 1 post MIA injection and on d 3 and 7 ($P < 0.10$) for rats fed the combination of NEM+ Ch-MIN relative to rats fed the negative control. Day 3 caliper measurements of knees indicated reductions in swelling in rats fed the combination of NEM+ Ch-MIN ($P < 0.05$) relative to rats fed NEM or Ch-MIN only ($P < 0.05$). CTXII, a marker of cartilage degradation was decreased in rats fed NEM d 7 ($P < 0.10$) and d 14 ($P < 0.05$). A reduction in CTXII was also observed d 7 for rats fed the combination of NEM+ Ch-MIN ($P < 0.10$). Reductions in COMP were also observed d 14 in rats fed Ch-MIN or the combination Ch-MIN + NEM ($P < 0.05$). Based on cartilage biomarkers, swelling and weight shift measurements, the combination of NEM + Ch-MIN was more effective than either NEM or Ch-MIN fed singly.

Keywords: Osteoarthritis, Rat, CTXII

Zinc deficiency increases Ca and P deposition in rat aortic primary vascular smooth muscle cells

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The vascular smooth muscle cells (VSMCs) in mature animals whose principal function is contraction and regulation of blood vessel tone diameter have been implicated in a major role in the progression of vascular calcification. Thus, primary cultures of VSMC can be an invaluable tool in studying molecular mechanisms underlying vascular diseases. The present study describes the isolation and cell culture of primary VSMCs and the effect of zinc on its viability and calcification. Primary VSMCs were isolated from the aortas of 4-month male Sprague-Dawley rats. The phenotype and purity of the isolated cultures were assessed by Western blotting for specific markers. Zn deficiency was induced in vitro either by using chelexed serum or TPEN [N,N,N',N'-tetrakis(2-pyridylmethyl)ethylenediamine] in the culture media and varying levels of Zn were appropriately added. Normal growth media was used as control. The cell viability was measured using MTT assay within 27d of Zn treatment. Ca and P deposition was visualized by Alizarin red and von Kossa staining, respectively. Our results show that the isolated primary VSMCs possesses smooth muscle phenotype as indicated by the abundant expression of marker proteins SM22 α and calponin. The purity of the cultures was confirmed by the absence of the endothelial marker von Willebrand factor. We also show that the viability of cultured primary VSMCs decreased dose-dependently with decreasing zinc concentrations. The accumulation of Ca deposits increased with decreasing Zn concentrations on the cultured pVSMCs as examined by Alizarin red staining. The P accumulation was likewise increased by decreasing Zn levels as visualized by von Kossa staining. Taken together, our findings indicate the importance of Zn on VSMC viability and implicate its crucial role for regulating vascular calcification by increasing Ca and P deposition in VSMCs.

Keywords: Zinc, VSMCs, Calcification

Zinc deficiency suppresses matrix mineralization and retards osteogenesis transiently with catch-up possibly through Runx2 modulation

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A characteristic sign of zinc deficiency is retarded skeletal growth, but the role of zinc in osteoblasts is not well understood. Two major events for bone formation include osteoblast differentiation by bone marker gene expression, which is mainly regulated by bone-specific transcription factor Runx2 and extracellular matrix (ECM) mineralization by Ca deposits for bone nodule formation. We investigated whether zinc deficiency down-regulates bone marker gene transcription and whether this might occur through modulation of Runx2. We also investigated whether zinc deficiency decreases ECM mineralization in osteoblastic MC3T3-E1 cells. In the presence of 5 µmol/L TPEN as zinc chelator, zinc deficiency (ZnD: 1 µmol Zn/L) decreased bone marker gene (collagen type I, osteopontin, alkaline phosphatase, osteoclastin and parathyroid hormone receptor) expression, as compared to normal osteogenic medium (OSM) or zinc adequate medium (ZnA: 15 µmol/L) ($P < 0.05$) both at 5 days (proliferation) and 15 days (matrix maturation). Decreased bone marker gene transcription by zinc deficiency could be caused by decreased nuclear Runx2 protein ($P = 0.05$) and transcript ($P < 0.05$) levels in ZnD. Furthermore, within the first 24 h of differentiation when Runx2 expression is induced, maximal Runx2 mRNA and nuclear protein levels were delayed in ZnD compared to OSM and ZnA. ECM Ca deposition was also lower in ZnD, which was also indirectly confirmed by detection of decreased cellular (synthesized) and medium (secreted) ALP activity as well as matrix ALP activity. Zinc deficiency attenuated osteogenic activity by decreasing bone marker gene transcription through reduced and delayed Runx2 expression and by decreasing ECM mineralization through inhibition of ALP activity in osteoblasts. Changed Runx2 expression and ECM mineralization in osteoblasts by zinc deficiency may explain the retarded skeletal growth which is the major zinc deficiency syndrome.

Keywords: Zinc, Runx2, Osteoblast Differentiation Gene

γ -Poly-glutamic acid improves iron bioavailability in rats

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The effect of γ -poly-glutamic acid (γ -PGA) on iron bioavailability was assessed in rats. Male Wistar rats were fed for 3 weeks on a low-iron diet (<0.7 mg Fe/kg diet) to induce iron deficiency anemia. Then the anemic animals were divided into three groups and fed normal diets (35mg Fe/kg diet) containing γ -PGA (0, 0.1% or 0.2%) for 21 d. Hemoglobin, red blood cell count, hematocrit, liver, spleen and femur iron concentration, serum total iron-binding capacity were determined. The results showed that the femur relative weight of the 0.1% PGA group and liver and spleen relative weight of the 0.2% γ -PGA group were higher than control. Serum iron concentration significantly increased ($P < 0.01$), serum total iron-binding capacity of 0.2% γ -PGA group was significant higher than other groups. The liver, spleen and femur iron concentration of 0.2% γ -PGA group were significantly higher than the control. There was no significant effect on average daily gain, hemoglobin, red blood cell count or hematocrit. We conclude that γ -PGA can effectively improve iron bioavailability.

Keywords: γ -Poly-Glutamic Acid (γ -PGA), Iron Bioavailability, Rat

Study on the contents of selenoprotein and Se-polysaccharide in selenium-enriched *Lentinan edodes*

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The cultivation of *Lentinan edodes* as a carrier for Se, low concentrations of sodium selenite solution were added directly to the medium to inorganic selenium compound into the mushroom body, and selenium-enriched *Lentinan edodes* can be got. Using selenium-enriched mushrooms as raw material, it was preliminarily studied that patterns of occurrence of selenium and the contents of Selenoprotein and Se-polysaccharide in their fruiting bodies of mushrooms. Various extraction solvents were used to distill and separation Se-polysaccharide and Se-protein of the *Lentinan edodes*, and atomic absorption spectrometer was used to determine the selenium contents of all component parts. The results showed that *Lentinan edodes* have the ability of enrichment selenium and can convert inorganic selenium in the environment into organic selenium. The main group of Selenium mushrooms containing selenium is organic state. Among them the content of protein for existence form of selenium is higher, selenium also have the distribution in the nonprotein or polysaccharide. The selenium in protein occupied the total selenium 40.09%, In the four components of selenium protein, water-soluble proteins of selenium is main (21.65% of the total selenium). The selenium in polysaccharide occupied the total selenium 27.83%. Mass fraction of acid-soluble Se-polysaccharide than in water-soluble Se-polysaccharide and alkali-soluble Se-polysaccharide is higher (13.52% of total selenium). The main distributed form of the selenium is from the organic matter in the analyzed *Lentinan edodes*, the combined selenium in protein was higher.

Keywords: Selenium-enriched *Lentinan Edodes*, Selenoprotein, Se-polysaccharide

Use of chelated trace minerals to improve bone health in poultry

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Zn and Cu promote collagen synthesis and crosslinking, a primary contributor to bone strength. Zn is a cofactor in matrix metalloproteinase enzymes during invasion of the cartilage matrix by osteoblasts prior to endochondral ossification, and is a cofactor for the Gli2 transcription factor which promotes endochondral ossification. Mn is essential for the formation of mucopolysaccharides that form the ground substance of the cartilage model of developing bone. Trace mineral supplementation important for poultry production, as leg bone developmental problems such as tibial dyschondroplasia (TD), bone breakage and lameness are common in birds selected for rapid growth. Chelated trace minerals, often more bioavailable than trace mineral salts, are often fed in poultry diets. Zn, Cu and Mn chelated by the methionine hydroxy analogue represent a new class of chelated minerals. Two trials tested these chelates for the ability to improve leg and bone problems in turkeys. Treatments in the first study were diets containing commercial levels of supplemental Zn, Cu and Mn as salts, or salts and 20ppm Zn, 20ppm Mn and 10ppm Cu from chelates. Control turkeys exhibited lameness that involved TD, pododermatitis and synovitis. The incidence was typical of that seen in commercial turkeys, with relatively minor foot and leg problems seen early and progressing to overt lameness at 14 weeks and beyond. Lameness was positively correlated with synovitis ($P<0.05$). Birds fed diets containing chelates had reduced ($P<0.05$) TD incidence, synovitis and pododermatitis, and increased ($P<0.05$) tibial breaking strength in the heaviest birds (>30 kg). Cortical bone thickness was greater in the birds when chelates were fed ($P<0.10$). In the second trial, turkeys were assigned to 4 treatments consisting of a 2x2 factorial arrangement of 2 concentrations of chelates (0 vs. 40, 40, 20 and 0.3ppm of chelated Zn, Cu, Mn and organic Se respectively, partially replacing trace mineral salts) and 2 concentrations of 25-hydroxycholecalciferol (HyD; 0 vs. 92ppm). Bending stress required for tibias to break were increased with chelate supplementation ($P<0.05$), especially when HyD was also added ($P=0.05$). In addition, the chelates increased bone thickness ($P=0.001$) at the site of breakage. Thus, chelated trace minerals can be used to improve bone development and health in poultry.

Keywords: Trace Minerals, Turkey, Bone

Putative expression mechanism of the novel transcripts of human frataxin, causing neurodegenerative disease

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Friedreich ataxia is an autosomal recessive disease with an estimated incidence of 1:40,000, caused by the reduced expression levels of the frataxin gene (FXN) due to the expansion of triplet nucleotide GAA repeats in the first intron of FXN. FXN is a mitochondrial iron-binding protein required for Fe-S cluster assembly, whose deficiency causes a range of metabolic disturbances. Clinical statistics shows that the lesions occur mainly in the central nervous system such as the cerebellum and spinal cord associated with myocardial damage (90%). Our recent work revealed that expression of two novel transcripts of FXN existed in specific tissues such as cerebellum and heart. NCBI database and other bioinformatic database support the existence of these transcripts in tissue-specific manner. The position of the two first exons of FXN gene suggested that transcription of the two transcripts were driven by different promoters with the effect of transcription factors. It was predicted that the human FXN gene has 5 promoters, each of which contains the binding sites of some putative transcription factors including HMX2, HMX3, EGR3, and CTCF. The results revealed that promoter one and two showed the highest promoter activities and mutation of the putative HMX2, HMX3, and EGR3-binding sites, except CTCF-binding site, on FXN promoter one and two dramatically decreased luciferase activity. Over-expression of HMX2, HMX3, and EGR3 significantly increased frataxin mRNA and protein levels. Conclusion: The putative transcription factors HMX2/HMX3/EGR3 may be very important for promoter activity and can regulate expression of human FXN gene. The results provide new mechanistic insights into the molecular factors influencing FXN expression.

Keywords: Friedreich Ataxia, Frataxin, Promoter

A randomized controlled trial investigating the effect of calcium supplementation on iron status in Chile

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Despite that it is widely accepted that calcium inhibits iron absorption from a meal. We found no inhibitory effect of 800 mg calcium on the absorption of 5 mg iron, when minerals were ingested on an empty stomach (Ca:Fe molar ratio ~ 220:1). On the other hand, a calcium-iron supplement for children would have a Ca:Fe molar ratio around 16:1, and it may be ingested on an empty stomach. Thus, in terms of anemia reduction, the efficacy of calcium-iron, or iron supplements would be similar. The aim of this study was to evaluate if the supplementation of 700 mg of calcium plus 30 mg of iron during 3 month has the same effect on iron status in children aged 6 to 8 years old compared with the supplementation of 30 mg of iron. We included 194 apparently healthy children (6-8 y). It was conformed two groups that were randomly assigned to receive 700 mg of calcium as calcium carbonate and 30 mg of iron as ferrous sulphate. The second group received 30 mg of single iron as ferrous sulphate. Follow up was for a duration of 3 months. The prevalence of anemia was evaluated pre and post-supplementation period. At the base line, the prevalences of anemia in the iron and the calcium-iron supplemented groups were 21.5 and 15.5 %. After follow up, the prevalence of anemia was 3.3 % in both groups (χ^2 ; NS). A combined calcium-iron supplement may be useful to increase calcium intake and to reduce the incidence of anemia in children.

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Keywords: Iron, Anemia, Calcium, Supplementation

Correlations between Se-status biomarkers during military training

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Selenium is an important element in military nutrition particularly due to its antioxidant properties. No single reliable biomarker exists for selenium status, thus it is beneficial to study several biomarkers and their interrelations. Whole blood Se, total plasma Se, Se in selenoprotein P, Se in plasma glutathione peroxidase, erythrocyte and serum glutathione peroxidase activity and total serum glutathione were analysed to monitor selenium status during three months of intense military training. Samples of whole blood and plasma were obtained from a group of fifteen soldiers at the beginning, in the middle (immediately after extra strenuous stressful physical activity) and at the end of the training. Statistical Analysis Software (SPSS) was used for calculation of parametric (ANOVA, Duncan) or nonparametric (Kruskall-Wallis) tests. Spearman and Pearson correlation coefficient were used for testing correlations. Linear regression models were used and regression equations were calculated for pairs at each of three blood samplings if at least weak correlation ($r^2 > 0,5$) was found at least at one of three blood samplings. Medium strong correlation was found at pair Se in blood and Se in plasma at first and second sampling and weak correlation at third sampling ($r^2=0,77$; $r^2=0,58$; $r^2=0,52$). The strongest correlation at first sampling, which was decreasing with the next samplings, could be a consequence of different individual adaptation to stress. As plasma is part of blood this correlation was expected. Similar correlations were found between Se in plasma (ng/g) and Se in SelP (ng/g) of all three samplings. The strongest correlation of first sampling was slowly decreasing with time of exposure to stress ($r^2=0,56$; $r^2=0,37$; $r^2=0,39$). Important is also statistically significant correlation at pair plasma Se and total glutathione at second sampling ($r^2=0,78$). Since no statistically significant correlation of this pair was found at first or third sampling, this one could be explained with good protection against oxidative stress after very strenuous activity. Diverse data of correlations between Se-status biomarkers, found in the literature, can not be compared to our study because of different conditions of the studies and insufficient data on physical activity.

Keywords: Selenium Status, Biomarkers, Correlations, Military, Stress

Manganese source affects manganese transport and divalent metal transporter one expression in the small intestine of broilers

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Manganese is an essential trace element in animals, with particular importance for fast-growing poultry. No information is available regarding the mechanism of Mn transport from organic Mn complexes in the small intestine of broilers. It has been found that solubilized Mn released from the stomach into the duodenum was transported across the microvilli via a divalent metal transporter 1 (DMT1). However, the effects of dietary Mn concentration and Mn source on the regulation of DMT1 mRNA expression have not been studied in chicks before. Two experiments were conducted using the in situ ligated duodenum and intact broiler model, respectively. In Expt. 1, a total of 220 Mn-deficient broilers (28 d-old) were selected and randomly assigned by body weight to 1 of 22 treatments (10 birds each) in 1 control plus 3 (Mn sources) × 7 (Mn concentrations) factorial arrangement of treatments. The duodenal loops of these chicks were perfused with solutions containing 0.13, 0.27, 0.54, 1.09, 2.18, 4.37, and 8.74 mmol Mn/L from either MnSO₄ or 2 organic complexes of Mn and amino acids with moderate (OM), or strong (OS) chelation strength up to 30 min. The mucosa was collected in duodenal loops treated with 2.18 mmol Mn/L (close to the dietary Mn requirement (120 mg Mn/kg diet) of broilers). In Expt. 2, a total of 256 Mn-deficient chicks (14 d old) were randomly divided into 4 treatment groups with 8 replicate cages (8 chicks per cage) for each treatment. Broilers were fed the basal diet (about 13 mg Mn/kg diet) and the basal diet supplemented with 100 mg Mn/kg as the above three Mn sources for 14 days. Mn uptake from different Mn sources followed the saturable process in the ligated duodenum by analyzing the concentration-dependent uptake profile, while the Michaelis constant (K_m) and the maximum transport rate (J_{max}) values for OM and OS were higher (P<0.001) than those for MnSO₄. As determined by quantitative real-time PCR, DMT1 mRNA level in duodenal loops was decreased by Mn treatment after short-time perfusion, but in the proximate intestine of chicks was increased by dietary Mn after longer-term feeding. Among Mn sources, DMT1 mRNA level also was higher (P<0.01) for OM and OS than for MnSO₄ in the above two cases. These results indicated that DMT1 might be involved in the regulation of organic Mn transport in the proximal intestine of broilers.

Keywords: Organic Manganese Transport, Divalent Metal Transporter One, Gene Expression, Small Intestinal Loops, Broilers

Influence of SelR gene silence on peroxynitrite induced cell apoptosis in human lens cells

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Peroxynitrite (ONOO⁻) rapidly breaks down at physiological pH to yield the hydroxyl radical (\cdot OH) and nitrogen dioxide radical (\cdot NO₂). The endogenous peroxynitrite can be formed in various tissues of the eye, and then lead to the formation of cataracts. Methionine sulfoxide reductases (Msrs) including MsrA and MsrB, can reduce the methionine-S-sulfoxide and methionine-R-sulfoxide, respectively. MsrA has been shown to play an important role in protection of lens cells against oxidative damage and it has been shown to be required for the maintenance of lens transparency. MsrB1 is a selenoprotein named SelR, but its role in cellular protection against peroxynitrite-induced human lens epithelial (HLE) cell damage remains to be evaluated. In present study, the effect of SelR gene silence on peroxynitrite-mediated cell apoptosis in HLE cells was examined. The results showed that the cells viability was obviously increased by low concentrations of peroxynitrite (50, 100 μ M) and decreased in a dose dependent by high concentrations of peroxynitrite (200-500 μ M) compared with normal cells; the apoptotic fraction of the group treated with 300 μ M peroxynitrite fore-and-aft SelR gene silence were 8.39% and 16.81%, respectively ($p < 0.01$); the Grp78 protein levels were significantly increased in HLE cells under peroxynitrite stress after SelR gene silence ($p < 0.001$), and the ROS and MDA levels were increased to approximately 4.4- and 3.8-fold after SelR gene silence, respectively, compared with untreated control cells; the DNA strand breaks fore-and-aft SelR gene silence were 43.5% and 62.1%, respectively ($p < 0.001$); the activity of caspase-3 was increased to approximately 1.5- and 2.1-fold fore-and-aft SelR gene silence, respectively ($p < 0.001$), compared with untreated control cells. And the levels of ERK1/2 phosphorylation were significantly decreased ($p < 0.001$). In conclusion, the results suggested that MsrB1 played important roles in regulating redox balance and mitigating ER stress induced by oxidative stress under physiological conditions as well as in protecting HLE cells against peroxynitrite-induced apoptosis by inhibiting activation of caspase-3 and oxidative damage of DNA, improving ERK phosphorylation under pathological conditions. * This work was supported by grant from the NSFC (Project No. 30870555)

Keywords: SelR, ER Stress, Oxidative Stress, Cell Apoptosis, Cataract

A preliminary study on the antioxidant activity of selenoprotein in *Cordyceps militaris* rich in selenium

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Utilize different solvents to extract and salt out soluble protein from the *Cordyceps* rich in selenium which is artificially cultivated, thus obtaining different types of selenoproteins contained in it, and then pyrogallol autoxidation method is applied to determine their antioxidant activity, meanwhile, double-channel atomic fluorescence is used to detect the materials and their selenium content. The results show that: various proteins of *Cordyceps* rich in selenium all contain selenium, followed by alkali-soluble selenoprotein > alcohol-soluble selenoprotein > salt-soluble selenoprotein > water-soluble selenoprotein; their ability to remove superoxide anion is followed by water-soluble protein > alkali-soluble protein > salt-soluble protein > alcohol-soluble protein, the clearance rate of selenoprotein with different salting points on superoxide anion is shown as follows: salting selenoprotein with the rate of 70% > salting selenoprotein with the rate of 100% > salting selenoprotein with the rate of 90% > salting selenoprotein with the rate of 80% > salting selenoprotein with the rate of 50% > salting selenoprotein with the rate of 60% ; therefore, selenoprotein of *Cordyceps* rich in selenium is a kind of natural resource with good antioxidant activity as well as broad application prospects.

Keywords: *Cordyceps Militaris*, Selenium, Selenoprotein, Antioxidant Activity

Studies on photosynthetic characteristics of *Cardamine* growing in different site conditions in the high selenium area in Yutangba

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Cardamine, the *Cruciferae Cardamine* plant, is 1-2 years herb, and the whole plant is for wild edible, medicinal dispersing heat, diuretic and detoxifying, cure dysentery enteritis, chyluria and various bleeding. Its seed can be extracted oil. The study found that the *Cardamine* grows in Enshi Yutangba area has a strong capability in enriching the selenium content from environment, showed plexiform distribution group, an area of about 0.03km². So this study selected the hillsides, selenium slag, streamsides and streams (the selenium concentrations were elevated) four site conditions in the net photosynthetic rate, transpiration rate and other photosynthetic parameters; plant height, dry weight, and biological parameters chlorophyll, soluble sugar content, provide a basis with a view to the development and utilization of selenium-rich plants. The results show that under different site conditions, net photosynthetic rate of *Cardamine* showed a single peak curve, there is no significant "lunch break" phenomenon. Photosynthetic capacity of the basic rendering is streamsides > streams > hillsides > selenium slag. The *Cardamine* growth in the streamsides and streams has higher net photosynthetic rate、 Water use efficiency and chlorophyll、 soluble sugar content, but the intercellular CO₂ concentration and transpiration rate is lower, indicating that the two site conditions *Cardamine* can use more solar energy and water chestnut, to better adapt to the environment. In addition, the *Cardamine* grow in different site conditions plant height, root length, fresh weight and dry weight, there are obvious differences, basically as the selenium concentration increased and increased, which grows in the streamsides these four parameters higher than the other three site conditions. Thus, the selenium concentration is moderate, and semi-dry environment is more appropriate for *Cardamine* growth.

Keywords: Selenium, Cardamine, Photosynthesis

Antioxidant activity in vitro of selenium polysaccharide of *Thlaspi caerulescens* L. rich in selenium

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The antioxidant capacity of the human body is closely related to its ability of disease resistance and anti-aging. It is a current research focus to find effective anti-oxidants used in medicine, food, health care, beauty make-up from natural plants. In this paper, we studied the content of selenium in selenium polysaccharide and its antioxidant activity in vitro of *Thlaspi caerulescens* L. produced from Yutangba of Enshi selenium mining area. The double tracts atomic fluorescence spectrometry is used to detect the total selenium content in the sample and that of selenium polysaccharide in the active ingredient of the sample. The salicylic acid method and pyrogallol autoxidation method are used to detect the scavenging activity of selenium polysaccharide on hydroxyl radicals and superoxide anion. Experiments show that the total amount of selenium in *Thlaspi caerulescens* L. is $708\mu\text{g}\cdot\text{g}^{-1}$, while the amount of selenium in selenium polysaccharide is $98.1\mu\text{g}\cdot\text{g}^{-1}$, accounting 13.86% of the total selenium content. Meanwhile, selenium polysaccharide in samples is with significant antioxidant capacity, and it shows a certain dose-effect relationship. Selenium polysaccharide has stronger anti-oxidation ability than pure polysaccharide compared with non-selenium polysaccharide. Therefore, plants rich in selenium are better natural antioxidants. This study will provide the necessary experimental basis for the effective and rational development and utilization of *Thlaspi caerulescens* L. rich in selenium.

Keywords: *Thlaspi Caerulescens* L., Selenium Polysaccharide, Antioxidant

Identification and verification of transcriptional networks involved in iron homeostasis and oxidative stress damage activated by copper in *Enterococcus faecalis*

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Copper and iron are trace elements required by prokaryotic and eukaryotic organisms; both are used as a cofactor in metallo-enzymes involved in different cellular processes. On the other hand, an excess of these metals can induce the generation of free radicals through the Haber–Weiss and Fenton reactions. In previous work using a microarray approach, we showed that the exposure of copper can induce the expression of genes involved in iron homeostasis and oxidative stress response. Using the bacterial model of *E. faecalis*, this work identified and verified transcriptional regulatory networks involved in these metabolic processes that respond to the copper stimulus. Consensus-Patser and Motif Sampler-Scan algorithms were used to search promoter region of genes related with iron (n=7) and stress response (n=5) different transcription factor binding sites described in other bacteria. As a result, we identified two transcriptional networks, the Fur network composed of 4 target genes involved in iron uptake, and the LexA network composed of 3 target genes related with DNA damage. To verify the connectivity predicted *in silico*, we constructed two independent *E. faecalis* mutants of these two transcriptional repressors. Subsequently, using real time PCR, we compare the expression profiles for the target genes between the wild type strain and its corresponding transcription factor mutant. In both experiments, all of the target genes transcript abundance increases significantly in the mutant strain, confirming the repression by Fur and LexA on genes activated by copper. These data show for the first time *in vivo* evidence of two transcription networks involved in iron homeostasis and oxidative stress damage able to respond to copper exposure. Also, we present two systems of transcriptional coordination expression, activated directly or indirectly by the presence of copper, suggesting a putative transcriptional connectivity between iron homeostasis, copper homeostasis and oxidative stress mechanisms. Fondecyt-1110427, FONDAP-15090007 and Conicyt fellowship (ML).

Keywords: Transcriptional Networks, Copper, Iron, Oxidative Stress Damage

Speciation and bioavailability of selenium in soil from Enshi, China

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The mobility and bioavailability of selenium (Se) in soil are controlled by its speciation. Enshi district is well-known for selenosis in human reported in 1960s, which was attributed to Se accumulation in maize-corn. In fact, Se uptake and accumulation in plants depends on Se content and speciation in soil. Seleniferous soil is widely distributed in Enshi area. However, few studies investigated the speciation of Se in arable soil. Although both single and sequential extraction methods have been used to evaluate Se speciation and bioavailability, the results are variable and even contradictory for some cases. Thus, a comprehensive study is needed to determine the most simple and efficient method to quantify Se speciation in soil. In this study, three representative sites in Enshi areas were selected (Yutangba (YTB), Bajiao (BJ) and Changping (CP)).for collection of soil samples. Seven single extraction and one sequential extraction methods were employed to evaluate Se speciation and bioavailability.. The results show Se concentrations in Yutangba soils are significantly higher than those in Bajiao and Changping soils, with the total Se content 2.15, 0.57 and 0.15 mg/kg in three sites. Compared the efficiency of single extractions with different extractant, phosphate buffers seemed to be the most efficient for Se and the most promising for routine monitoring purposes of our soils. Further speciation analysis indicates Se in Yutangba soil is more mobile than that in Bajiao soil, indicating higher bioavailability.

Keywords: Selenium, Soil, Bioavailability

Study on the Correlation between Selenium Levels and APOE Gene Polymorphism in Aged People in Rural Areas of Sichuan Province

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To investigate the correlation between selenium levels and APOE gene polymorphism in aged people in rural areas of Sichuan Province, 500 volunteers aged above 65 were recruited by cluster sampling from rural areas in each of two locations with moderate (Qionglai City) and low (Jian'ge County) environmental selenium levels. Additionally, selenium levels in venous blood of 50 senile volunteers were determined. Correlation analysis of blood and fingernail selenium levels of 50 old people in each of Qionglai and Jian'ge demonstrated good correlativity between finger selenium and blood selenium ($r=0.496$, $P<0.05$). Statistical test indicated that fingernail selenium levels of old people in the two places were significantly different ($P<0.001$) and so were the frequency distribution patterns of APOE gene polymorphism ($P<0.0001$). The 1000 surveyed old people were assigned into two groups by the fingernail selenium content. Frequencies of genes E2/2, E2/4 and E3/4 of old people in the group with fingernail selenium <0.259 $\mu\text{g/g}$ were significantly lower than in the group with fingernail selenium ≥ 0.259 $\mu\text{g/g}$ ($P<0.05$); frequencies of alleles E2, E3 and E4 of fingernail selenium ≥ 0.259 $\mu\text{g/g}$ were higher than in the group with fingernail selenium <0.259 $\mu\text{g/g}$ ($P<0.05$). In grouped analysis by both location and fingernail selenium level, inter-group differences were found in all of the three alleles (E2, E3 and E4) of APOE. In comparison of gene polymorphism frequency distribution, differences between the two groups of old people established by region were statistically significant in five gene types (E2/2, E2/4, E3/3, E3/4 and E4/4); in grouped comparison by finger selenium level, significant differences were found in only three gene types (E2/2, E2/4 and E3/4). Whether the correlation between selenium levels and APOE gene polymorphism and allele frequency distribution is common in middle-aged and old people needs further verification. It is of interest that E2/2 was found in only old people with high selenium levels and in none of the 500 old people from the low-selenium region (Jian'ge County). * Sponsored by NIH (R01 AG019181)

Keywords: Selenium, Gene polymorphism, Aged people in rural

Determination of selenium in food by atomic fluorescence spectrometry

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The object of this work was to establish a method for the determination of selenium in food using atomic fluorescence spectrometry. After collection samples were digested by heating in acid, hydrogen selenide (SeH_2) was generated using sodium borohydride as the reducer and introduced with the carrier into the atomizer for atomization. Under irradiation of a hollow cathode selenium lamp, ground state selenium atoms were excited to high-energy state and, when returning to the ground state after deactivation, emitted fluorescence of characteristic wavelengths. The fluorescence intensity was proportional to the content of selenium and, based on this, quantification was performed against a standard series. Good linearity was obtained within the selenium concentration range of $1.0\mu\text{g/L}$ - $20.0\mu\text{g/L}$; the regression equation was $y=177.421x-11.782$ ($r=1.0000$). For determination of selenium by atomic fluorescence spectrometry, the limit of detection could be as low as ppb; the limit of detection of AFS9800 spectrometer was $0.0989\mu\text{g/L}$. The method has the advantages of high sensitivity, high accuracy, high precision, wide linear range, simple operation and low reagent toxicity and, therefore, can be widely used for determination of selenium in food and water.

Key words: Atomic fluorescence spectrometry, food and water, selenium

AUTHOR INDEX

Name	Series	Name	Series
Finn Achmann	M05	Karima Benkhedda	B01
Grant Aaron	G05	Gérard Bertin	L03
Christian C Abnet	PS14, C09, Se-F3	Erwan Bezard	K04
Youssef Aboussaleh	PT36	Zulfiqar A. Bhutta	G03
Baseer Achakzai	G03	Weixia Bian	E05
Raghunath Acharya	P08	Isabel Blanco-Penedo	N09, PT48, PT49
Leigh Ackland	PS03, B09	Gabrielle Blundell-Pound	PS15
Namanjeet Ahluwalia	A01	Christopher J. Boehler	PT17
Chunxiang Ai	B06, L07	Alemtsehay Bogale	PT26
Didar Alam	G03	Fakira Borkovec	PT32
Ethel Alcantara	E04, E06, PT52	Erick Boy	J01, J04
Keith Allen-Redpath	E07	Rafael Brandao	G06
Christine Allmang	M02	Markus Brielmeier	E02
Maneesha Aluru	J07	Regina Brigelius-Flohe	C01
Agnes Amichalczyk	PS03	Margaret Broderius	PS04
Amanda Amorim	G06	Craig Browdy	B08
Peng An	I11	Kenneth H. Brown	G05, H07, J10, G01
Greg Anderson	PS07	S. Bruggraber	A09, N07, O07
Monica Andrews	PS05	Peter Buckett	K08
Venkata Ramana Reddy	P08	Sidooun Bun	G07
Annareddy		Raymond F. Burk	PS10, Se-F2
Magdalena Araya	PS05	Ashley Bush	F02
Andrei ASkalny	PT20	Johan Buyse	PT33
Cindy Atwell	PT51	Yunqing Cai	PT46
Marie-Caroline Augueres	O09	Gillian Campbell	E07
Dagfinn Aune	C10	Valeria Candia	PT12, PT58
Sasa Badzek	PT20	Hong Cao	G07
Shiping Bai	B03, PT60	Bradley A. Carlson	C04, M01, M07
Karl B. Bailey	G04	Fernando Carrasco	A06, A07
Yongping Bao	C03	Amelie Casgrain	A05
Zhengyu Bao	Se-F6, PT66	Cristina Castillo	PT21
Waldemar Barchewsky Jr.	G06	Adail Castro	G06
Lawrence Barrera	C03	J. S. Caton	L04
Karen Basfi-fer	A06, A07	Colin Cercamondi	PT40
Sarah Bath	H04	Zhifang Chai	N02
John H. Beattie	E03, E07, G08, M09, P05, PT53	Yanzhong Chang	K04
M. Beckmann	P05	Yo Ying Chang	PT47
Jose Luis Benedito	N09, PT21, PT49	Chunying Chen	N02, PT11
		Dan Chen	F08
		Xingxiang Chen	B05

14th International Symposium on Trace Elements in Man and Animals

Hongjie Chen	PT41	GrainneO' Donoghue	G08
Hua Chen	PT22	J. Draper	P05
Ping Chen	F04	Mary Drewnoski	L08
Shouwen Chen	PT54	Stephane Durosoy	A08
Xiaofang Chen	PT67	Ines Egli	PT40
Yu Hsin Chen	PT18	Tafere G. Egziabher	PT26
Zupei Chen	H05	Ulf Emanuelson	PT48
Wen-Hsing Cheng	C06	P.W. Emery	P05
Bharati Chimmad	O10, PT27	Reina Engle-Stone	G05, H07
Jazmin Chiu-Ugalde	I08	Robert Steven Esworthy	I05
Young-Eun Cho	PT53	Barbara E. Etschmann	P01
Je-Yong Choi	PT53	Joseph Evans	PT51
Hyo-Taek Chon	N05	Ojeiru F. Ezomo	PT30
Fong-Fong Chu	I05	Susan J.	A05, C10
An-Sik Chung	C02	Fairweather-Tait	
Lynne Clark	PT29	Nils Fall	PT48
Kevin A. Cockell	B01, PT25	Ingrid Falnoga	PT59
Juana Codoceo	A06, A07	Jin-Hu Fan	C09
Rachel Collings	A05, C10	Meirong Fan	B10
James Collins	K06	Zhaoxin Fan	PT05
Gerald Combs Jr.	H03, PT32	Zhiyong Fan	L06
Marcia Cooper	PT19	Rejun Fang	L06
Nick Costa	L09, L10	N.J.R. Faria	A09
Robert Cousins	PS01	Nuno Faria	O07
Attila Csendes	A06, A07	Xinbin Feng	N01
Wujin Cuomu	L10	Elaine L. Ferguson	G04, O08
Xiaoman Dai	F07, PT57	Anatoly Fesyun	F10, PT03
Bui Chau Truc Dan	B08	John Finley	J05, L05, Se-F5
Deepak Darshan	K03	Dmitri E. Fomenko	C04
R. S. Dass	B11	Dianne Ford	PS03
Cindy D. Davis	C04	Neal D Freedman	C09
Sanford M Dawsey	PS14, C09, Se-F3	David Freestone	B09
Benjamin Dehay	K04	Scott Fry	PS06
Seden Demirci	PT28	Lijuan Fu	K04
Fuqing Deng	PT15	Diego Gaitán	H10, H11, PT12, PT58
Veronique Dermauw	PT33		
Julia Dibner	PT56	Lorraine Gambling	PS08
Ellen S. Dierenfeld	PT33	Ujjawal Gandhi	M06
Alexander Dikiy	M05	Junquan Gao	H02
Li Ding	PT63, PT55	Shuo Gao	H05
Shi-bin Ding	N10	Yuxi Gao	N02
Ti Ding	C09	Marco García-Vaquero	PT21, PT49
Xueqing Ding	B10, PT06	A. K. Garg	B11
Olena Dobrovolska	M05	Yan Ge	B10
Daoyin Dong	I10	Rosalind S. Gibson	G04

14th International Symposium on Trace Elements in Man and Animals

Alex Giroux	B01	Lee Hooper	A05, C10
Vadim N. Gladyshev	PS12, M05, C04, PT04, PT44	Graham Horgen	G08
Natalya Gluschenko	PT07	Christine Hotz	G02
Bo Gong	I09	Jianglong Hou	PT50
Yi Gong	A11	Daryl L. Howard	P01
Mauricio Gonzalez	PT65	Yi-Shen Hsu	M08
Margaret-Jane Gordon	M09, E07	Yun-Hsin Hsu	M08
Andrei Grabeklis	PT03	Nan Hu	C09
Sevil Grabeklis	PT03	Xiaobo Hu	A11 PT16, PT37
Robin Graham	D02	Yandan Hu	F09, PT16, PT37
Andrew R Gray	O08	Chengyu Huang	J03, PT16, PT37
Darren Greenwood	C10	Jian Huang	O01
Eliseo Guallar	PS15	Jiaqiang Huang	PT39
Fucun Guo	G07	Kaixun Huang	PS16, E05, I04, PT61, PT41
Xin Guo	I11	Kehe Huang	B05
Yu Guo	PT66	Qibin Huang	PT62
Yuming Guo	G07	Ruicheng Huang	J06
Zijian Guo	P02	Yang Huang	J08
Betiana Gutiérrez	PT21	Yiqiang Huang	PT15
Jere Haas	J02	Junsheng Huo	H08, O01
Edwin Habeych	O09	Richard Hurrell	PT40
Atif Habib	G03	Rachel Hurst	C10
Beth Halfyard	H05	Imtiaz Hussain	G03
K Michael Hambidge	A02, A06, A07, J04, PT26	Kwang Yeon Hwang	PT44
Pengfei Han	PT50	Jorge Inostroza	A06, A07
Stephanie Hansen	L08, B04	Yassir Islam	J04
Robert J. Harrell	B08	Irina Ivanova	I12
Linda J. Harvey	A05, C10	Igor Ivashkiv	F10
Dolph L. Hatfield	C04, M01, M07	Matthew Jackson	H03
Jianhua He	L06	Sumit Kumar Jaiswal	P08
Weihong He	PT01	Jaeho Jeong	PT44
Zisen He	P07	Feng Ji	B03
Anne-Louise M Heath	O08	Fengjie Ji	G07
Shailaja Hegde	M06	Zhixia Ji	PT54
Pushpa Bharati	O10	Xuming Jia	K08
Hemlatha S		Yi Jia	I04, PT61
Joaquín Hernández	PT49	Jon-Hang Jiang	H09
John Hesketh	M03	Liang Jiang	PT22
Sonja Y. Hess	G01	Yugang Jiang	F09, PT13, PT16, PT37
Kristina E. Hill	PS10, Se-F2	Yunxia Jiang	B06, L07
Emily Ho	B02	Wenqian Jing	PT34
Ye-Shih Ho	I05	Melanie Jokinen	PS04
C. Hogstrand	P05	Martin D. de Jonge	P01

14th International Symposium on Trace Elements in Man and Animals

Geoffrey Judson	L09, L10	Xue Leng	F09
Darren Juniper	L03, PT29	Bai Li	PT11
Taiho Kambe	PS03	Dailin Li	PT39
Y. James Kang	B10, E01, I10, PT01, PT05-06, PT08, PT38, PT43, PT50	Dan Li	C03, N10
		Fei Li	D04
		Hui Li	PT63, PT55, PT66
Young-Hee Kang	PT53	Jing Li	PT13, PT16, PT37
Anumantha Kanthasamy	F08	Jungang Li	M10
Suman Kapila	PT02	Kuanyu Li	F07, PT57
Sarojani Karakannavar	A10	Ping Li	PT67
Galina Karpova	M02	Qifeng Li	PT01
Hitoshi Kawamoto	PT30	Ribang Li	Se-F7
Byung-Wook Kim	I05	Rui Li	PT43
Heejeong Kim	K01	Shengfu Li	PT08
Hwa-Young Kim	M05, PT44	Shun Li	PT05, PT08
Jin Young Kim	M07	Sufen Li	B03, PT14
Jong-Han Kim	K08	Weidong Li	C11
Moon-Jung Kim	PT44	Wenjie Li	PT13, PT37
Takayuki Kimura	PT30	Wenxian Li	H08
Marc O. Klein	I08	Yi Li	I04, PT61
Mitchell Knutson	K05	Yufeng Li	N02, PT11
Halina Kobryn	L09, L10	Yanghua Liao	PT15
Ravindra Kodihalli	M06	Chaoke Liang	PT67
Josef Köhrle	I01, I08, Se-F4	Yih-Fong Liew	H09, M08, PT47
Olga Kossinova	M02	Chao-Hsiang Lin	N04
Kavita Kotagi	PT27	Jing Lin	N02, PT11
Nancy Krebs	A06, A07, G08, A02	Ling Lin	H08
Alain Krol	M02	Shih-Wen Lin	C09
Lukas C. Kühn	K03	Yu-Shun Lin	M08
Loveleen Kumar	PS03	Zhiqing Lin	D04
Suleyman Kutluhan	PT28	Changwei Liu	PT46
In-Sook Kwun	E04, E06, E07, PT52, PT53	Hongmei liu	E05
		Hsiao-Ching Liu	B04
Mary R L'Abbe	PS09, B01, H06	Jiayu Liu	H05
Gijs Du Laing	PT33	Jie Liu	PT35
Christine Lang	PS08	Qiong Liu	F04, PT22
Pascal Lapointe	PT25	Sihao Liu	K08
Mauricio Latorre	PT65	Xiaoli Liu	M10
Rosa Lau	C10	Xinping Liu	PT64
Byung Cheon Lee	PT44	Ying Liu	D04
Jaekwon Lee	K01	Zehui Liu	PT14
Kong-Joo Lee	PT44	Zonglie Liu	Se-F7
Xin Gen Lei	I02, I07, M10, P04, PT39	Ria-Ann R. Lomeda	PT53
		Bo Lonnerdal	A04, H10
Zairong Lei	PT35	Marta López-Alonso	N09, PT21, PT48

14th International Symposium on Trace Elements in Man and Animals

W. Y. Wendy Lou	PS09, H06, PT19	Hyeyoung Nam	K05
Hao Lu	F09, PT13, PT16, PT37	Martin Nankap	G05, H07
Lin Lu	B03, L09, PT14, PT60	Salvador Naranjo-Suarez	C04
Mei Po Lu	PT18	Mustafa Naziroglu	F06, PT24, PT28
Shijun Lu	PT13	Alex Ongla Ndjebayi	G05, H07
Xiaoqi Lu	P07	Shakira Nelson	M06
Thomas Lundh	PT48	Sam Newton	J04
Jenea Lunneman	PT51	Jiazuan Ni	F04, PT22
Kunli Luo	Se-F7	Fergus Nicol	M09
Xugang Luo	B03, L09, L10, PT14, PT60	Shaoping Nie	A11
Xu Ma	PT11	Caixiang Niu	Se-F7
Zhenzhen Ma	PT66	Graeme F. Nixon	E07
Alejandro Maass	PT65	Vahid Noaman	PT45
P. K. Malik	B11	Nadir Nogueira	G06
Deqian Mao	C11	Teresa Norat	C10
Dilina Marreiro	G06	Kimberly O'Brien	A03
Harry J. McArdle	PS08	Manuel Olivares	A06, A07, H10, H11, PT12, PT58
Kevin McPhee	PT32	Gary E. Olson	PS10
Marcos Medina	PS05	Ei Lin Ooi	B08
Catherine Méplan	M03	Ou Ou	E07, M09, P05
Bianca I Mergler	A09, O07	Bor-Rung Ou	N04
Shunsuke Meshitsuka	N06, PT30	Guangtang Pang	J03
Zoltan Mester	P03	Wei Pang	F09, PT13, PT16, PT37
Agnes Michalczyk	B09	Zuoquan Peng	Se-F7
Martin Michel	O09	Karin Papapietro	A06, A07
Yasunari Miki	PT30	Winsome R. Parnell	G04
Dennis Miller	O04	Roberto Pastor-Barriuso	PS15
Leland Miller	A02	David Paterson	P01
Ninoslav Mimica	P09, PT20	Anasuya Patil	A10
Marta Miranda	N09, PT49	Madhu Patted	O10
Melissa Miranda-Durán	H11	Dora I. A. Pereira	A09, O07
Sergey Miroshnikov	PT07	Jianhua Piao	O03, O05
Berislav Momčilović	H01	Antonio Pinto	PT09
Semiramis Monte	G06	Fernando Pizarro	A06, A07, H10, PT12, PT58
Linda Morgan	PT29	Danielle Pogge	L08
Sandra Morovic	P09	Larisa Pograjc	PT59
Elise Mostad	PS04	Valentina Polyakova	PT07
Amy K. Motley	PS10	J. J. Powell	A09
Anna Mraines	PS13	Jonathan Powell	N07, O07
Afework Mulugeta	PT26	K. Sandeep Prabhu	M06
Barbara E. Murray	PT65	Ranjana Prakash	P08
Rama Naik	PT27	Tejo Prakash	P08

14th International Symposium on Trace Elements in Man and Animals

Juraj Prejac	P09, PT20	Young Rok Seo	C07
Joseph R. Prohaska	PS04	Ning-Sing Shaw	M08
Markus Purtzki	C05	Jun Shen	H05
Su Qi	L09	Yi Ting Shih	PT18
Ying Qi	PS09, H06, PT19	Hong-In Shin	PT53
Xifeng Qiao	F04	Mee-Young Shin	E04, E06, PT52
Youlin Qiao	Se-F3, PS14, C09	Richard F. Shore	N09
Yu Qiao	D06	Qin Shuai	D06, J06
Fei Qin	E05	Elena Shumilina	M05
Bin Qiu	PT11	Yu Shunxiang	L09, L10
Liyang Qiu	PT06	Helmut Sies	PT09, PT29
Anna M. Raines	Se-F1, PT17	Elena Sizova	PT07
Linwu Ran	B05	Margarita Skalnaya	PT23
Ahmad Reza Ranjbari	PT45	Anatoly Skalny	P06, P09, PT03, PT07
Mohsen Rasti	PT45		
G.A. Ravishankar	O02, O06	Andrey Skalny	F10
Margaret Rayman	PS15, H04, PT29	Sheila A Skeaff	O08
Manju Reddy	F08, J07, PT02	Sajid B. Soofi	G03
D. A. Redmer	L04	Jerry Spears	PS06, B04, L01
Martin D. Reid	M09	Bodo Speckmann	PT09
L. P. Reynolds	L04	Nicole Spiegel	L09, L10
Jung Rho	PT65	Hemalatha Sreeramaiah	A10, PT02
Shelley Rhodes	G08	Holger Steinbrenner	I03, PT09, PT29
Marcelo Ribeiro	G06	Sylvia Stephen	G08
James Richards	B08, PT31, PT56	Vekoslava Stibilj	PT59
Larry Richman	K03	Barbara Stoecker	PT26
Alison Richmond	PS08	Saverio Stranges	PS15
Erin Richter	L08	Bo Su	PT01
Lothar Rink	PS02	Miriam Suazo	PS05
Mary R L'Abbe	PT19	Jing Sun	H08, O01
Bruce Robertson	B01	Lvhui Sun	I07, PT39
André Robichaud	PT25	Xiaorong Sun	PT38
Steve Rodermel	J07	Roger A. Sunde	PS13, PT17, Se-F1
Vladimir Rodionov	I12	Ewa A. Szymlek-Gay	O08
Pamela Rojas	A06, A07	Akiko Takeuchi	M02
Daniel López de Romaña	H10, H11, PT12, PT58	Jiaan Tan	Se-F7
Tracey Rouault	F07, K04	Jian Tan	H05
Manuel Ruz	A06, A07	Long Tan	H05
Chris G. Ryan	P01	Chengkang Tang	PT01
Nazhao Sang	H05	Jiayong Tang	M10
Mert Sanil	PT29	Zezheng Tang	C09
Remy Sapin	I08	Nyima Tashi	L09, L10
Lutz Schomburg	I08	Philip R Taylor	PS14, C09, Se-F3
Ulrich Schweizer	F03, I08	Pushparajah Thavarajah	J08, PT32
		Dil Thavarajah	PT32

14th International Symposium on Trace Elements in Man and Animals

Nguyen Huu Thinh	B08	Gerardo Weisstaub	PS05
Peter Thomson	L09, L10	Ross Welch	D01
Chong Tian	N10	Xiaorong Wen	PT38
Kexiong Tian	L06	Marianne	K08
Yuan Tian	O05	Wessling-Resnick	
Ryuta Tobe	M01	Jamie Westcott	A06, A07, G08
Katalin Toth	F01	Noela Wilson	G04
Alexey Trefilov	I12	Virginia P. Winfrey	PS10
Petra A. Tsuji	C04	Peter Winship	N07
Anton Turanov	M01	Eva. K. Wirth	I08
Nguyen Thi Kieu Tuyen	B08	Lianghuan Wu	D03
Abdulhadi Cihangir	PT24	Min-Hsuan Wu	N08
Uguz		Wen-Mein Wu	N08
A. Cihangir Uguz	PT28	Xianshi Wu	B05
Wilfried Vahjen	A08	Yun Wu	PT55, PT63
Alejandra Valencia	A06, A07	Yuntang Wu	H05
Louise J. Valentine	G08	Laurence Wurth	M02
Liviu Vanoaica	K03	Lin Xi	PT14, PT60
Vjeran Visnjevic	P09, PT20	Xinjie Xia	C11, M10, PT39
K. A. Vonnahme	L04	Yiming Xia	PS11, Se-F2
Biao Wang	I10	Chuanxiao Xie	J03
Chao Wang	F04	Hua Xu	B06, L07
Chia-Yu Wang	K05	Huiqi Xie	B10, I10, PT01,
Fudi Wang	I11, K02, K09		PT05, PT06, PT08,
Jiangyun Wang	M04		PT38, PT43, PT50
Jun Wang	O03, O05	Ming-yong Xie	A11
Kangning Wang	J03, PT39	Huibi Xu	PS16
Peizhong Wang	H05	Minghou Xu	D06
Quanxin Wang	J08	Shengrui Xu	J06
Runlian Wang	PT60	Xinhua Xu	I10
Shikui Wang	P04	Xiuju Xu	I09
Shumin Wang	K04	Xue-Ming Xu	C04, M01, M07
Tao Wang	B10	Zhaoming Xu	C05
Tianyuan Wang	M04	Jinting Yan	PT11
Wei Wang	C03	Sen Yan	J06, PT66
Xiaoxi Wang	K07	Xi Yan	I07
Yanqing Wang	PT54	Feili Lo Yang	PT18
Yanxin Wang	N03	Henian Yang	E07, M09, P05
Yuanxing Wang	A11	Hongpeng Yang	F09, PT13, PT37
Zhanyou Wang	F05	Lichen Yang	O03, O05
Guoo-Shyng Wang-Hsu	N08	Wenjie Yang	C11
Emorn Wasantwisut	J09	Xiangliang Yang	PS16
Xiaobin We	K01	Xiaoguang Yang	O03, O05
Jeremy Weaver	P04	Yu Sheng Yang	PT47
Karen Wedekind	B07, PT31, PT51	Zhaixiao Yao	H05

14th International Symposium on Trace Elements in Man and Animals

Ting Ye	L06	Lili Zhang	PT67
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Yu-Te Yeh	H09	Ningbo Zhang	PT34
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Kechero Yisehak	PT33	Weijun Zhang	PT15
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Kai Yu	C09	Zhuzhen Zhang	I11
Yu Yu	K09	Hua Zhao	M10
Ding Yuan	PT38	Junmei Zhao	B08
Linxi Yuan	D05	Ying Zhao	O08
Vasily Yurasov	PT23	Zhuqing Zhao	PT42
Vedat Ali Yurekli	PT28	D. Zheng	P05
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Geoffrey I. Zanton	B08	Dingyou Zhou	PT67
Christophe Zeder	PT40	Ji-Chang Zhou	M10
Huawei Zeng	C08	Shaobo Zhou	M09, P05
Jiangyong Zeng	L10	Xiang Zhou	PT50
Tao Zeng	D06	Yijing Zhou	PT46
Yu Zeng	M07	Lan Zhu	PT67
Jürgen Zentek	A08	Le Zhu	O04
Ning Zhao	K04	Nianhua Zhu	PT15
Caixia Zhang	PT54	Se Zhu	L09, L10
Chi Zhang	PT62	Yuanyuan Zhu	P07
Fan Zhang	I11	Yumei Zhu	M10
Jiahua Zhang	PT10, PT35	Zhiwu Zhu	I06
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14th International Symposium on Trace Elements in Man and Animals

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14th International Symposium on Trace Elements in Man and Animals

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14th International Symposium on Trace Elements in Man and Animals

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14th International Symposium on Trace Elements in Man and Animals

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14th International Symposium on Trace Elements in Man and Animals

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14th International Symposium on Trace Elements in Man and Animals

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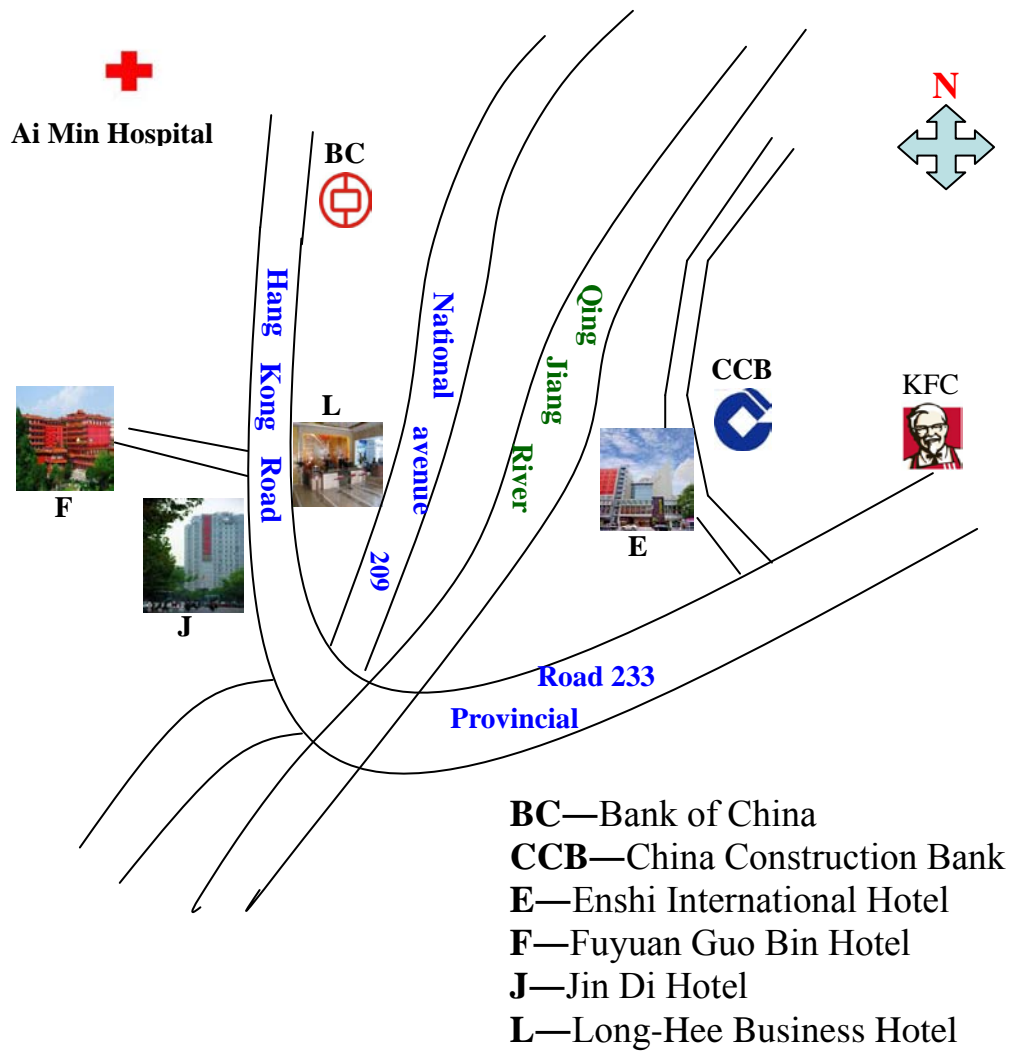
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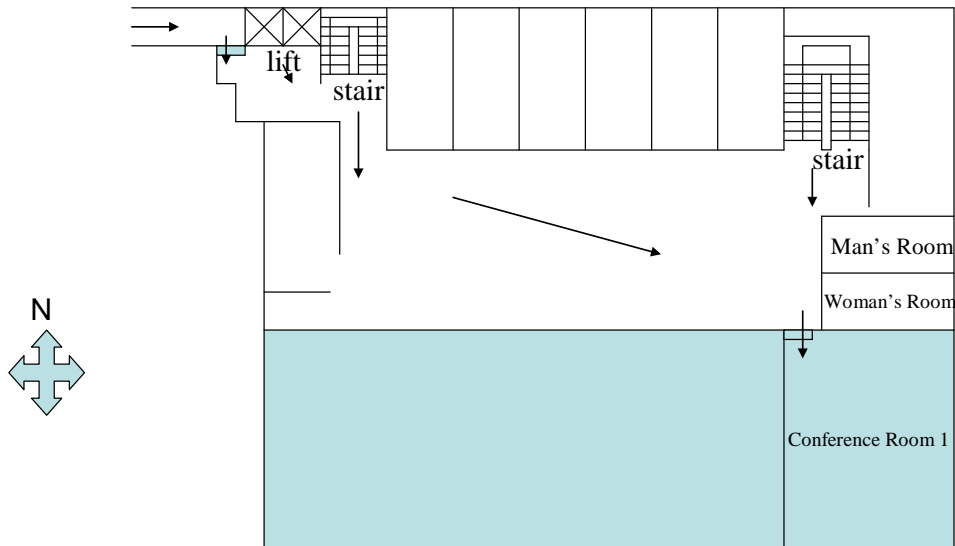
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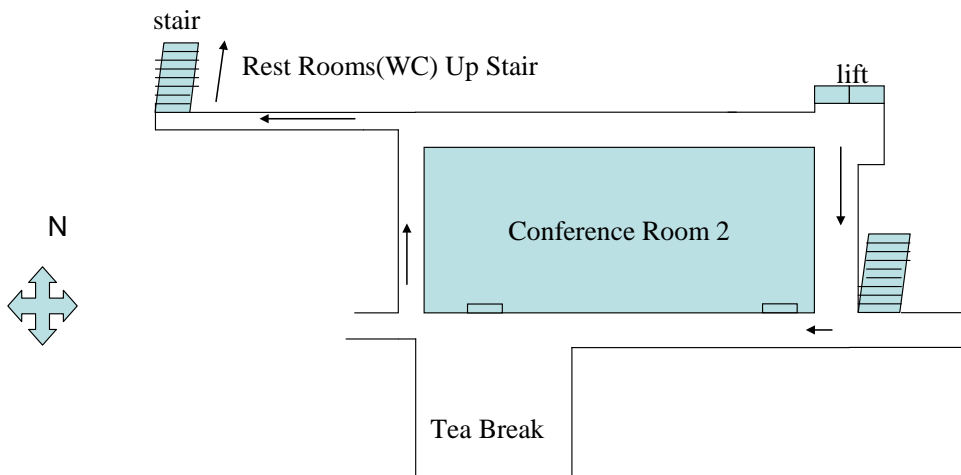
Schematic Drawing of the Meeting Hotel Location in Enshi



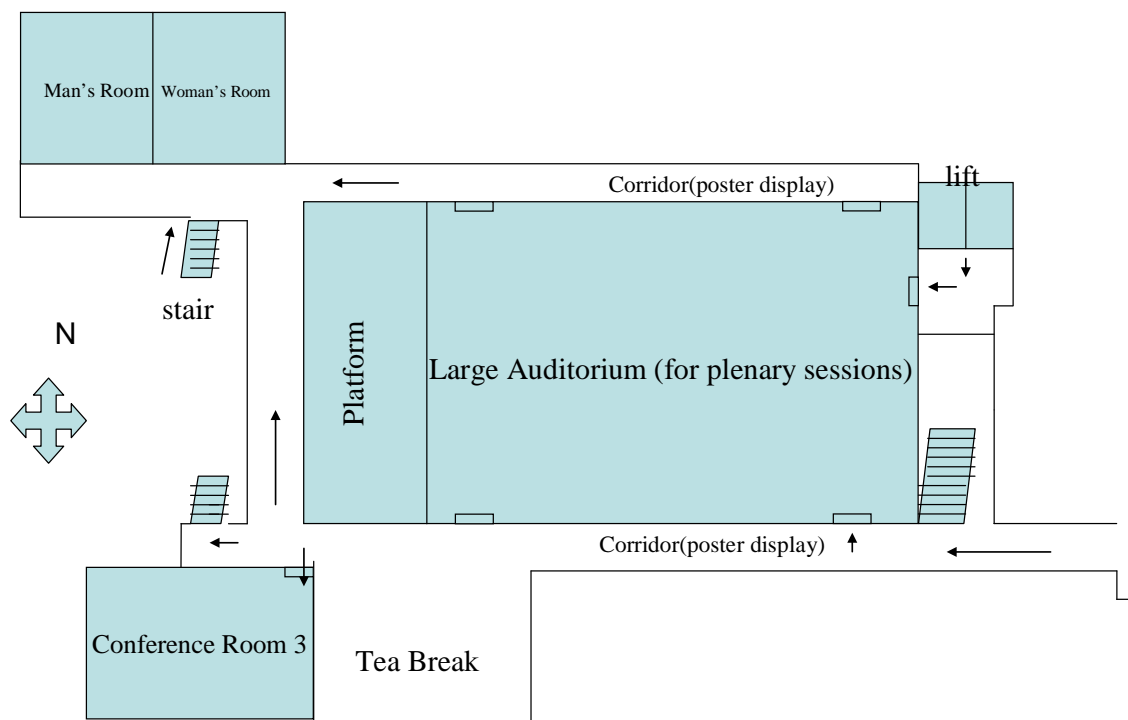
Schematic Drawing of the Meeting Rooms



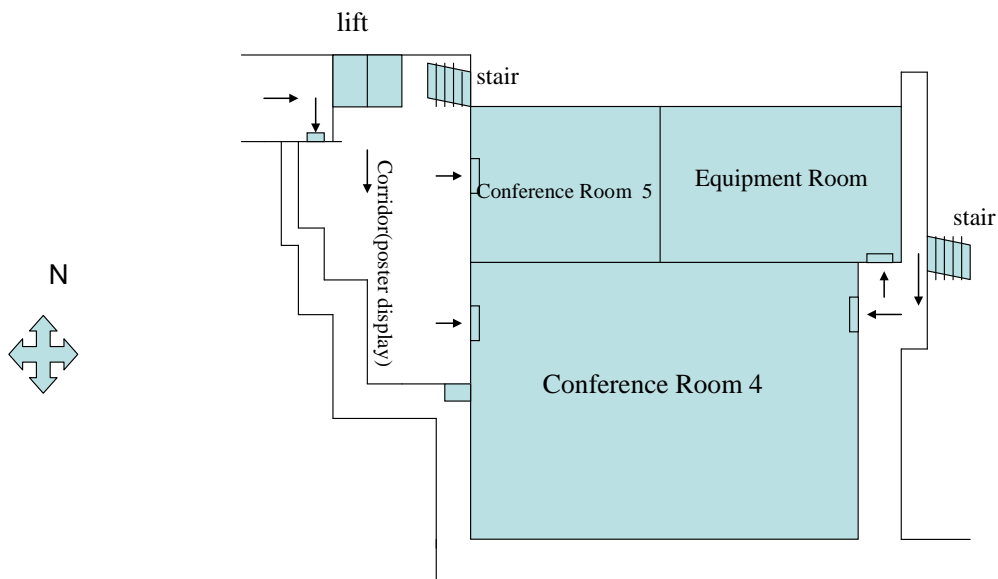
Conference 1 (on the second floor of wing building)



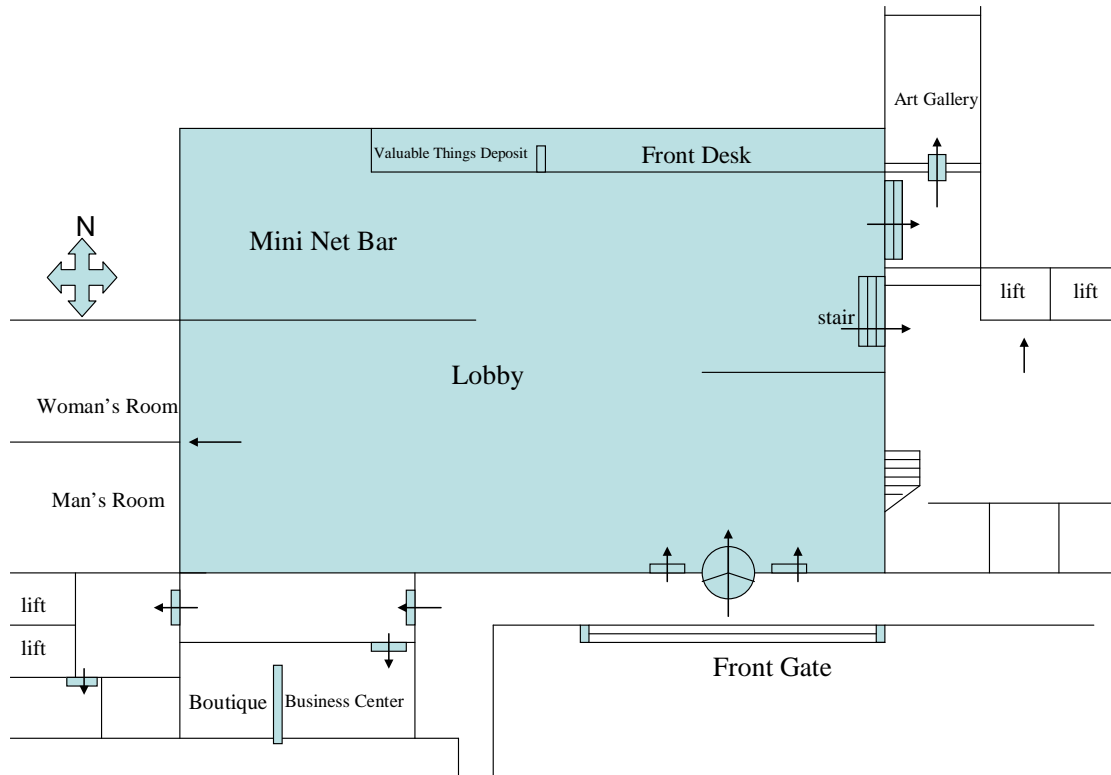
Conference 2 (on the sixth floor of main building)



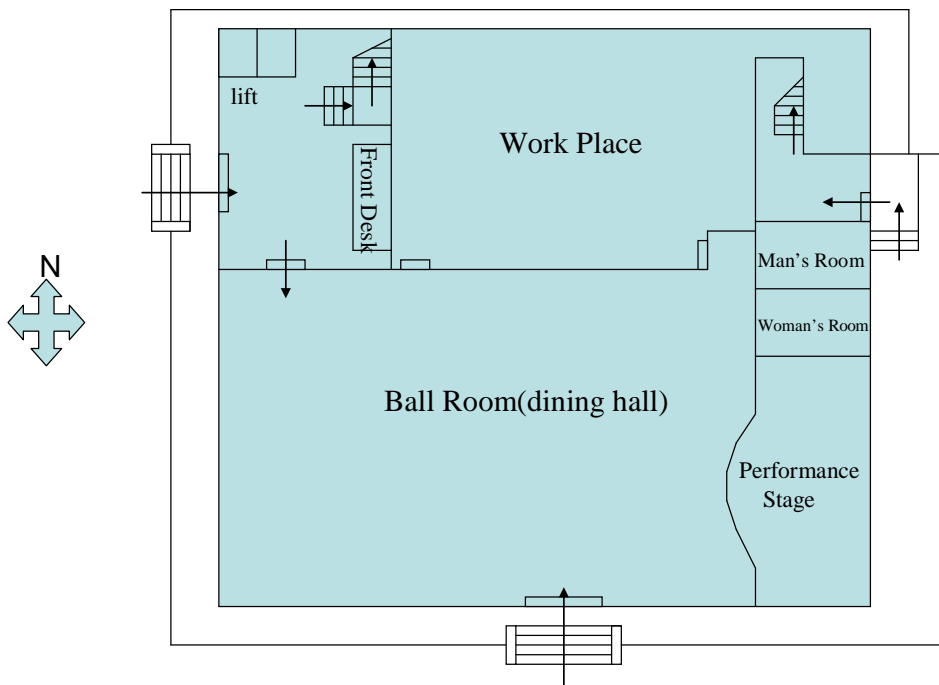
Large Auditorium, Poster Display and Conference 3
(on the seventh floor of main building)



Conference 4 and 5 (on the eighth floor of wing building)



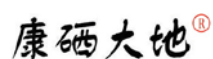
Registration (on the first floor of main building)



Ball Room (on the first floor of wing building)

Acknowledgements

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White Tiger is the totem of Tujia People, decedents of Baren. In Tujia culture they believe that their very first ancestor is the incarnation of white tiger and his descendants also become white tiger after death. They worship white tiger from generation to generation.