

BELLE presents

NON-LINEAR DOSE-RESPONSE RELATIONSHIPS IN BIOLOGY, TOXICOLOGY AND MEDICINE

An International Conference

June 11-13 2002

University of Massachusetts, Amherst, MA

Conference Directors: Edward J. Calabrese, Ph.D., Paul T. Kostecki, Ph.D.

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HORMETIC • NON-MONOTONIC • U/J-SHAPED • PARADOXICAL**

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PLATFORM PRESENTATIONS

TUESDAY, JUNE 11, 2002

Morning

8:45am WELCOME

PLENARY

Moderator: Paul T. Kostecki, *University of Massachusetts, Amherst, MA*

8:50am **Biphasic Dose Responses in the Biological Sciences**

Edward J. Calabrese, *University of Massachusetts, Amherst, MA*

9:30am **Implications of Non-Linearity for Ecotoxicological Risk Assessment**

Keith Solomon, *University of Guelph, Guelph, Ontario, Canada*

10:10am **Break**

10:40am **Evolutionary Foundations of Non-Linearity**

Lorenz Rhomberg, *Gradient Corporation, Cambridge, MA*

11:20am **Risk Assessment Implications of Non-Linear Dose-Responses**

William F. Greenlee, *Chemical Industry Institute of Toxicology, Research Triangle Park, NC*; Frederick J. Miller, *CIIT Centers for Health Research, Research Triangle Park, NC*; Rory B. Conolly, *Center for Computational Biology & Extrapolation Modeling, Research Triangle Park, NC*

Noon

LUNCHEON SPEAKER

REPORTING ON TOXICOLOGY AND RISK ASSESSMENT

Joscelyn Kaiser, *Science News Reporter, Science*

Afternoon

CHEMICAL

Moderator: John DeSesso, *Mitretek Systems, Inc., Falls Church, VA*

1:30pm **Complex Shapes of Dose-Response Curves as the Summation of Underlying Low-Dose-Linear and Saturable Processes**

Rory Conolly, *CIIT Centers for Health Research, Research Triangle Park, NC*

David W. Gaylor, *Sciences International, Inc., Little Rock, AR*

Kevin W. Gaido, *CIIT Centers for Health Research, Research Triangle Park, NC*

Werner K. Lutz, *University of Wurzburg, Wurzburg*

1:50 pm **From Mice to Men, Cancers Are Not Certain at Old Age**

Francesco Pompei & Richard Wilson, *Harvard University, Cambridge, MA*

2:10pm **Implications of Hormesis in Developmental Toxicology Risk Assessment**

Mehdi Razzaghi, *Bloomsburg University, Bloomsburg, PA*

2:30pm **Using Dose and Time to Predict Acute and Chronic Toxicity**

Karl Rozman, *University of Kansas Medical Center, Kansas City, KS*

2:50pm **Experiences with Non-Linear Dose-Response Relationships in Chemical Evaluations**

Dennis Jones, *ATSDR, Atlanta, GA*

3:10pm **Break**

3:40pm **Risk Modeling Implications of Mechanistic Differences between Low and High Dose Effects of Arsenic**

Christopher Wells, Tracey M. Slayton, Barbara C. Beck & Thomas A. Lewandowski, *Gradient Corporation, Cambridge, MA*

4:00pm **Hormesis, Low Dose Carcinogenicity and Low Dose Anti-Carcinogenicity Occur in the Same Animal and with the Same Chemical**

Richard Wilson, *Harvard University, Cambridge, MA*

4:20pm **Data for Trichloroethylene-Induced Kidney Tumors in Rodents Suggest an Epigenetic Mechanism of Action**

Amy Lavin, *International Life Sciences Institute, Washington, DC*

Catherine F. Jacobson & John M. DeSesso, *Mitretek Systems, Inc., Falls Church, VA*

4:40pm **Quantitation of the Dose Response for Formation of DNA Adducts in Rat Liver by 2-Acetylaminofluorene**

Gary Williams, Michael J. Iatropoulos, Jian-Dong Duan & Alan M. Jeffrey, *New York Medical College, Valhalla, NY*

5:00pm **End**

PLATFORM PRESENTATIONS

WEDNESDAY, JUNE 12, 2002

Morning

RADIATION

Moderator: Klaus Becker, *Berlin, Germany*

- 8:30am **Impact of Cellular Defense Mechanisms and Bystander Effects on a Multi-Stage Carcinogenesis Model**
Helmut Schollnberger, *University of Salzburg, Salzburg, Austria/Europe*; Margaret G. Menache, *University of New Mexico, Albuquerque, NM*; Rod Stewart, *Pacific Northwest National Laboratory (PNNL), Richland, WA*; Werner Hofmann, *University of Salzburg, Salzburg, Austria/Europe*
- 8:50am **Human Cells Respond to Changes in Background Radiation by Inducing Specific Heat Shock Protein Members**
Satya P. Saxena, Neerad C. Mishra, & Steven P. Allen, *Lovelace Respiratory Research Institute, Albuquerque, NM*; Raymond A. Guilmette, *Los Alamos National Laboratory, Los Alamos, NM*
- 9:10am **Low-Dose Protective Mechanisms: Implications for Risk Assessment**
Bobby R. Scott, Dale M. Walker, Vernon Walker, James Aden, & Yohannes Tesfaigzi, *Lovelace Respiratory Research Institute, Albuquerque, NM*
- 9:30am **Non-Linear Dose-Response Curves in the Immune System Following Whole-Body X-Irradiation**
Shu-Zheng Liu, *Norman Bethune University of Medical Sciences, Changchun, China*
- 9:50am **The Hormetic Health Effects of Radiation Observed in the Incident of Co-60 Contaminated Apartments in Taiwan**
Y.C. Luan, M.C. Shieh, S.T. Chen, K.L. Soong, & W.K. Wang, *Nuclear Science & Technology Association, Taipei, Taiwan, ROC*; C.M. Tsai, *Atomic Technology Foundation, Taipei, Taiwan, ROC*; W.L. Chen, T.S. Chou, S.H. Mong, J.T. Wu & C.P. Sun, *NBC Protection Society, Taipei, Taiwan, ROC*
- 10:10am **Break**
- 10:40am **Dose-Response Relationship: Chromosome Aberrations in Residents at the High Background Radiation Areas in Ramsar, Iran**
S.M. Javad Mortazavi & Takaji Ikushima, *Kyoto University of Education, Kyoto, Japan*; P. Andrew Karam, *University of Rochester, Rochester, NY*
- 11:00am **Residential Radon in U.S. Counties vs. Lung Cancer in Women who Predominantly Never Smoked**
K.T. Bogen, *Lawrence Livermore National Laboratory, Livermore, CA*; J. Cullen, *University of California Berkeley, Berkeley, CA*
- 11:20am **Treatment of Confounding Factors in Ecological Study Test of Linear-No Threshold Theory**
Bernard Cohen, *University of Pittsburgh, Pittsburgh, PA*
- 11:40am **The Bolton-Brush Radiographic Growth Studies**
B. Holly Broadbent & P.S. Rao, *Case Western Reserve University, Cleveland, OH*

Noon

LUNCHEON SPEAKER

RISK ASSESSMENT MILESTONES

John Doull, M.D., Ph.D., *Dept of Pharmacy, Toxicology and Therapeutics, University of Kansas Medical Center*

Afternoon

ULTRA-LOW DOSES AND MEDICINE

Moderator: Wayne Jonas, *Samueli Institute, Alexandria, VA*

- 1:30pm **Effects of Low Dose Cadmium on Stress Proteins and Survival in Human Prostrate Cells**
Jaya Gaddipati, Rajesh Kumar NV, *Uniformed Services University of the Health Sciences, Bethesda, MD*; William Achanzar, *NCI at NIEHS, Research Triangle Park, NC*; Radha K. Maheshwari, Wayne Jonas, *Uniformed Services University of the Health Sciences, Bethesda, MD*
- 1:55 pm **Non-Immunological Sensitization: A Nonlinear Host Dose-Response to Repeated Low Level Chemical Exposures**
Iris Bell, *The University of Arizona College of Medicine, Tucson, AZ*; Carol Baldwin, Gary E. Schwartz, *University of Arizona, Tucson, AZ*
- 2:20pm **Ultra-low Doses and Biological Responses: A Review of the Literature and Recent Experiments**
Wayne B. Jonas, *Samueli Institute, Alexandria, VA*
- 2:45pm **High Sensitivity ¹H-NMR Studies of Homeopathic Remedies: Unexplained Peaks in the Spectra of Some Samples**
David Anick, *Harvard University, Cambridge, MA*
- 3:10pm **Break**
- 3:40pm **Challenges to the Investigation of Low and Ultra-Low Dose Effects**
Roeland van Wijk, *University of Utrecht, Geldermalsen, The Netherlands*
- 4:05pm **Low Dose Effects in Pulmonary Disease**
Rebecca Bascom, *Penn State Milton S. Hershey Medical Center, Hershey, PA*
- 4:30pm-6:30pm **POSTER SESSION**
(see listing of posters at the end of the program)

PLATFORM PRESENTATIONS

THURSDAY, JUNE 13, 2002

Morning

BIOMEDICAL

Moderator: David Diamond, *University of South Florida, Tampa, FL*

- 8:00am **Non-Linear Functions between Stress Hormones, Brain Plasticity and Memory**
David Diamond, *University of South Florida, Tampa, FL*
- 8:20am **Biphasic Effects of Progesterone Treatment on Proliferation of Normal and Malignant Human Ovarian Surface Epithelial Cells**
Viqar Syed & Shuk-Mei Ho, *University of Massachusetts Medical School, Worcester, MA*
- 8:40am **Two Examples of Paradoxical Pharmacology Using *In Vivo* Animal Models of Disease**
Kenda LJ Evans, Zsuzsanna Callaerts-Vegh, *University of Houston, Houston, TX*; Felix Shardonofsky, *Texas Children's Hospital, Houston, TX*; Heather Giles, *GlaxoSmithKline, Herfordshire, UK*; Richard Bond, *University of Houston, Houston, TX*
- 9:00am **Using *C. elegans* to Model Induced Stress Resistance and Life Span Hormesis**
James Cypser & Thomas E. Johnson, *University of Colorado, Boulder, CO.*
- 9:20am **Biological Aging and Its Hormetic Modulation by Repeated Challenge**
Suresh Rattan, *University of Aarhus, Aarhus, Denmark*
- 9:40am **Hormetic vs Inhibitory Effects in Sea Urchin Bioassays**
Giovanni Pagano, *Istituto Nazionale Tumori, Naples, Italy*
- 10:00am **Break**
- 10:30am **Non Linear Factors Affecting Exposure and Risk to Anthrax**
Dennis Jones, *ATSDR, Atlanta, GA*
- 10:50am **Biphasic Effects of Cardiac Glycosides (Ouabain) on Vascular Smooth Muscle Cell Proliferation**
Julius Allen, Joel Abramowitz & Ashihan Aydemir-Koksoy, *Baylor College of Medicine, Houston, TX*
- 11:10am **Altered Phenotype in Glial Cells Underlies the Low-Dose Neuroprotection Against Neurotoxicity**
Victor M. Pentreath, *University of Salford, Salford, UK*; Mark R. Cookson, *Mayo Clinic, Jacksonville, FL*; Carole Mead, *Christie Hospital, Manchester, UK*; Debbie Slamon, *AstraZeneca Pharmaceuticals, Cheshire, UK*
- 11:30am **Is the Hygiene Hypothesis an Example of Hormesis?**
John A. Bukowski, *ExxonMobil Biomedical Sciences, Inc., Annandale, NJ*; Philip G. Lewis, *Rohm and Haas Company, Bristol, PA*
- 1150am **Tissue-Specific Dysfunction Induced by Menadione in Blood Vessels: Mechanisms for U-shape Dose-Response Curve**
Jin-Ho Chung & Jee-Yeon Han, *Seoul National University, Seoul, Korea*
- 12:10 **Lunch**

RISK ASSESSMENT

Moderator: Gary Marchant, *Arizona State University, Tempe, AZ*

1:30pm Non-Linear Dose Response: Legal Standards for the Admission of Novel Scientific Theories in Regulatory Decision-Making

Gary Marchant, *Arizona State University College of Law, Tempe, AZ*

1:50 pm Implications of Hormesis for Industrial Hygiene

Michael Jayjock, *Rohm and Haas Company, Spring House, PA*; Philip G. Lewis, *Rohm and Haas Company, Bristol, PA*

2:10pm Do We Need any Legal Limits for Radon below about 500 Bq/m³?

Klaus Becker, *Berlin, Germany*

2:45pm Some Thoughts about How to Incorporate Hormesis into the Risk Assessment Process

Brent L. Finley, *Exponent, Santa Rosa, CA*; Dennis J. Paustenbach, *Exponent, Menlo Park, CA*

2:50pm Radiation Hormesis: Molecular-Cellular Biology, Epidemiology, and Prevention and Therapy of Cancer

Myron Polycove, *University of California, North Bethesda, MD*; Ludwig E. Feinendegen, *Heinrich-Heine-University Duesseldorf, Lindau, Germany*

3:10pm Basic Research Needs Panel (DOE, NIEHS, CIIT, Air Force, Pharmaceutical Industry)

Kenneth A. Mundt, *Applied Epidemiology, Inc., Amherst, MA*

Wayne Jonas, *USUHS, Bethesda, MD*

Klaus Becker, *Berlin, Germany*

Antone L. Brooks, *Washington State University, Richland, WA*

Rory B. Conolly, *Center for Computational Biology & Extrapolation Modeling, Research Triangle Park, NC*

POSTER SESSIONS

4:30 - 6:30PM

WEDNESDAY, JUNE 12, 2002

Neurobehavioral Hormesis: The Exclusion of Compounds that Activate Arousal Systems in the Brain

Marni Y.V. Bekkedal, Glenn D. Ritchie, Kenneth R. Still & John Rossi III, *Naval Health Research Center Detachment (Toxicology), Wright-Patterson Air Force Base, OH*

Debates Over Linearity: Much Ado About Evidence; Not Enough About Relevance Nor Preference

Kevin P. Brand, *University of Ottawa, Ottawa, ON, Canada*; Lorenz Rhomberg, *Gradient Corporation, Cambridge, MA*

Effects of Superlow Doses

Elena B. Burlakova & Alexander A. Konradov, *Russian Academy of Sciences, Moscow, Russia*

New Approaches to Modeling of Living Systems Response to Ultra Weak Actions

Elena B. Burlakova, *Russian Academy of Sciences, Moscow, Russia*

Effects of a 'Lead-free' Environment on Fertility and Reproductive Function in Female Mice

Ivo Iavicoli, Giovanni Carelli & Nicolo Castellino, *Catholic University of the Sacred Heart, Rome, Italy*

Pseudo Hormesis: An Explanation in Search of a Manifestation

Susan M. Chemerynski & Jonathon Borak, *Yale University, New Haven, CT*; Greg Sirianni, *University of New Haven, West Haven, CT*; Bernard L. Cohen, *University of Pittsburgh, Pittsburgh, PA*

Usefulness of Very Low-Doses of Cisplatin in Regulation of Animal and People Health Conditions

Elzbieta Deranalowicz-Malarczyk, Martyna Kandefer-Szerszen, Anna Jarosz-Wilkolazka, Agnieszka Szuster-Ciesielska & Liliana Borowska, *Marie Curie-Sklodowska University, Lublin, Poland*

The Effect of Low-Dose of Guaiacol on Enzymatic Activity of Fungal Cells

Elzbieta Deranalowicz-Malarczyk, Anna Jarosz-Wilkolazka & Janina Kochmanska-Rdest, *Marie Curie-Sklodowska University, Lublin, Poland*

Ultra-weak Secondary Radiation Chemiluminescence of Humic Acid Induced by Gamma-irradiation

Wieslaw Goraczko & Janusz Slawinski, *Poznan Univeristy of Techical, Poznan, Poland*

Linear and Non-linear Effects of Lead on Behavior of *Drosophila melanogaster*

Helmut V.B. Hirsch, John D. Mercer, Tara Torno, Diane Stark & Helen Ghiradella, *The University at Albany, SUNY, Albany, NY*

Extracellular Replication of Bacteria in Presence of Cytokines or Lipopolysaccharide(LPS): Linear and Non-Linear Responses

Siva Kanangat, Umberto Meduri, Elizabeth A. Tolley, Arnold E. Postlethwaite & Dennise R. Schaberg, *University of Tennessee Memphis, Memphis, TN*

A Mathematical Model for Curve-Fitting Allelochemical Dose-Responses

D.L. Liu, *NSW Agriculture, Wagga Wagga, NSW, Australia*; M. An, *Charles Sturt University, Wagga Wagga, NSW Australia*; J.V. Lovett, *University of New England, Armidale, NSW, Australia*

Nectophotometer: A New Instrument for Observing Hormesis

Richard W. Lo Pinto & John Santelli, *Fairleigh Dickinson University, Teaneck, NJ*

Adaptive Response in Two Populations of Uranium Miners Exposed to Low and High Doses of Radiation

Jose Henrique Pereira Luis, *Nuclear and Technological Institute, Sacavem, Portugal*

Bimodal Type of Regulation of Protein Kinase C by Antioxidants Down to Ultra-Low Doses

Elena L. Maltseva & Nadya P. Palmina, *Institute of Biochemical Physics RAS, Moscow, Russia*; Konstantin Gurevich, *Lomonosov Moscow University, Moscow, Russia*

Adaptation to Radiation: Reductions in Risk after Low Doses *in vivo*

R.E.J. Mitchel, *Atomic Energy of Canada, Ltd, D.R. Boreham, McMaster University*

The History of Chemical Hormesis and Potential Implications for Modern Risk Assessment and Epidemiology

Kenneth A. Mundt, *Applied Epidemiology, Inc., Amherst, MA*

Edward J. Calabrese & Linda A. Baldwin, *University of Massachusetts, Amherst, MA*

The Development of a Reproducible Toxicological Bioassay to Elucidate Hormesis

Marc A. Nascarella, John G. Stoffolano, Jr. & Edward J. Calabrese, *University of Massachusetts, Amherst, MA*

Hyperbolic Radiopathogenic Processes for Chernoboyl-touched Children

Eugene A. Neyfakh, *Institute of Biochemical Physics, Moscow, Russia*

Continuous Low Dose-Rate Gamma-Irradiation Induce Non-Linear Changes of DNA-Protein Cross-Links in Lymphocytes of Mice

Andreyan N. Osipov & Alexander L. Elakov, *Moscow SIA "Radon", Moscow, Russia*; Galina Ya. Kolomijtseva, *M.V.Lomonosov Moscow State University, Moscow, Russia*; Vyacheslav D. Sypin, *Moscow SIA "Radon", Moscow, Russia*

The Effect of Antioxidants in Ultra Low Doses on Lipid Peroxide Oxidation in Biological Membranes

Nadezhda P. Palmina, Lyubov V. Kledova & Tatyana V. Pankova, *Emanuel Institute of Biochemical Physics RAS, Moscow, Russia*

Nonlinear Dose-Response Behavior and Multiple Solutions for a Model of the Menstrual Cycle

Paul M. Schlosser, *CIIT Centers for Health Research, Research Triangle Park, NC*; James F. Selgrade & Leona Harris, *North Carolina State University, Raleigh, NC*

Extremely Low Frequency Electromagnetic Field (ELF-EMF)-Sress Induced DNA Damage in Human Peripheral Blood Leukocytes Evaluated by Comet Assay

Ravindra K. Tiwari, *New Science College, Hyderabad, India*; K. Iravathy Goud, *Bhagwan Mahavir Medical Research Centre, Hyderabad, India*; K. Suryanarayana, *Research Center Imarat, Hyderabad, India*; S.C Bhargava & Y. Rahuja, *Bhagwan Mahavir Medical Research Centre, Hyderabad, India*

Non-Linear Dose-Response of Alcohol Drinking in a Large Population

Natalia Udaltsova & Arthur L. Klatsky, *Kaiser Permanente Medical Care Program, Oakland, CA*

Season of Birth and Human Longevity in a Large Population

Natalia Udaltsova, Gary D. Friedman & Arthur L. Klatsky, *Kaiser Permanente Medical Care Program, Oakland, CA*; Germaine Cornelissen, *Halberg Chronobiology Center, University of Minnesota, Minneapolis, MN*; Franz Halberg, *Halberg Chronobiology Center, University of Minnesota, Minneapolis, MN*

Gamma Variate (Indicator Dilution Curve): Analogy to Describing Selected Hormesis Effects

J.A. Vento & R.P. Spencer, *Univ. of Connecticut Health Center, Farmington, CT*