

BELLE presents

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

An International Conference

May 28-30 2003

University of Massachusetts, Amherst, MA

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

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PLATFORM PRESENTATIONS

WEDNESDAY, MAY 28, 2003

Morning

Session I: GENERAL PRINCIPLES

Moderator: Russell Keenan, *AMEC, Portland, ME*

- 8:30am **Biomedical Implications of Hormesis**
Edward J. Calabrese, University of Massachusetts, Amherst, MA
- 9:00am **Biological Switching Mechanisms and Dose Response Relationships**
Melvin Andersen, CIIT-Center for Health Research, Research Triangle Park, NC
- 9:30am **The Bystander Effect: Recent Developments and Implications for Understanding the Dose-Response**
Ronald Mitchel, Atomic Energy of Canada, Ltd., Chalk River, ON
- 10:00am **Break**
- 10:30am **The Potential Impact of Hormesis on Risk Assessment**
Russell Keenan, AMEC, Portland, ME
- 11:00am **The Implications of Non-Linear Effects in Risk Assessment Harmonization**
John A. Bukowski & R. Jeffrey Lewis, ExxonMobil Biomedical Sciences, Inc., Annandale, NJ
- 11:30am **Economic Implications of Hormesis**
Jim Hammit, Harvard University School of Public Health, Boston, MA

Noon **LUNCHEON SPEAKER** 1009 CAMPUS CENTER

**YOU HAVE A BRAIN IN YOUR HEAD, FEET IN YOUR SHOES,
STEER YOURSELF ANY DIRECTION YOU CHOOSE (DR. SEUSS)**

Dr. Joseph Borzelleca, Medical College of Virginia, Richmond, VA

Afternoon

Session II: RADIATION

Moderator: Ludwig E. Feinendegen, *Heinrich-Heine-University Düsseldorf, Germany*

- 1:30pm **Assessment of Low-Dose Radiation Risk in Europe: Diverging Authorities and Scientists**
Klaus Becker, Radiation, Science & Health, Berlin, Germany
- 2:00pm **Responses to Low Doses of Ionizing Radiation in Biological Systems**
*Ludwig E. Feinendegen, Heinrich-Heine-University Düsseldorf, Germany
Myron Polycove, University of California San Francisco Medical School, San Francisco, CA*
- 2:30pm **Radiation-Induced Change in Cell Proliferation and its Neuroendocrine Regulation: Dose-Response Relationship and Pathophysiological Implications**
Shu-Zheng Liu, MH Radiobiology Research Unit, Jilin University Health Sciences Center, Changchun, China
- 3:00pm **Low-Dose Radiation and Genotoxic Chemicals Protect Against Stochastic Biological Effects**
Bobby R. Scott, Dale M. Walker & Vernon Walker, Lovelace Respiratory Research Institute, Albuquerque, NM
- 3:30pm **Break**
- 4:00pm **Low Dose Radiation Health and Medical Benefits: A Century of Hard Data and Soft Science**
Jim Muckerheide, Center for Nuclear Technology and Society, Worcester Polytechnic Institute, Worcester, MA

Session III: CHEMICAL CARCINOGENESIS

Moderator: Ludwig E. Feinendegen, *Heinrich-Heine-University Düsseldorf, Germany*

- 4:30pm **Dose-Response Curves in Chemical Carcinogenesis**
William J. Waddell, University of Louisville, Dept. of Pharmacology and Toxicology, Prospect, KY
- 5:00pm **Detoxication Strategy of Epoxide Hydrolase—The Basis for a Novel Threshold for Definable Genotoxic Carcinogens**
Franz Oesch & Michael Arand, Institute of Toxicology, University of Mainz, Mainz, Germany
- 5:30 - 7:30pm **POSTER SESSION / SOCIAL**
(see listing of posters at the end of the program)

PLATFORM PRESENTATIONS

THURSDAY, MAY 29, 2003

Morning

Session IV: BIOCHEMICAL

Moderator: Wayne Jonas, *Samueli Institute, Bethesda, MD*

- 8:30am **The Treatment of Chronic Prostatitis with Low Level Chorionic Gonadotropin**
John McLane & John McMichael, *Milkhaus Laboratory, Inc., Providence, RI*
- 9:00am **Non-Linear Dose-Response Effects of Neurosteroids on Brain Plasticity and Memory**
David M. Diamond, *University of South Florida and Veterans Hospital, Tampa, FL*
- 9:30am **Possible Clinical Implications of Hormesis**
Wayne Jonas, *Samueli Institute, Bethesda, MD*
- 10:00am **Break**
- 10:40am **Biphasic and U-Shaped Opioid Dose-Responses in the Immune System**
Burt M. Sharp, *University of Tennessee, Memphis, TN*
- 11:00am **Molecular Mechanisms of Anti-Aging Effects of Mild Heat Stress on Human Cells**
Dr. Suresh I.S. Rattan, *University of Aarhus, Denmark*
- 11:30am **Biphasic Response of Ciprofloxacin in Human Fibroblast Cell Cultures**
Filiz Hincal & Aylin Gürbay, *University of Hacettepe, Ankara, Turkey*
Alain Favier, *Université Joseph Fourier, France*

Noon

LUNCHEON SPEAKER

1009 CAMPUS CENTER

WHY THE COMPANY WHOSE STOCK YOU OWN DOESN'T CARE ABOUT RISK ASSESSMENT
Philip G. Lewis, MD, Vice President, Rohm and Haas Company, Bristol, PA

Afternoon

Session V: HIGH PROFILE TOXIC SUBSTANCES AND THE NON-LINEAR FEATURES OF THEIR DOSE RESPONSE RELATIONSHIPS

Moderator: Ralph L. Kodell, *U.S. Food and Drug Administration, Jefferson, AR*

- 1:30pm **Asbestos: Non-Linear Dose Response Relationships in in vitro Assays and Inhalation Experiments**
Brooke Mossman & Arti Shukla, Ph.D., *University of Vermont College of Medicine, Burlington, VT*
Pamela Vacek, PhD, *University of Vermont, Burlington, VT*
- 2:00pm **The Particulate Air Pollution Controversy**
Robert F. Phalen, *University of California, Irvine, CA*
- 2:30pm **Mechanistic Model Predicts Low-Dose Nonlinearity of Liver Tumor Risk in Mice Fed Fumonisin B1**
Ralph L. Kodell & Angelo Turturro, *U.S. Food and Drug Administration, Jefferson, AR*
- 3:00pm **Dioxin**
Thomas Starr, *TBS Associates, Raleigh, NC*
- 3:30pm **Break**
- 4:00pm **The Chloroform Saga: Science Trumps Policy?**
Jay Goodman, *Michigan State University, East Lansing, MI*
- 4:30pm **Justification, Application and Implication of Presumed Linearity for Dioxin and Dioxin-Like Compounds**
John D. Schell, *BBL Sciences, Tallahassee, FL*
- 5:00pm **Non-Linear Dose-Response Relationships in Endocrine Disruption**
John Ashby, *Syngenta Central Toxicology Lab, Cheshire, UK*
- 6:30pm **DINNER 1009 Campus Center**

PLATFORM PRESENTATIONS

FRIDAY, MAY 30, 2003

Morning

Session VI: TOXICOLOGY

Moderator: Louis Anthony Cox, Jr., *Cox Associates and University of Colorado, Denver, CO*

- 8:00am **Nonlinearity in the IQ-Blood Lead Relation: Redefining Low Level Exposure**
Richard L. Canfield, *Cornell University, Ithaca, NY*
Todd A. Jusko, *University of Washington, Seattle, WA*
Charles R. Henderson, Jr., *Cornell University, Ithaca, NY*
- 8:30am **Non-Linear Dose-Response Relationships in Experimental Neurotoxicology**
Victor W. Pentreath, *University of Salford, Salford, U.K.*
- 9:00am **Nonlinear Low-dose Hematotoxicity**
Louis Anthony Cox, Jr., *Cox Associates and University of Colorado, Denver, CO*
- 9:30am **Break**

10:00am-
Noon

Session VII: REGULATORY FORUM ON NON-LINEAR DOSE RESPONSE

Moderator: Myron Harrison, *ExxonMobil Corporation, Irving, TX*

Chris DeRosa, *ATSDR, Atlanta, GA*
James Muckerheide, *Radiation Science and Health, Needham, MA*
Michael Bolger, *FDA, Washington, DC*
Matt Bogdanffy, *Dupont, Newark, DE*
Scott Stoner, *Department of Environmental Conservation, Albany, NY*

WEDNESDAY, MAY 28, 2003

The Influence of Lead and Mercury on Beta-Amyloid Aggregation and Cytotoxicity

M.D. Basha, W. Wei & N.H. Zawia, *University of Rhode Island, Kingston, RI*

Effect of Hydroperoxide and Water Specimens of Different Composition and Physicochemical Properties on the Structure of Membranes and Activity of Membrane Enzymes

Elena B. Burlakova, Alexander N. Goloshchapov, Elena M. Molochkina & Lyudmila D. Fatkhulina, *Emanuel Institute of Biochemical Physics, Moscow, Russia*

Metallothionein as an Adaptive Protein Prevents Diabetes and its Toxicity

Lu Cai, *Department of Medicine, University of Louisville, KY*

Hormesis at NTP: Evidence of Hormetic Dose Responses in NTP Dose-Range Studies

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

Effects of Low-Dose Exposures to X-rays on the Non-Specific Anti-Tumor Responses in Mice

Aneta Cheda, Jolanta Wrembel-Wargocka, Emil Lisiak, Ewa Nowosielska, Maria Marciniak & Marek K. Janiak, *Military Institute of Hygiene and Epidemiology, Warsaw, Poland*

Experimental Study of Subchronic Toxicity of Lanthanum Nitrate on Liver in Rats

Dong Chen, Ying Liu & Yu-Xiu Nie, *Jilin University, Changchun, Jilin, PR China*

The Immune Effects of Radiation Observed from the Incident of Co-60 Contaminated Apartments in Taiwan

W.L. Chen, Y.C. Luan, S.H. Mong, J.T. Wu, C.P. Sun & H.Y. Shen, *Nuclear Science & Technology Association, Taipei, Taiwan, ROC*
 M.C. Shieh, T.S. Chou, S.T. Chen, K.L. Soong, Y.C. Yeh & W.K. Wang, *Nuclear, Biological and Chemical Protection Society, Taipei, Taiwan, ROC*
 C.M. Tsai, *Atomic Technology Foundation, Taipei, Taiwan, ROC*
 M.L. Shen, *National Taiwan University, Taipei, Taiwan, ROC*

Health Risks from Fluoridated Water

Myron J. Coplan, *Intelleguity Technology Services, Natick, MA*

Secondary Ultraweak Luminescence from Humic Acids Induced by Gamma Radiation

Wieslaw Goraczko & Janusz Slawinski, *Poznan University of Technology, Poznan, Poland*

Non-Linear Dose Response Relationships in the Definition of Occupational Exposure Limits

Ivo Iavicoli & Giovanni Carelli, *Institute of Occupational Health, Università Cattolica del Sacro Cuore, Roma, Italy*

Heterogeneous Exposure Dose Levels Unable to Induce Harmful Effects of Life Expectancy and Blastomogenesis

Valentina S. Kalistratova, Lev A. Buldakov, Petr G. Nisimov & Irina B. Romanova, *State Research Center of Russia, Moscow, Russia*

Alcohol and Blood Pressure: a Complex Nonlinear Relationship

Arthur L. Klatsky, MD, *Kaiser Permanente Medical Center, Oakland, CA*
 Natalia V. Udaltsova, PhD, *Kaiser Permanente Division of Research, Oakland CA*

Stress Response and Cellular Longevity: The Prolonged Lifespan of Cushing's-Syndrome-Patients, Fibroblasts

Dimitris Kletsas, Harris Pratsinis, Irene Zervolea & Dimitri Stathakos, *National Centre for Scientific Research "Demokritos", Athens, Greece*
 Fivos Giannakopoulos, Nikos Thalassinos & Stylianos Tsagarakis, *Evangelismos Hospital, Athens, Greece*

Hormetic Effects at Clinical Levels

Marios Kyriazis MD, *British Longevity Society, Hemel Hempstead, UK*

Synergy—The Effect of Combining Non-Linear Dose Profiles: The Prediction and Quantification of the Potentiation of EDTA with Antimicrobials

R. J. W. Lambert, *R2-Scientific, Sharnbrook, Beds, UK*
 Stephen P. Denyer & Geoff W. Hanlon, *University of Brighton, Brighton, UK*

Effect of Single WBI with Low Doses of X-rays on the Development of and Blood Supply to the Pulmonary Tumor Colonies in Mice

Emil Lisiak, *Military Institute of Hygiene and Epidemiology, Warsaw, Poland*
 Mirosław Dziekiewicz, *Clinical Hospital of Military Medical University, Warsaw, Poland*
 Krzysztof W. Zielinski, *Military Medical University, Lodz, Poland*
 Aneta Cheda, *Military Institute of Hygiene and Epidemiology, Warsaw, Poland*
 Jolanta Wrembel-Wargocka, *Military Institute of Hygiene and Epidemiology, Warsaw, Poland*
 Sebastian Dominiak, *Military Medical University, Lodz, Poland*
 Marek K. Janiak, *Military Institute of Hygiene and Epidemiology, Warsaw, Poland*

Effect of Low and Very Low Doses of Simple Phenolics on Plant Peroxidase Activity

Elzbieta Malarczyk, Janina Kochmanska-Rdest & Marzanna Pazdziuch-Czochra, *Maria Curie-Skłodowska University, Lublin, Poland*

The Use of Streptolysin O for the Treatment of Scars, Adhesions and Fibrosis

Stephen W. Mamber, Vit Long, Ryan G. Rhodes, Sunthorn Pond-Tor, Lyn R. Wheeler, Kellie Fredericks, Brian Vanscoy, Jean-Frederic Sauniere & John McMichael, *Milkhaus Laboratory Inc., Providence, RI*
 Remy Steinschneider & Jean-Claude Laurent, *Bio Expertise Technologies, Marseille, France*

Comparison in vivo Study of Genotoxic Action of High versus Very Low Dose-Rate γ -Irradiation

Andreyan N. Osipov, *Moscow SIA "Radon", Moscow, Russia*
 Dmitry Yu. Klovok, *Institute of Theoretical and Experimental Biophysics, Moscow Region, Russia*
 Alexander L. Elakov, *Moscow SIA "Radon", Moscow, Russia*
 Olga M. Rozanova & Svetlana I. Zaichkina, *Institute of Theoretical and Experimental Biophysics, Moscow Region, Russia*

The Use of Low Dose Thimerosal for the Treatment of Herpesvirus Infections

Sunthorn Pond-Tor, Ryan G. Rhodes, Albert E. Dahlberg & John McMichael, *Milkhaus Laboratory, Inc., Providence, RI*

Effect of Low Dose of Cadmium on Transformation of Normal Human Prostate Cells

N.V. Rajeshkumar, Jaya P. Gaddipati, Jason C. Grove & Radha K. Maheshwari, *Uniformed Services University of the Health Sciences, Bethesda, MD*
 Wayne B. Jonas, *Samueli Institute for Information Biology, Alexandria, VA*

Hormetic Modulation of Aging and Longevity in Fruitflies

Dr. Suraj P. Sharma, *Guru Nanak Dev University, Amritsar, India*
 Dr. Suresh I.S. Rattan, *University of Aarhus, Aarhus, Denmark*

Particulate Matter (PM) Increments may not be Causal in Mortality and Morbidity

Peter A. Valberg, *Gradient Corporation, Cambridge, MA*

Epidemiological Evaluation of the Threshold Model for Hexavalent Chromium

Edwin van Wijngaarden, Rose S. Luippold & Kenneth A. Mundt, PhD, *Applied Epidemiology, Inc., Amherst, MA*

Hematopoietic Hormesis and Adaptive Response Induced by LDR is Likely Due to Up-Regulation of Hematopoiesis-related Cytokines

Guangjun Wang, *The First Hospital of Jilin University, PR China*
 Lu Cai, *The First Hospital of Jilin University, PR China and University of Louisville, KY*

The APP Promoter Responds to Pb Exposure in Transfected PC12 Cells

W. Wei, M.D. Basha & N.H. Zawia, *University of Rhode Island, Kingston, RI*

Low Doses Gamma-Radiation Induce Non-Linear Dose Response in Mammalian and Plant Cells

Svetlana I. Zaichkina, Olga M. Rozanova, Gella F. Aptikaeva, Asia Ch. Achmadiyeva & D. Ju Klovok, *Institute of Theoretical and Experimental Biophysics, Moscow Region, Russia*

Effect of Mixed Rare Earth Changle Crossing Placenta Membrane on Embryo Cell DNA Damage

Li Zhou, Li Shulei & Nie Yuxiu, *Jilin University, Changchun, Jilin Province, PR China*