

The 11th Annual International Conference on

DOSE-RESPONSE 2012:

**Implications for Toxicology,
Medicine, and Risk Assessment**

*The Annual Meeting of the
International Dose-Response Society*

April 24-25 2012

University of Massachusetts, Amherst, MA

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



**THRESHOLD • ADAPTIVE • BIDIRECTIONAL • BIPHASIC
HORMETIC • NON-MONOTONIC • U/J-SHAPED • PARADOXICAL**

PLATFORM PRESENTATIONS

TUESDAY, APRIL 24, 2012

Morning

Session I: BIOMEDICAL

Moderator: Jaap Hanecamp, *Roosevelt Academy, Middelburg, The Netherlands and University of Massachusetts, Amherst, MA*

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|--------|---|---------|---|
| 8:30am | Welcome | 9:45am | Hormesis in the Modeling of Locally Implanted Anti-Cancer Therapy
Hava Siegelmann, <i>University of Massachusetts, Amherst, MA</i> |
| 8:45am | Non-Ionizing Radiofrequency Fields-Induced Adaptive in Mammalian Cells
Maria Rosaria Scarfi, <i>CNR-Institute for Electro-magnetic Sensing of Environment, Napoli, Italy</i>
Yi Cao, <i>School of Public Health, Soochow University, Suzhou, Jiangsu, P.R. China</i>
Vijayalaxmi, <i>University of Texas Health Science Center, San Antonio, TX</i> | 10:15am | Break |
| 9:15am | Stress Adaptation to Enhance Neural Progenitor Cells Viability
Guanghu Wang, <i>Georgia Health Sciences University, Augusta, GA</i>
Kannan Krishnamurthy, <i>Cold Spring Harbour Laboratories, New York, NY</i>
Dantera Tangpisuthipongsa, <i>Georgia Health Sciences University, Augusta, GA</i> | 10:45am | Postconditioning Hormesis; Mild Stress Stimulates Recovery in Cells
FAC Wiegant and R. van Wijk, <i>Utrecht University, The Netherlands</i> |

Session II: PLENARY

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

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|---------|---|------|--|
| 11:15am | Food Safety and Chemophobia
Gordon Gribble, <i>Dartmouth College, Hanover, NH</i> | Noon | Lunch
Amherst Room, 10th Floor Campus Center |
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Afternoon

Session II: PLENARY (cont.)

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|--------|---|
| 1:00pm | For Nuclear Accidents, What is the Appropriate Dose-Rate Limit for Remedial Actions?
Jerry Cuttler, <i>Cuttler & Associates Inc., Mississauga, ON, Canada</i> |
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Session III: TOXICOLOGY / RISK ASSESSMENT I

Moderator: Brooke Mossman, *University of Vermont College of Medicine, Burlington, VT*

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|--------|---|--------|--|
| 1:45pm | Beyond Dose-Response: Concentration-Responses and Food
Jaap Hanecamp, <i>Roosevelt Academy, Middelburg, The Netherlands and University of Massachusetts, Amherst, MA</i>
Aalt Bast, <i>Maastricht University Medical Centre, The Netherlands</i> | 2:30pm | Break |
| 2:15pm | Chemical Hormesis in Plant Pathogenic Fungi and Fungus-Like Oomycete
Carla Domenica Garzon and Francisco Flores, <i>Oklahoma State University, Stillwater, OK</i> | 3:45pm | Pseudoscientific Aspects of Fine Particulate Matter (PM2.5) Epidemiology, 1993-2012
James Enstrom, <i>University of California, Los Angeles, CA</i> |
| 2:45pm | Dose Response Molecular Responses to Asbestos and Silica in Human Lung Cells
Brooke Mossman, Jedd Hillegass, Paul Peeters, Timothy N. Perkins, and Arti Shukla, <i>University of Vermont College of Medicine, Burlington, VT</i> | 4:15pm | Tannins: Hormetic Longevity-Triggers or Just Energy-Allocators
Nadine Saul and Kerstin Pietsch, <i>Humboldt-Universität zu Berlin, Germany</i>
Stephen R. Stürzenbaum, <i>King's College London, London, United Kingdom</i>
Ralph Menzel and Christian E. W. Steinberg, <i>Humboldt-Universität zu Berlin, Germany</i> |

PLATFORM PRESENTATIONS (cont.)

WEDNESDAY, APRIL 25, 2012

Morning

Session I: TOXICOLOGY / RISK ASSESSMENT II

Moderator: José E. Manautou, *University of Connecticut, Storrs, CT*

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|--------|--|---------|---|
| 8:30am | Gene Expression Patterns and Adaptive Response as Mechanistic Background of Hormesis
Christian E.W. Steinberg, Kerstin Pietsch, Nadine Saul and Ralph Menzel, <i>Humboldt-Universität zu Berlin, Germany</i>
Stephen R. Stürzenbaum, <i>King's College London, London, United Kingdom</i> | 9:30am | Dose-Response Assessment for Arsenic: A Case Study for Why the LNT Doesn't Work
Barbara Beck and Ari S. Lewis, <i>Gradient, Cambridge, MA</i> |
| 9:00am | Promotion of Metabolic Health and Lifespan by Transiently Increasing Oxidative Stress
Michael Ristow, <i>University of Jena, Germany</i> | 10:00am | Break |

Session II: RADIATION

Moderator: Jerry Cuttler, *Cuttler & Associates Inc., Mississauga, ON, Canada*

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|---------|---|---------|---|
| 10:30am | Gene Expression Profiles of Radiation Threshold Effects in <i>Drosophila melanogaster</i>
Michael Antosh, David Fox, Nicola Neretti and Leon Cooper, <i>Brown University, Providence, RI</i> | 11:30am | The New Radiobiology: Returning to Our Roots
Brant Ulsh, <i>Colorado State University, Cincinnati, OH</i> |
| 11:00am | Chronic Radiation Exposure Induces Cellular Adaptive Response in Interventional Cardiologists
Gian Luigi Russo, Idolo Tedesco, Maria Russo, Carmela Spagnuolo and Maria Grazia Andreassi, <i>Institute of Food Sciences, National Research Council, Avellino, Italy</i>
Eugenio Picano, <i>Pisa, Italy</i> | Noon | Lunch
Amherst Room, 10th Floor Campus Center |

Afternoon

Session II: RADIATION (cont.)

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|--------|---|--------|---|
| 1:00pm | Effect of Low Doses of Low-LET Radiation on the Innate Anti-tumor Reactions in Radioresistant and Radiosensitive Mice
Ewa Nowosielska, Aneta Cheda, Jolanta Wrembel-Wargocka and Marek K. Janiak, <i>Military Institute of Hygiene and Epidemiology, Warsaw, Poland</i> | 2:00pm | Low-Dose-Radiation Benefits, a New Paradigm
Bobby R. Scott, <i>Lovelace Respiratory Research Institute, Albuquerque, NM</i> |
| 1:30pm | Exposures Involving Perturbations of the EM Field Have Non-Linear Effects on Radiation Response and Can Alter the Expression of Radiation Induced Bystander Effects
Carmel Mothersill and Colin Seymour, <i>McMaster's University, Hamilton, ON, Canada</i> | 2:30pm | Hormesis and the Adaptive Response
Colin Seymour and Carmel Mothersill, <i>McMaster's University, Hamilton, ON, Canada</i> |

TUESDAY EVENING

POSTER SESSION & SOCIAL

5:00pm – 6:30pm • 10th Floor Campus Center

DINNER 6:30pm • Amherst Room, 10th Floor Campus Center

A Partial List Of Poster Presentations

Flawed Human Health Effects Epidemiology: The California Air Resources Board's Diesel Truck Emission Rules

Jerome Arnett, Jr., MD. *The Heartland Institute, Chicago, Ill.*

Interactions of Low-Dose Radiation and the Carcinogen

Benzo[a]pyrene in A/J Mice

Veronica R. Bruce, *University of New Mexico, Albuquerque, NM and Lovelace Respiratory Research Institute, Albuquerque, NM*
Katherine Gott, Bobby Scott and Julie Wilder, *Lovelace Respiratory Research Institute, Albuquerque, NM*

Hormesis and the Salk Polio Vaccine

Edward J. Calabrese, Ph.D., *Department of Public Health, University of Massachusetts, Amherst, MA*

Key Historical Studies Serving as the Basis for the Linear Dose Response Challenged

Edward J. Calabrese, Ph.D., *Environmental Health Sciences, University of Massachusetts, Amherst, MA*

The Role of X-rays In the Treatment Of Gas Gangrene: A Historical Assessment

Edward J. Calabrese and Gaurav Dhawan, *University of Massachusetts, Amherst, MA*

Production of Cytokines by Splenocytes and Macrophages after Single or Fractionated Low-level Irradiations with X-rays

Aneta Cheda, Ewa M. Nowosielska, Jolanta Wrembel-Wargocka and Marek K. Janiak *Military Institute of Hygiene and Epidemiology, Warsaw, Poland*

Shifting the Paradigm in Radiation Safety

Mohan Doss, *Fox Chase Cancer Center, Philadelphia, PA*

Bystander Signal Propagation via Serotonin-Mediated Calcium Uptake

Jennifer Fazzari, Anna Mersov, Colin Seymour and Carmel Mothersill, *McMaster University, Hamilton, ON, Canada*

Revisiting Assumptions of Linearity for Radiation-Induced Cancer: Implications for Chemical Cancer Risk Assessment

R. Golden, *ToxLogic LLC, Potomac, MD USA*
E. Calabrese, *School of Public Health, Environmental Health Sciences, University of Massachusetts, Amherst, MA USA*

Cancer Mortality, Natural Background Radiation, and other Selected Predictors

John Hart, *Sherman College of Chiropractic, Spartanburg, SC*
Seungeun Hyun, *University of South Carolina Upstate, Spartanburg, SC*

Effect of Internal Contamination with HTO on the Innate Anti-Tumour and Inflammatory Reactions in Mice

Ewa M. Nowosielska, Aneta Cheda, Jolanta Wrembel-Wargocka and Marek K. Janiak, *Military Institute of Hygiene and Epidemiology, Warsaw, Poland*

Threshold Doses of Single or Fractionated X-rays for Stimulation of Natural Anti-Neoplastic Cells in Mice

Ewa M. Nowosielska, Aneta Cheda, Jolanta Wrembel-Wargocka and Marek K. Janiak, *Military Institute of Hygiene and Epidemiology, Warsaw, Poland*

Low-dose Gamma Irradiation Inhibits IL-6 Secretion from Fibroblasts that Promotes HBEC Transformation by Cigarette Smoke

Wenshu Chen, Xiuling Xu, Lang Bai, Mabel T. Padilla, Bobby R. Scott and Yong Lin, *Lovelace Respiratory Research Institute, Albuquerque, NM*

Non-Targeted Radiation Effects with High Dose Rate (HDR) Brachytherapy

Christine Pinho, *McMaster University, Hamilton, Ontario, Canada*
Ranjan K. Sur and Raimond Wong, *Juravinski Cancer Centre, Hamilton, Ontario, Canada*
Carmel Mothersill and Colin Seymour, *McMaster University, Hamilton, Ontario, Canada*
Joseph E. Hayward and Thomas J. Farrell, *Juravinski Cancer Centre, Hamilton, Ontario, Canada*

Biphasic Dose Responses to Phytoestrogens: An Evaluation of Mechanisms

Miles A. Sarill, *University of Massachusetts, Amherst, MA*
Edward J. Calabrese, *University of Massachusetts, Amherst, MA*

2012 INTERNATIONAL DOSE-RESPONSE SOCIETY AWARDS

OVERVIEW

*The International Dose-Response Society is proud to announce the recipients of the annual awards for **Outstanding Career Achievement, Outstanding New Investigator and Outstanding Leadership**. These awards are presented to individuals in each category who have made outstanding contributions to the field of **Dose Response**. The awards committee selecting the recipients was Barbara Callahan, University Research, Helmut Hirsch, University at Albany, Ken Mundt, Environ.*

*This year's awards go to: **Roger O. McClellan** for Outstanding Career Achievement; **Julie E. Goodman, Ph.D., DABT** for Outstanding New Investigator; and **Lynn Hlatky** for Outstanding Leadership. Congratulations to all.*

2012 INTERNATIONAL DOSE-RESPONSE SOCIETY AWARDS

AWARDEE PROFILE: CAREER ACHIEVEMENT



ROGER O. McCLELLAN

DVM, MMS, DSc (Honorary),

Diplomate-ABT, Diplomate-ABVT,

Fellow-ATS, AAAR, SRA, HPS and AAAS

Member – Institute of Medicine

He received his Doctor of Veterinary Medicine degree from Washington State University in 1960 and joined the Hanford Laboratories, Richland, WA, staff to conduct research on radionuclide toxicity in domestic animals. As a U.S. Atomic Energy Commission staff scientist (1965-1966), he provided oversight for the AEC's radionuclide toxicity program. Beginning in 1966, he provided scientific leadership for the inhalation toxicology program of the Lovelace organization in Albuquerque, NM. This program achieved international recognition for research on the health effect of airborne radioactive materials and chemicals. As President of the Chemical Industry Institute of Toxicology (1988-1999), the Institute achieved international recognition for understanding how the mode of action of chemicals influences exposure-response relationships and informs extrapolation from animals to humans. Since 1999, he has served as an advisor to both public and private organizations on air quality issues, including the development of improved and safer technologies and products.

He has served as Adjunct Professor at eight universities and been active in a number of professional organizations, including service as President of the Society of Toxicology and the American Association for Aerosol Research. He is a Diplomate of the American Board of Toxicology and the American Board of Veterinary Toxicology and a Fellow of Academy of Toxicological Sciences, Society for Risk Analysis, Health Physics Society, Society for Risk Analysis, and American Association for Aerosol Research.

In 1990, he was elected to membership in the Institute of Medicine of the National Academy of Sciences. He received the International Aerosol Fellow Award for his contributions to aerosol science and technology and the Society of Toxicology's Merit Award and Founders Award. In 2005, The Ohio State University awarded him an Honorary Doctor of Science degree. In 2008, he received the Washington State University Regents Distinguished Alumnus Award. He is a strong advocate of risk-based decision-making and the need to integrate data from epidemiological, controlled clinical, laboratory animal and cell studies to evaluate dose-response relationships for different technologies and products and to inform policy makers in developing standards and guidance to protect the health of workers and the public.



DR. LYNN HLATKY

Dr. Hlatky is an internationally known radiobiologist and cancer biologist. She received her PhD from the University of CA, Berkeley and trained in heavy ion radiobiology at Lawrence Berkeley Laboratory. She then was recruited to Harvard Medical School where she was faculty in Dept. of Radiation Oncology for a decade and half, before founding a Center of Cancer Systems Biology at Tufts Univ. School of Medicine. Dr. Hlatky has long been involved in the quantitative and empirical study of radiation damage effects at the cellular and chromosomal levels, as well as the dynamical aspects of tumor development. For radiations demonstrating linear kill kinetics, she was the first to establish that any form of protracted dosing to an asynchronous cell population would be asymptotically more suppressive than an acute dose of the same magnitude [Hahnfeldt P and Hlatky L. *Cell resensitization during protracted dosing of heterogeneous cell populations. Radiat Res 150:681-687, 1998*]. She followed this up by showing

that uniform dosing was optimal in this regard [Hahnfeldt P, Folkman J and Hlatky L. *Minimizing long-term tumor burden: the logic for metronomic chemotherapeutic dosing and its antiangiogenic basis. J Theor Biol 220: 545-554, 2003*]. Her lab has considerable expertise in angiogenesis and was also the first to show the expression of the major angiogenic factor, vascular endothelial growth factor (VEGF) in cells following irradiation [Hlatky L, Hahnfeldt P, Tsiou C, Coleman CN. *Vascular endothelial growth factor: environmental controls and effects in angiogenesis. Br J Cancer 74(Suppl. XXVII):S151-6, 1996*]. These earlier works highlighted the role of both endothelial and stromal cells in the radiation response of tumors. In the decade that followed, Dr. Hlatky's lab uncovered many novel corollaries in both the angiogenic and radioresponse of tumor populations. Demonstrating a novel relationship between diversity in radioresponse over tumor populations under cell stress, her lab demonstrated the diversity in cellular radioresponse under conditions of environmental stress (using "sandwich cultures" designed to develop a self-imposed, graded ischemia across the cell population) was reduced, then sharply increased, after mimicking reperfusion through introduction of oxygen/nutrients to the cultures [Hlatky L, Van Buren T, Hahnfeldt P. *Quantifying intercellular radioresponse diversity in irradiated sandwich cultures via micronucleus expression. Int J Radiat Biol 1995;67:541-8*]. Her latest work, in collaboration with Professor Rainer K. Sachs, refutes the long-held paradigm of a single-cell origin for chronic myelogenous leukemia, a notable radiation-inducible cancer. They demonstrated a statistically better fit to CML incidence when CML is considered to have a two-cell origin [Sachs RK, Johnsson K, Hahnfeldt P, Luo J, Chen A, Hlatky L. *A multicellular basis for the origination of blast crisis in chronic myeloid leukemia. Cancer Res 71(8):2838-47, 2011*]. The study has far-reaching implications on the role of cell-cell interactions in carcinogenesis. Dr. Hlatky's lab currently focuses on the study of cancer systems biology, with focus on investigations integrating carcinogenesis with radiobiology.

INTERNATIONAL DOSE-RESPONSE SOCIETY MEMBERSHIP

The INTERNATIONAL DOSE-RESPONSE SOCIETY is a professional society designed to enhance understanding of the nature of the dose response and its implications for science and society. Those Individuals with a professional interest in these areas are invited to join the Society. Applications for membership can be found at www.dose-response.org.

As part of the INTERNATIONAL DOSE-RESPONSE SOCIETY membership, each member will receive a

subscription to the e-journal Dose-Response, which is a peer-reviewed quarterly journal. In addition, there is a Society Newsletter developed for the membership. Members will receive a 25% reduction in registration fees to Dose-Response 2012: Implications for Toxicology, Medicine, and Risk Assessment, the Annual Meeting of the International Dose-Response Society.

To Become a Member, Visit www.dose-response.org

2012 INTERNATIONAL DOSE-RESPONSE SOCIETY AWARDS

AWARDEE PROFILE: NEW INVESTIGATOR ACHIEVEMENT



DR. JULIE GOODMAN

Dr. Julie Goodman, an epidemiologist and a Diplomate of the American Board of Toxicology, is a principal at Gradient, an environmental consulting firm. She is also on the adjunct faculty in the department of epidemiology at the Harvard School of Public Health. Her primary responsibilities at Gradient include the design, oversight, analysis, and interpretation of epidemiology studies as well as the evaluation of chemical toxicology data, apparent disease clusters, and chemical exposures.

Much of Dr. Goodman's work focuses on assessing the weight of evidence regarding chemical exposures and potential health risks. She also has done considerable work evaluating the shape of dose-response curves at low doses, the toxicological significance of functional changes, and the use of epidemiology and toxicology data to address questions regarding appropriate dose-response models and the identification of responses at ambient exposures.

Dr. Goodman has authored and co-authored over 50 original research articles, review articles, and book chapters on a wide variety of topics related to epidemiology, toxicology, and risk assessment. She also has presented scientific findings and analyses to community groups and regulatory and legislative bodies, including the US Congress.

Topics on which she has published and presented include an evaluation of health risks from low doses of bisphenol A, commentary on the proposal for linear low-dose extrapolation for non-cancer health effects, and assessments of health risks (and differentiating adverse vs. non-adverse effects) from the criteria pollutants (NO₂, O₃, PM, and SO₂) at low exposure levels.

Before joining Gradient, Dr. Goodman was a Cancer Prevention Fellow at the National Cancer Institute. She received an SB degree in Environmental Engineering from the Massachusetts Institute of Technology in 1996, and an Sc.M. in Epidemiology in 2000 and a Ph.D. in Environmental Health Sciences/Toxicology in 2002 from the Johns Hopkins Bloomberg School of Public Health.

ANNOUNCEMENT

The 12th International Conference on

DOSE-RESPONSE 2013: IMPLICATIONS FOR TOXICOLOGY, MEDICINE, AND RISK ASSESSMENT

The Annual Meeting of the International Dose-Response Society

APRIL 23-24, 2013

University of Massachusetts at Amherst

- *Adaptive* • *Bidirectional* • *Biphasic* • *Hormetic* • *Non-Monotonic* • *Yerkes-Dodson Law (Psychology)*
- *U-Shaped* • *J-Shaped* • *Subsidy-Stress Gradient (Ecology)* • *Reverse Dose-Responses*

TOPICS WILL INCLUDE:

- Molecular mechanisms
- Pharmacological effects
- Chemical and radiation toxicology
- Risk assessment implications
- Low-dose modeling
- Evolutionary foundations
- Ecological effects
- Clinical/therapeutic effects
- Psychological/behavioral responses
- Bioengineering processes
- Exercise science
- Epidemiology of low doses
- Industrial hygiene
- Legal implications

Please visit our website for more information, Abstract Submission Guidelines and Abstract Submission

www.dose-response.org

For further information contact Edward J. Calabrese, Ph.D. or Paul T. Kostecki, Ph.D.
Environmental Health Sciences • Morrill I, N344 • University of Massachusetts Amherst, MA 01003
Phone: (413) 545-3164 • FAX: (413) 545-4692 • edwardc@schoolph.umass.edu

DEADLINE FOR SUBMISSION - December 13, 2012

E-mail to dleonard@schoolph.umass.edu

INTERNATIONAL DOSE-RESPONSE SOCIETY

2012 Membership Form for New and Renewing Members

Renewal Membership New Membership

Please choose one membership category (Payment in US Funds):

- Individual Membership \$125–1 year
Individual Membership \$225–2 years
Retiree Membership \$75–1 year
Retiree Membership \$125–2 years
Post-Graduate Membership \$75–1 year (up to three years post-graduation)
Post-Graduate Membership \$125–2 years (up to three years post-graduation)
Student Membership \$10–1 year
Student Membership \$15–2 years
Sustaining Member \$1000/year
Corporate Membership \$5000/year

Please type or print clearly in ink only:

Last Name: _____ Middle Initial(s): _____

First Name: _____ Date of Birth: _____

Title: _____

Address: _____

Organization

Department

Street / P.O. Box

City: _____ State: _____

Country: _____ Postal Code: _____

Telephone: _____ / _____ / _____
Country code Area code Number

Fax: _____ / _____ / _____
Country code Area code Number

Email Address: _____

Payment (check one credit card type):

American Express Master Card Visa Discover Check (Payable to Univ. of Mass. Dose-Response)

Account Number: _____ Expiration Date: _____

Completed application forms should be mailed, emailed or faxed to:

Dose-Response/BELLE Offices
Environmental Health Sciences Program, School of Public Health
Morrill 1, Room N344
University of Massachusetts
Amherst, MA 01003

Telephone: 413-545-3164 • Fax: 413-545-4692 • Email: Sorensen@ehs.umass.edu