PRECONDITIONING ADAPTIVE RESPONSES IN BIOLOGY AND MEDICINE

Building Biological Shields Against Disease and Injury

The Annual Meeting of the International Dose-Response Society

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

April 22-23, 2014
University of Massachusetts
Amherst, MA

Threshold
Adaptive
Bidirectional
Biphasic
Hormetic
Non-Monotonic
U/J Shaped
Linear



PLATFORM PRESENTATIONS

TUESDAY, APRIL 22, 2014

Morning

8:00am Welcome

Carmel Mothersill, McMasters University, Hamilton, ON, Canada

Session I: PRE-CONDITIONING AND THE DOSE RESPONSE

Chair: John Ives, Samueli Institute, Alexandria, VA

8:15am Intermittent Energetic Challenges,

Adaptive Responses and Health: Lessons

from the Brain

Mark Mattson, National Institute on Aging,

Baltimore, MD

8:45am Adaption by Low Dose Radiation Exposure:

A Look at Scope and Limitations for

Radioprotection

Ronald Mitchel, Atomic Energy of Canada Ltd,

Chalk River, ON, Canada

9:15am Optimizing Pre- and Post-conditioning

Clinical Outcomes: A Dose Response

Perspective

Edward Calabrese, University of Massachusetts,

Amherst, MA

9:45am **Discussion**

10:00am Break

Session II: CARDIOVASCULAR PRE- AND POST-CONDITIONING

Chair: Jeff Gidday, Washington University School of Medicine, St. Louis, MO

10:30am Remote Ischemic Conditioning: From

Inspiration to Clinical Translation

Karin Przyklenk, Peter Whittaker, Wayne State

University School of Medicine, Detroit MI

11:00am Assessing the Promise of Remote

Conditioning for Cardioprotection: New

Clinical Developments

Andrew Redington, University of Toronto,

Toronto, ON, Canada

11:30am Cardioprotection: Challenges and

Possibilities

Derek Haulsenloy, University College, London, UK

12:00pm Cellular Mechanisms Underlying the

Cardioprotective Effects of Exercise

Rick J. Alleman, David Brown, Eastern Carolina

University, Greenville, NC

12:30pm **LUNCH**

Amherst Room, 10th Floor Campus Center

Afternoon

Session III: NEUROLOGICAL PRE- AND POST-CONDITIONING

Chair: James Giordano, Georgetown University, Washington, DC

2:00pm Ischemic Tolerance and Neurological

Protection

John M. Hallenbeck, National Institute of Health,

Bethesda, MD

2:30pm Post-conditioning and the Transition

from Animal Models to Humans for the

Treatment of Stroke

Roger Simon, Morehouse School of Medicine,

Atlanta, GA

3:00pm Extending Injury- and Disease-Tolerant

Phenotypes by Repetitive Conditioning: Promoting Long-Lasting Protection in the

CNS

Jeff Gidday, Lihong Zhang, Yanli Zhu, Washington

University School of Medicine, St. Louis, MO

3:30pm **Discussion**

TUESDAY EVENING

POSTER SESSION & SOCIAL 4:30pm - 6:00pm • 10th Floor Campus Center

PLATFORM PRESENTATIONS (cont.)

WEDNESDAY, APRIL 23, 2014

Morning

Session I: PRE- POST-CONDITIONING AND MEDICAL AND PUBLIC HEALTH IMPLICATIONS

Chair: TBA

8:30am Preconditioning Strategy for Improved
Therapeutic Potential of Stem Cell
Transplantation Therapy after

Ischemic Stroke

Shan Ping Yu, Emory University, Atlanta, GA

9:00am Implementation of Intermittent Fasting

Prescriptions: Breaking Through

the Barriers

Mark Mattson, National Institutes on Aging,

Baltimore, MD

9:30am Pre-conditioning with Low Level Laser

(Light) Therapy

Tanupriya Agrawal, Massachusetts General Hospital and Harvard Medical School,

Boston, MA

James D Carroll, Thor Photomedicine Ltd,

Chesham, UK

Michael Hamblin, Massachusetts General Hospital, Harvard Medical School, and

Harvard-MIT, Boston, MA

10:00am Break

10:30am Dose-Response Effects of Low-Level Light

Therapy on Brain and Muscle

Francisco Gonzalez-Lima, University of Texas at

Austin, Austin, TX

11:00am Neuromodulation With Weak Transcranial Electrical Stimulation: Small Things Making

a Big Difference

Marom Bikson, City College of New York, NY

11:30am Increased Threat Detection, Learning and

Attention using Low-Level Transcranial Direct Current Stimulation (tDCS)

Vincent P. Clark, University of New Mexico,

Albuquerque, NM

12:00pm **LUNCH**

Afternoon

Session II: INTEGRATIVE DISCUSSION:

How Can Pre-Post-conditioning be Used?

Chair: James Watson, Los Angeles, CA

1:15pm 1. Therapeutic Application

2. Protecting Military Personnel

3. Preventing Athletic Injuries and Enhancing Recovery

4. Enhancing Athletic and Job Performance

5. Improving Public Health

Participants:

Wayne Jonas, Samueli Institute, Alexandria, VA

Andrew Redington, University of Toronto,

Toronto, ON, Canada

Jeff Gidday, Washington University School of

Medicine, St. Louis, MO

John Hallenbeck, National Institute of Health,

Bethesda, MD

2:15pm CONFERENCE TECHNICAL SUMMARY

Jay Mitchell, Harvard University, Boston, MA

2:30pm FINAL CONFERENCE PERSPECTIVES

Colin Seymour, McMasters University, Hamilton, ON, Canada

A Partial List Of Poster Presentations

Drosophila melanogaster Show a Threshold Effect in Response to Radiation

Michael Antosh, David Fox, Thomas Hasselbacher, Brown University, Institute for Brain and Neural Systems, Providence, RI Robert Lanou, Brown University, Department of Physics, Providence, RI Nicola Neretti, Leon N Cooper, Brown University, Department of Molecular Biology, Cell Biology and Biochemistry and Institute for Brain and Neural Systems, Providence, RI

How Radiotherapy Was Historically Used to Treat Pneumonia: Could it be Useful Today?

Edward J. Calabrese, Rachna Kapoor, Gaurav Dhawan, School of Public Health and Health Sciences, University of Massachusetts, Amherst, MA

Use of X-rays to Treat Shoulder Tendonitis/Bursitis: A Historical Assessment

Edward J. Calabrese, Gaurav Dhawan, Rachna Kapoor, School of Public Health and Health Sciences, University of Massachusetts, Amherst, MA

Model Uncertainty in Cancer Risk Assessment

Edward J. Calabrese, University of Massachusetts, School of Public Health and Health Sciences, University of Massachusetts, Amherst, MA Dima Yazji Shamoun, Mercatus Center at George Mason University, Austin, TX

Risk Assessment Report Card

Edward J. Calabrese, University of Massachusetts, School of Public Health and Health Sciences, University of Massachusetts, Amherst, MA Dima Yazji Shamoun, Mercatus Center at George Mason University, Austin, TX

Low-dose Radiation Prevents Diabetic Complications

Jie Cheng, The First Hospital of Jilin University, Changchun 130021, China Lu Cai, Kosair Children's Hospital Research Institute, the Departments of Pediatrics, Radiation Oncology and Pharmacology and Toxicology, University of Louisville, Louisville, KY

Protection of Hearts Against Ischemic Insult: Changes in Iron Homeostasis Explain Myocardial Response to Preconditioning

Mottie (Mordechai) Chevion, The Dr. W. Ganz Chair of Heart Studies, The Hebrew University of Jerusalem Faculty of Medicine, Israel Vladimir Vinokur, Baruch Bulvik, Eduard Berenshtein, Department of Biochemistry and Molecular Biology, The Hebrew University of Jerusalem Faculty of Medicine, Israel

Correcting Deficiencies in Our Societal Infrastructure for the Application of Science in Medicine

Ron Eliashar, Head and Neck Surgery, Hadassah University Hospital, Israel

Mohan Doss, Fox Chase Cancer Center, Philadelphia, PA

Investigation of the Cellular and Molecular Mechanisms of Radiation-induced Bystander Effects in a Human Keratinocyte Cell Line

Hayley Furlong, Dublin Institute of Technology, Centre for Radiation and Environmental Science, Focas Research Institute, Dublin Institute of Technology, Dublin, Ireland

Richard Smith, Department of Biology, McMaster University, Hamilton, ON, Canada

Jiaxi Wang, Queen's Mass Spectrometry and Proteomics Unit, Department of Chemistry, Queen's University, Kingston, ON, Canada Colin Seymour, Carmel Mothersill, Department of Medical Physics and Applied Radiation Sciences, McMaster University, Hamilton, ON, Canada Orla Howe, Dublin Institute of Technology, Centre for Radiation and Environmental Science, Focas Research Institute, Dublin Institute of Technology, Dublin, Ireland

Astrocyte Preconditioning by Severe Stress is Glutathione- but not Heat Shock Protein 70-Dependent

Amanda M. Gleixner, Elena Serpico, Deepti B. Pant, Jessica M. Posimo, Rehana K. Leak, *Duquesne University, Graduate School of Pharmaceutical Sciences, Mylan School of Pharmacy, Pittsburgh, PA*

Low Level Radiation and Heart Disease Death Rates in Four States: An Ecological Study

John Hart, Sherman College of Chiropractic, Department of Research, Spartanburg, SC

Inter-Relationships between Low Dose Hypersensitivity, Induced Radioresistance and Bystander Effects in Human Cell Lines

Cristian Fernandez-Palomo, Colin Seymour, Carmel Mothersill, Department of Medical Physics and Applied Radiation Sciences, McMaster University, Hamilton, ON, Canada

Comparative Acute Toxicity of Silver Nanoparticles Produced by Physical (Top-Down) and Chemical (Bottom-Up) Methods in Zebrafish (Danio rerio)

Seyed Ali Johari, Aquaculture Department, Natural Resources Faculty, University of Kurdistan, Sanandaj, Kurdistan, Iran

Ultraviolet-A Photoemission from Cells upon β-irradiation and Consequent Bystander Effects

Michelle Le, Fiona McNeill, Colin Seymour, McMaster University, Medical Physics and Applied Radiation Sciences, Hamilton, ON, Canada Andrew J. Rainbow, McMaster University, Department of Biology, Hamilton, ON, Canada

Carmel Mothersill, McMaster University, Medical Physics and Applied Radiation Sciences, Hamilton, ON, Canada

Physiological Conditioning Hormesis Improves Post-Irradiation Performance in Young and Aging Fruit Flies

Giancarlo Lopez-Martinez, Department of Biology, New Mexico State University, Las Cruces, NM

Daniel A. Hahn, Department of Entomology/Nematology, University of Florida, Gainesville, FL

Communication of Protective Signals from Fish Sub-Lethally Challenged with *Vibrio anguillarum* VIB1 to Naïve Fish

Carmel Mothersill, McMaster University, Department of Medical Physics and Applied Radiation Sciences, Hamilton, ON, Canada Dawn Austin, Institute of Aquaculture, School of Natural Sciences, University of Stirling, Scotland, UK

Colin Seymour, McMaster University, Department of Medical Physics and Applied Radiation Sciences, Hamilton, ON, Canada Niall Auchinachie, Institute of Aquaculture, School of Natural Sciences, University of Stirling, Scotland, UK

Cris Fernandez Palomo, McMaster University, Department of Medical Physics and Applied Radiation Sciences, Hamilton, ON, Canada Brian Austin, Institute of Aquaculture, School of Natural Sciences, University of Stirling, Scotland, UK

Pre-Operative Stress Conditioning: Role for Hyperbaric Oxygen Therapy

George A. Perdrizet, Kent Hospital Wound and Hyperbaric Medicine Center, Warwick, RI, and the Univ. of Connecticut, Storrs, CT

Assessing Predictive Factors and Radiation-Induced Non-Targeted Effects in Blood Serum from Cancer Patients

Christine Pinho, McMaster University, Hamilton, ON Emilia Timotin, Juravinski Cancer Centre, Medical Physics & Applied

Radiation Science, Hamilton, ON

Ranjan K. Sur, Raimond Wong, *Juravinski Cancer Centre, Department of Oncology, Hamilton, ON*

Joseph E. Hayward, Thomas J. Farrell, *Juravinski Cancer Centre, Medical Physics & Applied Radiation Science Hamilton, ON*Colin Seymour, Carmel Mothersill, *McMaster University, Medical Physics & Applied Radiation Science Hamilton, ON*

The Effects of Chronic Exposure to Low Levels of Alpha-Emitting Radionuclides on the Health and Reproductive Fitness of Mammals

Meloja Satkunam, McMaster University, Department of Medical Physics and Applied Radiation Sciences, Hamilton, ON, Canada Marilyne Stuart, Atomic Energy of Canada Limited, Chalk River, ON, Canada Ben Su, Colin Seymour, Carmel Mothersill, McMaster University, Department of Medical Physics and Applied Radiation Sciences, Hamilton, ON, Canada

CONFERENCE ADVISORY COMMITTEE

Jeff Gidday, Washington University in St Louis James Giordano, Georgetown University Walter Kozumbo, AFOSR (retired) Mark P. Mattson, National Institute on Aging Kenneth I Maynard, Sanofi-Aventis US Inc James R. Mitchell, Harvard School of Public Health James P. Watson, Plastic Surgery Heng Zhao, Stanford University School of Medicine

2014 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 contribution to the field of Dose-Response.

This year's awards go to: **Mark P Mattson** for Outstanding Career Achievement; **Rehana K. Leak** for Outstanding New Investigator; and **Mohan Doss** for Outstanding Leadership. Congratulations to all.

AWARDEE PROFILE: CAREER ACHIEVEMENT



MARK P MATTSON

Chief, Laboratory of Neurosciences, National Institute on Aging

After receiving his PhD degree from the University of Iowa, Dr. Mattson completed a postdoctoral fellowship in Developmental Neuroscience at Colorado State University. He then joined the Sanders-Brown Center on Aging at the University of Kentucky College of Medicine where he advanced to Full Professor. In 2000, Dr. Mattson took the position of Chief of the Laboratory of Neurosciences at the National Institute on Aging in Baltimore. He is also a Professor in the Department of Neuroscience at Johns Hopkins University School of Medicine where he is the director of a course on the Neurobiology of Aging. Dr. Mattson leads a multi-faceted research team that applies cutting-edge technologies

in research aimed at understanding molecular and cellular mechanisms of brain aging and the pathogenesis of Alzheimer's, Parkinson's and Huntington's diseases, and stroke. His work has elucidated how the brain responds adaptively to challenges such as fasting and exercise, and he has used that information to develop novel interventions to promote optimal brain function throughout life. He has published more than 500 original research articles and numerous review articles, and has edited 10 books in the areas of signal transduction, cellular stress responses, neurodegenerative disorders and mechanisms of aging. Dr. Mattson has been the most highly cited neuroscientist in the world during the past 20 years with an 'h' index of over 160. He has received many awards including the Metropolitan Life Foundation Medical Research Award, the Alzheimer's Association Zenith Award, the Santiago Grisolia Chair Prize and the Tovi Comet-Walerstein Science Award. He was elected an AAAS Fellow in 2011. He is Editor-in-Chief of Ageing Research Reviews and NeuroMolecular Medicine and has been/is a Managing or Associate Editor of Nature Communications, the Journal of Neuroscience, Trends in Neurosciences, the Journal of Neurochemistry and the Neurobiology of Aging. For more information visit: http://www.irp.nia.nih.gov/branches/lns/mcnu.htm.

2014 INTERNATIONAL DOSE-RESPONSE SOCIETY AWARDS

AWARDEE PROFILE: NEW INVESTIGATOR



REHANA LEAK

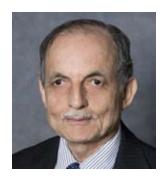
Rehana Leak is an Assistant Professor of Pharmacology at Duquesne University and studies stress-induced adaptations or toxicity in models of neurodegeneration. Dr. Leak was trained in Neuroscience at Barnard College (B.A., graduated magna cum laude with Phi Beta Kappa induction) and the University of Pittsburgh (M.S., Ph.D., National Science Foundation graduate scholarship). Following a brief post-doctoral fellowship with an NIH trainee award, she took a career hiatus to take care of her young children while her husband was on active military duty. After returning to science with an NIH career reentry award, Dr. Leak focused on adaptive defenses in models of Parkinson's disease and then opened her own lab in 2010. The Leak lab is currently examining the impact

of sublethal and lethal protein-misfolding stress as a function of brain region and cell type, because neurons and astrocytes from different brain regions are differentially vulnerable to protein inclusions in neurodegenerative disorders.

Dr. Leak has published 41 original research papers, 9 review articles, 5 book chapters, and 3 editorials. Her work has been cited 1593 times. Dr. Leak is currently funded by the Michael J. Fox foundation and the Pennsylvania Department of Health. In the past, she has received funding from the American Parkinson's Disease Association. Dr. Leak was voted Professor of the Year by the Duquesne pharmacy class of 2015 and received the Faculty Award from the university in 2013. She is a member of the Society for Neuroscience and the International Dose-Response Society.

A summary presentation of Dr. Leak's work on adaptive responses in astrocytes can be found at the link below. As described in the video, the Leak lab discovered that severe stress can elicit protection against a second challenge in the survivors of the original insult. These findings challenge the traditional view that severe stress only weakens defenses and broaden the range of stressor doses that are able to elicit adaptive

AWARDEE PROFILE: LEADERSHIP



DR. MOHAN DOSS

Dr. Mohan Doss received B.Sc. degree in Physics from Madras University, India and his M.Sc. degree in Physics from Indian Institute of Technology, Kanpur, India. He obtained M.S. and Ph.D. degrees in Physics from Carnegie-Mellon University. After 10 years of post-doctoral research in USA and Canada, he became a Medical Physicist in the Nuclear Medicine Department of Regina General Hospital in Regina, Canada. In 2001, he joined Diagnostic Imaging Department of Fox Chase Cancer Center in Philadelphia where he is presently an Associate Professor. Dr. Doss has board certification from the Canadian College of Physicists in Medicine.

Dr. Doss began a detailed study of the health effects of low dose radiation (LDR) to investigate the claims of increased cancer risk from diagnostic imaging based on the linear no-threshold (LNT) model. He noted that although considerable amount of evidence exists for the disease preventive effect of LDR, the atomic bomb survivor data had been used to raise LDR carcinogenic concerns in many publications. Dr. Doss's analysis of the latest update to the atomic bomb survivor data showed that these data no longer support the LNT model but are consistent with a threshold or hormesis model. The LNT model however continues to be used for radiation safety worldwide.

There is increasing realization in the scientific community of the tremendous harm from the use of the LNT model, e.g. casualties due to prolonged evacuations in Fukushima, missed diagnoses in patients due to LDR concerns, and barriers to study of LDR for disease prevention in spite of considerable evidence in pre-clinical studies. Dr. Doss is pleased to be a member of a group called Scientists for Accurate Radiation Information (SARI) that has been formed recently to attempt to reduce such harm by dispelling misinformation and encouraging a change in the radiation safety paradigm.

ANNOUNCEMENT

The 14th International Conference on

Adaptive Responses/Preconditioning The Annual Meeting of the International Dose-Response Society

APRIL 21-22, 2015

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:

PRE- POST-CONDITIONING

Alzheimer's Disease/Dementia Parkinson's Disease Depression and PTSD Concussions/Traumatic Brain Injury Improving Surgical Outcomes Stroke/Cardiovascular Disease Diabetes Glaucoma Stem Cell Transplantation Therapy

HEALTHY LIFESTYLES, AGING AND LIFE EXTENSION

Intermittent Fasting
Exercise
Chemical/Nutritional Supplements
Low Dose Radiation and Longevity
Adaptive response-based cosmetics

ENHANCING HUMAN PERFORMANCE

Cognition
Endurance, Strength and Speed
Fatigue/Jet Lag: Prolong Onset/
Speed Up Recovery
Wound Healing Acceleration - skin,
tendon, muscle, bone, and vascular

ENHANCING HEALTHY LIVING AND PERFORMANCE

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

www.dose-response.org

For further Information contact:

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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 11, 2014

E-mail to dleonard@schoolph.umass.edu

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.

International Dose-Response Society

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. Members will receive a 25% reduction in registration fees to Dose-Response 2014: Implications for Toxicology, Medicine, and Risk Assessment, the Annual Meeting of the International Dose-Response Society.

INTERNATIONAL DOSE-RESPONSE SOCIETY

2014 Membership Form for New and Renewing Members

Please choose one membership car	tegory (Payment in US Funds):	
Individual Membership–1 year Individual Membership–2 years Retiree Membership–1 year Retiree Membership–2 years Post-Graduate Membership–1 year Post-Graduate Membership–2 years Student Membership–1 year Student Membership–2 years Sustaining Member Corporate Membership Additional Donation	□ \$125–1 year □ \$225–2 years □ \$75–1 year □ \$125–2 years □ \$75–1 year (up to three years p □ \$125–2 years (up to three years p □ \$10–1 year □ \$15–2 years □ \$1000/year □ \$5000/year □ \$25 □ \$50 □ \$10	post-graduation)
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Completed application form along Dose-Response/BELLE Offices Environmental Health Sciences Program Morrill 1, Room N344, University of M Amherst, MA 01003 Telephone: 413-545-3164 Email: So	, School of Public Health assachusetts	u US dollars should be mailed to
Signature of Applicant		Date