The 11th Biennial Meeting of the International Neurotoxicology Association

Neuroprotection and Promotion of Repair Following Neurotoxic Injury

June 10-15, 2007
Pacific Grove, California U.S.A.
Asilomar Conference Center

The 11th Biennial Meeting of the International Neurotoxicology Association (INA-11) will convene June 10-15, 2007 at the Asilomar Conference Center In Pacific Grove, California. The theme of INA-11 will emphasize mechanisms that confer neuroprotection and promote repair subsequent to injury of the nervous system. Although basic science in nature, the conference relates basic research in the neurosciences and toxicology to major issues confronting our understanding of neurodevelopmental disorders, neurodegeneration, and the impact of environmental exposures on human disease processes.

Traditionally an internationally recognized scientist who serves to integrate a major issue confronting human nervous system health launches the meeting with a keynote presentation. This year we are fortunate to have Dr. Fred Gage presenting the Keynote Lecture entitled, Promoting Recovery from Central Nervous System Injury in the Adult Organism. The overarching objectives of INA meetings are to 1) highlight the latest findings in neurotoxicology, 2) promote the development of the field by hosting symposia speakers from multiple subdisciplines, 3) provide a collegial setting for developing working relationships among scientists from different countries, and 4) recruit and energize young investigators to pursue careers in neurotoxicology. The INA meeting contributes an important venue for international scientific discourse on advances in the broad field of neurotoxicological research and has made this community unusually collaborative, cohesive, and truly international in scope. The INA11 meeting is being considered as a setting for satellite meetings by the Behavioral Toxicology Society and the Global Health Security Advisory Group (chemical group). INA and neurotoxicology in general also contributes to the discipline of neuroscience by developing new models for understanding how the nervous system is influenced by external stressors.

INA-11 has three major themes (1) how to enhance repair/regeneration in the nervous system (2) development of new neurotoxicity screening approaches in mammalian and non-mammalian models and (3) characterizing new neurotoxicological concerns.

Included below are the meeting agenda and an initial list of our proposed session chairs and established speakers that we plan to invite early.
I. The Hoissma Lecture (Sun, June 10): Fred H. Gage, University of California, San Diego, USA
Promoting Recovery from Central Nervous System Injury in the Adult Organism

Dr. Fred Gage, Ph.D. Vi and John Adler Chair for Research on Age-Related Neurodegenerative Diseases, The Salk Institute for Biological Sciences, San Diego, CA

Fred H. Gage, a professor in the Laboratory of Genetics, concentrates on the adult central nervous system and unexpected plasticity and adaptability to environmental stimulation that remains throughout the life of all mammals. His work may lead to methods of replacing or enhancing brain and spinal cord tissues lost or damaged due to Neurodegenerative disease or trauma.

Gage’s lab showed that, contrary to accepted dogma, human beings are capable of growing new nerve cells throughout life. Small populations of immature nerve cells are found in the adult mammalian brain, a process called Neurogenesis. Gage is working to understand how these cells can be induced to become mature functioning nerve cells in the adult brain and spinal cord. They showed that environmental enrichment and physical exercise can enhance the growth of new brain cells and they are studying the underlying cellular and molecular mechanisms, that may be harnessed to repair the aged and damaged brain and spinal cord.

Dr. Gage is a Fellow of the National Academy of Sciences, The Institute of Medicine, and the American Academy of Arts and Sciences.

II. THEME: HOW TO ENHANCE REPAIR/REGENERATION IN THE NERVOUS SYSTEM

IIa. Symposium 1 (Mon, a.m., June 11): The role of Metallothioneins in Neuroprotection

Co-chairs: Michael Aschner – Vanderbilt University School of Medicine, USA
Adrian K. West – University of Tasmania School of Medicine, AU

Metallothioneins (MTs) form a major protective system in the brain. Because of their high abundance of the thiol containing amino acid cysteine, MTs confer protection against both endogenous and exogenous toxicants. Disordered MT homeostasis has been associated with neurological disorders such as Parkinson’s disease (PD) Alzheimer disease (AD), amyotrophic lateral sclerosis (ALS) and stroke. Recently exogenous MT has been shown to ameliorate symptoms in a number of disease and injury models. Many unanswered questions remain about how and where MTs act in the brain. MT isoforms are differentially expressed in astrocytes and neurons of the hippocampus. Although deletion of any of any of the three known isoforms using gene targeting is largely asymptomatic in untreated animals, it enhances vulnerability to chemical or physical CNS injury. Exciting new results indicate that MTs have wider relevance in how glia and neurons interact in the face of injurious stimuli. The goal of this symposium is to discuss recent advances in our understanding of molecular mechanisms governing MT synthesis and distribution in the brain. The speakers will describe a broad spectrum of model systems ranging from the worm C. elegans to the rodent brain. Participation in this symposium will enable the audience to become acquainted with the latest information and scientific breakthroughs in this fast-paced research area and provide information that will also be germane to molecular mechanisms, risk assessment, and the role of MT in neuroprotection.

Presentation 1: Michael Aschner, Vanderbilt University School of Medicine, USA
Distribution, Classifications, and Biological Roles of Metallothioneins.

Presentation 2: Ed Levin, Duke University, USA
The role of metallothionein in susceptibility to cognitive impairment caused by developmental mercury exposure.

Presentation 3: Juan Hidalgo, Autonomous University of Barcelona, Spain
Brain Metallothioneins and Inflammation: Lessons Learned from MT Knockout Mice?

Presentation 4: Adrian West, School of Medicine, University of Tasmania, Australia

Protective Role of Metallothioneins in the Injured Mammalian Brain.

Presentation 5: To be determined

Poster Presentations: Two brief summaries to be chosen by session co-chairs

IIb. Symposium 2 (Tues, a.m., June 12): Neuroprotective Agents and Strategies for Replacing Damaged Cells in the Adult Nervous System

Co-chairs: Laurence Fechter – Loma Linda VA Medical Center USA

David Ray – MRC Applied Neuroscience Group University of Nottingham, UK

The identification of common pathways to neurotoxicity has made possible the identification of potential therapeutic strategies for promoting repair in the central nervous system or of limiting initial injury. The application of such strategies in toxicology has lagged behind that of CNS disease and traumatic damage. The presentations included in this symposium will identify several such approaches and demonstrate their efficacy in treating nervous system injury. The objective is to encourage toxicologists to begin to focus on gathering data essential to determining the efficacy of therapeutics in treating accidental neurotoxicant exposure.

Presentation 1: David Wright, Emory University School of Medicine, USA

Modulating Neurotoxicity with Neurosteroids

Presentation 2: Robert Floyd, Oklahoma Medical Research Foundation, USA


Presentation 3: Elias Aizenman, University of Pittsburgh, USA

Potassium Channels as Targets for Neuroprotection

Presentation 4: Yohash Raphael, Univ of Michigan Medical Center, USA

Strategies for Replacing Damaged Hair Cells in the Inner Ear

Poster Presentations: Two brief summaries to be chosen by session co-chairs

III. THEME: ADVANCES IN SCREENING FOR NEUROTOXICITY

Illa. Symposium 3 (Tues, p.m., June 12): Application of In vitro Neurotoxicity Testing for Regulatory Purposes

Chair: Anna Price – Institute for Health and Consumer Protection, Italy

In October 2003, the European Commission published its proposal for the regulation concerning registration, evaluation and authorisation of chemicals (REACH). This proposal addresses the lack of publicly available data on 30,000 of existing chemicals. The additional pressure comes from the 7th amendment to the Cosmetic Legislation as a complete ban on animal testing for cosmetic ingredients and the finished products will enter into force of the directive, from 2009. In view of current testing requirements for human health, neurotoxic effects are being identified during the evaluation of acute systemic toxicity, repeated-dose toxicity, subchronic, chronic and reproductive/developmental toxicity. Presently, no in vitro methods for evaluating the neurotoxic hazard of a chemical have been validated and the current OECD and EC guidelines for the assessment of neurotoxic effects of chemicals are based on in vivo studies that are both expensive and time consuming. Implementation of alternative in vitro tests in screening strategies to assess neurotoxic effects of compounds would accelerate the rate at which compound knowledge and mechanistic data are produced.

Presentation 1: Anna Price, EU-ECVAM, Ispra, Italy
ECVAM Strategy for In Vitro Neurotoxicity Testing in the Context of the new Political Challenges

Presentation 2: Dieter Weiss, University of Rostock, Rostock, Germany
Neuronal Networks In Vitro As High Content Neurotoxicity Screening Platform

Presentation 3: Cristina Sunol, Institut d’Investigacions Biomediques, CSIC, Barcelona, Spain
Ligand-Gated Ion Channel Toxicity

Presentation 4: Lucio Costa, University of Washington, Seattle, USA
Organophosphates; Acute and Long-Term Neurotoxicity

Poster Presentations: Two brief summaries to be chosen by session co-chairs

IIIb. Symposium 4 (Thurs, a.m. June 14): Use of Non-Mammals for Neurotoxicological Study

Chair: Toshsio Narahashi – Northwestern University Medical School, Chicago, USA

There was a time when non-mammals were thought to be far from ideal materials for the study of biomedical science because they are phylogenically too distant from humans. However, it has now become abundantly clear that some of the non-mammals are not only convenient materials but also are endowed with physiological and pharmacological properties common to humans. Thus, several such species have become very popular materials and are being used extensively as models. Here we would like to present a few such examples: Drosophila, Caenorhabditis elegans, cockroach, and zebrafish. Each of them is now being used not only for genetics, biochemistry, physiology and pharmacology of the nervous system but also for neurotoxicology.

Presentation 1: Randall Peterson, MGH, Harvard Medical School, Cambridge, USA
High-throughput Assessment of Small Molecule Bioactivity in the Zebrafish

Presentation 2: Richard Nass, Vanderbilt University, Nashville, USA
Toxicogeneic Analysis in a Novel C. elegans Model of Parkinson’s Disease and Manganism

Presentation 3: Jonathan Freedman, Duke University, Durham USA
Toxicologic Studies of Environmental Agents Using C. elegans

Presentation 4: Ke Dong, Michigan State University, E. Lansing, USA
Molecular Action of Pyrethroid Insecticides on the Insect Sodium Channel

Presentation 5: Toshsio Narahashi, Northwestern University, Chicago, USA
Glutamate-Activated Chloride Channels: Unique Chemical Target Present in Insects but not in Mammals

Poster Presentations: Two brief summaries to be chosen by session co-chairs

IIIc. Symposium 5 (Thurs, p.m., June 14): Neurobehavioral Testing in Human Risk Assessment

Co-Chairs: Diane Rohlman – Oregon Health Sciences University, Portland, USA
Christoph van Thriel – Institut fur Arbeitsphysiologie, Dortmund, Germany

Why is it of central interest? Neurobehavioral testing are being increasingly used in human risk assessment and there is a strong need for guidance. Are there new developments in this field that warrant a symposium at this time? Advances are available re the assessment of behavioral and sensory changes and the statistical treatment of neurobehavioral data. Is there a new synthesis of existing data to present? A synthesis of existing data will be provided during this Symposium, which is proposed by members of the ICOH Scientific Committee on Neurotoxicology and Psychophysics to continue and strengthen the collaboration with INA.

Presentation 1: Diane Rohlman, Oregon Health Sciences University, Portland, USA
Assessment of Neurobehavioral Affects in Vulnerable Populations: The Example of Pesticide Exposure in Children

Presentation 2: David Bellinger, Harvard School of Public Health, Boston, USA
Interpretation of Small Effect Sizes in Neurotoxicological Studies: Characterizing Individual versus Population Risk.

Presentation 3: Christoph van Thriel, Institut fur Arbeitsphysiologie, Dortmund, Germany
Neurobehavioral and Chemosensory Effects of Local Irritants

Presentation 4: Roberto Lucchini, University of Brecia, Brecia, Italy
Assessment of Neurobehavioral Effects from Lifetime Exposure to Cumulative Neurotoxicants: The Example of Manganese

Poster Presentations: Two brief summaries to be chosen by session co-chairs

IV. THEME: CHARACTERIZING NEW NEUROTOXICOLOGICAL CONCERNS

IVa. Symposium 6 (Thurs, p.m., June 14): Immunologic and Neurodevelopmental Susceptibilities of Autism

Co-Chairs: Isaac Pessah – University of California, Davis CA, USA
Benjamin Yee – Swiss Federal Institute of Technology Zurich, Switzerland

Inherited immune-system dysfunctions may represent one of the etiological cores of autism. Identifying common patterns of immunological dysfunction common to autism, or patterns specific to subphenotypes using transcriptional profiling and immune phenotyping in the context of epidemiological studies of autism is providing a powerful approach that is likely to identify early biomarkers of risk, yield a better understanding of environmental risk factors, and identify rational intervention strategies to mitigate these risks. The immune system of autistic children may therefore be especially susceptible to psychological stressors, exposure to chemical triggers, and infectious agents. Considering our emerging knowledge of how the immune system contributes to normal and pathological neurodevelopment, environmental triggers are likely to synergize existing genetic defects to adversely influence neurodevelopmental processes that contribute to the onset and severity of autism. The goal of this symposium is to (1) present new evidence that autistic children have a unique pattern of immune system markers that significantly differ from typically developing children and children diagnosed with mental retardation or developmental delays (MR/DD); (2) provide an update on transcriptional, genetic, epigenetic and xenobiotic markers associated with autism susceptibility, (3) provide an update on how animal models have contributed to our knowledge of autism susceptibility.

Presentation 1: Pamela Lein, Oregon Health and Science University, Portland, OR, USA
Polychlorinated Biphenyls (PCBs) Modulate the Development of Neuronal Connectivity

Presentation 2: Benjamin Yee, Swiss Federal Institute of Technology Zurich, Switzerland
Prenatal Immune Challenge Determines the Specificity of Inflammation-Mediated Brain and Behavioral Pathology.

Presentation 3: Janine LaSalle, University of California School of Medicine, Davis USA
Epigenetic influences on Autism Risk: A Role of GABA Receptor Dysregulation

Presentation 4: Isaac Pessah, University of California, Davis CA, USA
How Can Chemical Exposure Contribute to Autism Risk?

Poster Presentations: Two brief summaries to be chosen by session co-chairs

IVb. Symposium 7 (Fri, a.m., Jun 15): Air Pollution, Oxidative Stress, and Neurodegeneration

Co-chairs: Bellina Veronesi – U.S. EPA, Research Triangle Park, USA
Michelle Block – NIEHS, Research Triangle Park, USA

Neurodegenerative diseases are increasing within the population and epidemiological data suggest that environmental chemical exposures, combined with predisposing factors (e.g., genetics, diseased states, occupational, etc.) may play a role in these increases. This symposium
will present evidence that links oxidative stress, a type of air pollution known as particulate matter (PM) and neurodegeneration. PM is firmly associated with inflammatory driven morbidity (e.g., asthma) in the young and mortality in the elderly. PM particles contain numerous biological (e.g., bacterial) and chemical contaminants on their surface and convey free radical activity to target cells and tissues in the airways. Recent studies indicate that inhaled PM particles quickly exit the lungs, enter the systemic circulation and distribute to numerous organ systems, including the brain which is highly vulnerable to oxidative stress damage. A series of clinical and experimental reports will be presented that identify the brain as vulnerable to PM damage and implicates oxidative stress as a predisposing factor to neurotoxic susceptibility.

**Presentation 1:** Sheba Mohankumar, Michigan State University, E. Lansing, USA  
*Exposure to Concentrated Ambient Particles Increases Stress Axis Activity*

**Presentation 2:** Arezoo Campbell, University of California, Irvine, USA  
*Neurochemical Evidence of Oxidative Stress in Mouse Brain in Response to Urban Air Pollution*

**Presentation 3:** Michelle Block, NIEHS\NIH, Research Triangle Park, USA  
*Diesel Exhaust Particles Cause Microglia-Mediated Neurodegeneration in Mixed CNS Cultures*

**Presentation 4:** Bellina Veronesi, U.S. EPA, Research Triangle Park, USA  
*Particulate Matter Induces Oxidative Stress and Mediate Neurodegeneration in Transgenic Mice*

**Poster Presentations:** Two brief summaries to be chosen by session co-chairs

### IVc. Symposium 8 (Fri, a.m., June 15): Building a Scientific Framework for Studying Hormonal Effects on Development of Sexually Dimorphic Nervous System and on Adult Behavior

**Co-chairs:** Abby A. Li – Exponent, Oakland, USA  
L. Earl Gray – U.S. EPA, Research Triangle Park, USA

There has been increasing concern that low-dose exposure to hormonally active chemicals disrupts sexual differentiation of the brain and peripheral nervous system. There also has been active drug development research on the therapeutic potential of hormone therapy on behavior. These different research goals have in common the need to develop reliable animal models to study the effect of hormones on brain function and behavior that are relevant to humans. This symposium brings together scientists from diverse backgrounds (developmental toxicology, neurobehavior, psychosexual behavior) to discuss challenges and approaches to studying hormonal effects on sexual differentiation of the brain and behavior. This symposium will provide an overview of sexually dimorphic behavior including (a) research on the role of androgens and estrogens in the development of the brain and peripheral nervous system, (b) approaches to differentiate activational and organization effects on sexually dimorphic behavior and (c) research on differences and similarities between human and rodent sexual differentiation of the brain. Presentations will focus on building a rational scientific framework(s) to study the effects of hormones, environmental chemicals, nutriceuticals, and pharmaceuticals on the development of sexually dimorphic nervous system and behavior. Speakers will present approaches to validating animal models to study effects of environmental estrogens and androgens on sexual differentiation of the central and peripheral nervous system. Future research needs that integrate approaches used by scientists from reproduction/developmental backgrounds and neurobehavioral backgrounds will be discussed.

**Presentation 1:** L. Earl Gray, U.S. EPA, Research Triangle Park, USA  
*The Role of Androgens and Estrogens in the Development of Brain and Peripheral Nervous System: Approaches to Developing Animal Models for Sexually Dimorphic Behaviors*

**Presentation 2:** Abby Li, Exponent, Oakland, USA  
*Developing Animal Models: Lessons learned from a case study on bisphenol A*
Presentation 3: Mark Day, Wyeth Pharmaceuticals, Madison USA  
*From molecular mechanism to functional effects: Estrogen Receptor Beta Agonists Increase Hippocampal Neuronal Architecture and Improve Memory and Synaptic Plasticity*

Presentation 4: Michael Baum, Boston University, Boston, USA  
*Mammalian Animal Models of Psychosexual Differentiation: When is “Translation” to the Human Situation Possible.*

Poster Presentations: Two brief summaries to be chosen by session co-chairs

V. Student Symposium (Monday, p.m., June 11)

The Student Symposium consists of presentations by senior graduate students and individuals who have recently received their doctoral degrees. Participants are selected based upon submission of an outstanding extended abstract and recommendation letters submitted by individuals familiar with their research achievements. Individuals selected to participate in this program receive a stipend to cover travel, room and board, and registration at INA-11.

![Figure 1: Organization of the 11th International Neurotoxicology Conference (INA-11) to be held at Asilomar Conference Center, Pacific Grove, California, June 10-15.](image)