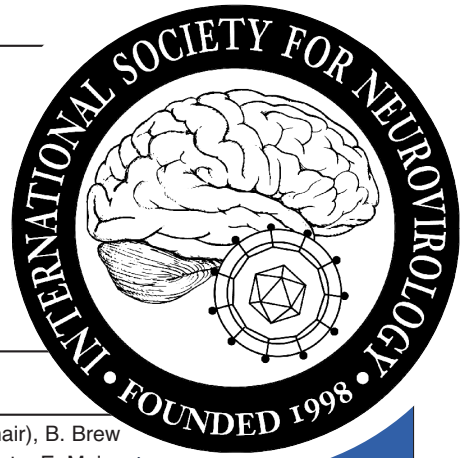


ISNV



International Society for NeuroVirology

Vol. 7(2)
October 2007

ISNV Publications Subcommittee: K. Khalili (Chair), B. Brew
J. Clements, P. Ferrante, E. Major

WELCOME TO SAN DIEGO

THE 8TH INTERNATIONAL SYMPOSIUM ON NEUROVIROLOGY

Peter Kennedy, M.D., Ph.D. • Glasgow, Scotland, UK
Igor Grant, M.D. • San Diego, CA
Brian Wigdahl, Ph.D. • Philadelphia, PA
Kamel Khalili, Ph.D. • Philadelphia, PA

On behalf of the international organizing committee, Chaired by Igor Grant, the President of the International Society for NeuroVirology, Peter Kennedy, the Chair of the ISNV Meetings Committee, Brian Wigdahl, and Chair of the Fundraising Committee, Kamel Khalili, we would like to welcome you to the 8th International Symposium on NeuroVirology! This year, the Symposium takes place in San Diego, a major metropolitan area in Southern California, and home to a large number of investigators working in the area of neurovirology and related disciplines at the University of California at San Diego and the Scripps Research Institute. The 8th Symposium represents the second time that the Symposium has been held on the west coast following a highly successful 3rd Symposium held in San Francisco in 2000 and organized by Lynn Pulliam. Under the organizational and scientific skills of Igor Grant and the International Organizing Committee, the 8th Symposium promises to be another exciting scientific interchange.

The primary goal of the 8th Symposium will be to examine the molecular mechanisms associated with viral-induced neurologic disease in humans and animal models to enhance understanding of common pathogenic themes and to facilitate the diagnosis, prevention, and treatment of neurologic disease. The central theme of the 8th Symposium will be to examine molecular mechanisms involved in degenerative

(continued on page 4)



8th International Symposium on NeuroVirology Major Sponsors

National Institute of Mental Health
National Institute of Neurological
Disorders & Stroke
National Institute of Drug Abuse
National Institutes of Health

Department of Microbiology & Immunology,
Institute for Molecular Medicine
& Infectious Disease
Drexel University College of Medicine

Office of the Vice President for Research,
Department of Neuroscience
Temple University School of Medicine

Sbarro Institute for Cancer Research
& Molecular Medicine

BIODEN IDEC

Journal of NeuroVirology

BOARD OF DIRECTORS

ADRIANO AGUZZI, SWITZERLAND
WALTER ATWOOD, USA
JOSEPH BERGER, USA
RUTH BRACK-WERNER, GERMANY
BRUCE BREW, AUSTRALIA
JANICE CLEMENTS, USA
ANTONINA DOLEI, ITALY
PASQUALE FERRANTE, ITALY
ROBERT FUJINAMI, USA
SUZANNE GARTNER, USA
JENNIFER GORDON, USA
ALAN C. JACKSON, CANADA
STEVEN JACOBSON, USA
PETER KENNEDY, UK
KAMEL KHALILI, USA
KRISTER KRISTENSSON, SWEDEN
MONIQUE LAFON, FRANCE
EHUD LAVI, USA
EUGENE O. MAJOR, USA
MITSUHIRO OSAME, JAPAN
LYNN PULLIAM, USA
WALTER ROYAL, III, USA
ISRAEL STEINER, ISRAEL
DAVID VOLSKY, USA
THOMAS WEBER, GERMANY
BRIAN WIGDAHL, USA

IN THIS ISSUE

- *Welcome to San Diego*
The 8th International Symposium on NeuroVirology
- *ISNV Highlight - Dr. Shilpa Buch*
- *ISNV Highlight - Dr. Françoise Gray*
- *ISNV Highlight - Dr. Kelly Jordan-Sciutto*
- *Friends of ISNV Highlight - Dr. Antonio Giordano and the SHRO*

ISNV Highlight - Shilpa Buch, Ph.D.

Dianne Langford, Ph.D. • Philadelphia, PA



As Associate Professor in the Department of Molecular & Integrative Physiology at Kansas University Medical Center, Dr. Buch's exemplary research record reflects diverse areas of expertise such as hyperoxic lung injury, virology, immunology, animal models of human disease and gene therapy. Shilpa graduated from MS University in Baroda, India in 1982, completed three years of post-doctoral training at Memorial University in Newfoundland, Canada followed by five years as a Research Scientist/ Research Associate at the University of Western Ontario and the Hospital for Sick Children in Toronto. She then joined the faculty of the Hospital for Sick Children in the Division of Lung Biology as Assistant Professor before accepting a position at Kansas University Medical Center. Recent studies in her lab address pathogenic mechanisms of HIV using the rhesus macaque model to investigate Simian Human Immunodeficiency Virus (SHIV). For example, studies from Dr. Buch's laboratory identified the chemokine, CXCL10 as an important factor for the development of SHIV-associated NeuroAIDS and SHIV-associated pneumonia, and described mechanisms involved in CXCL10-related pathogenic processes (Dhillon, et al., J Immunol 2007; Sui, et al., Eur J Neurosci 2006; Sui, et al., Amer J Pathol 2005). Dr. Shilpa suggests that these studies point to the possibility for similar molecular triggers that initiate pathologies in both the brain and lungs during infection. Likewise, in the therapeutics arena, Dr. Buch's laboratory reported the inhibition of SHIV replication by Interleukin-4 antisense DNA (Dhillon et al., Blood 2005).

When asked about plans for future research, Dr. Buch describes the important issues of intravenous drug use and HIV infections as "two global health crises linked by needle sharing." Shilpa hypothesizes that cocaine use will accelerate HIV Encephalitis progression by affecting viral replication and IL-10 production and intends to investigate potential synergy between viral factors and drugs of abuse.

Outside of the laboratory, Dr. Buch is active in the ISNV where she has chaired scientific sessions during the International Symposia. Recently, she was invited to serve on the Journal of Neurovirology Editorial Board and on an NIH study section. As reflected by her participation in the 2006 World AIDS Day in Tianjin, China, Shilpa also contributes significantly to international efforts for AIDS awareness and scientific advancement. Mentoring also plays an important part in Dr. Buch's scientific career as she provides guidance to diverse student populations including clinical and post-doctoral fellows, medical and summer interns for over 15 years.

Friends of ISNV Highlight - Antonio Giordano, MD, PhD and the SHRO

Kamel Khalili, Ph.D. • Philadelphia, PA

An internationally recognized researcher in the genetics of cancer and gene therapy, Antonio Giordano, MD, PhD, is the President and Chairman of the Board of the Sbarro Health Research Organization and Director of the Sbarro Institute for Cancer Research and Molecular Medicine at Temple University's College of Science and Technology. Founded in 1993 by Dr. Giordano, with the generous contributions of Mario Sbarro, owner of Sbarro, Inc., a successful fast food chain, the Sbarro Health Research Organization, Inc. (SHRO) (www.shro.org) is committed to funding excellence in basic genetic research to diagnose and cure cancer, cardiovascular diseases, diabetes and other chronic illnesses and to foster the training of young doctors in a spirit of professionalism and humanism. SHRO funds the Sbarro Institute for Cancer Research and Molecular Medicine located at Temple University in Philadelphia, Pennsylvania and at the University of Siena in Siena, Italy. Ongoing research includes work on the relationship between obesity and cancer and a new program on molecular therapeutics, which explores how molecular genetic research can be applied to the newest drug therapies and diagnostics. Since 1995, the Institute has organized and co-sponsored scientific meetings around the world. In particular, generous donations from Dr. Giordano and the SHRO have contributed to our continued success at ISNV.



Dr. Giordano also serves as the Director of the Scientific Advisory Committee for the Human Health Foundation (HHF), an Italian charity for basic medical research based in Terni, Italy. Dr. Giordano graduated from the University of Naples, Italy with an MD and PhD and held a post-doctoral appointment at Cold Spring Harbor, run by Nobel Prize winner James Watson, who helped to decode DNA. At Cold Spring, Dr. Giordano discovered the protein cyclin A, a substance that regulates growth in the cell cycle. Later, at the Fels Institute for Cancer Research at Temple University, he discovered Rb2/p130, a tumor suppressor gene active in lung, endometrial, brain, breast, liver and ovarian cancers, and Cdk9 and Cdk10, guardians of the human genome (Falco and Giordano Cancer Biol Ther 2002 (review); Giacinti and Giordano, Oncogene 2006 (review); Grana et al, Oncogene 1994). Other important studies aimed at the understanding of potential viral links with brain tumors in which Dr. Giordano has contributed include those showing the presence of human neurotropic JC virus DNA and expression of the viral oncogenic protein in pediatric medulloblastomas (Krynska et al., PNAS 1999 and White et al, Brain Res Reviews 2005). In addition, Dr. Giordano serves on the editorial board of numerous leading professional journals, including Frontiers in Bioscience, Cancer Biology and Therapy, the

(continued on page 4)

ISNV Highlight - Françoise Gray, MD, PhD.

Dianne Langford, Ph.D. • Philadelphia, PA

Having earned an MD in Paris in 1972 with specialties in Anatomic Pathology, Histopathology and Neurology, Dr. Françoise Gray went on to obtain a PhD in Human Biology in Marseille in 1983. She is now Head of the Department of Pathology and “Pole Laboratory, Imaging and Pharmacy” at Assistance Publique-Hôpitaux de Paris, Hôpital Lariboisière - University Paris VII. With a publication record boasting well over 300 research articles, Dr. Gray also has contributed to nearly 100 textbooks and references materials. Among the most successful is Escourolle and Poirier’s Manuel of Basic Neuropathology, 4th Edition that has been heralded on Amazon.com as “perfect for the residents of neurology today”. She has also served as Editor for 6 textbooks.

Although Françoise describes herself as “a general clinical neuropathologist with an interest in nearly all fields of neuropathology”, her main scientific interest has been the neuropathology of AIDS with a special interest in early central nervous system changes in asymptomatic HIV patients (Gray et al., Brain Pathology, 1996). More recently, Dr. Gray has focused on the changing patterns of HIV-associated neuropathology in the era of highly active anti-retroviral therapy and immune reconstitution syndrome as described in several detailed articles (Gray et al., Ann Indian Acad Neurol, 2007; Gray et al., J. Neurovirology, 2005; Gray et al., JNEN, 2003). In a historical review article published in Brain Pathology by Scaravilli et al (2007), Dr. Gray describes thoroughly factors that contribute to the pathophysiology of HIV dementia. Moreover, Françoise addresses the importance (and sometimes overlooked) issue of the time of arrival of HIV into the CNS after infection.

On a more fundamental note, Dr. Gray explains that her interest in neuronal death includes not only neuronal loss in AIDS, but in prion diseases, as well. Moreover, Dr. Gray has recently begun working with the team that originally described cerebral autosomal dominant arteriopathy with subcortical infarcts (CADASIL) at the Hôpital Lariboisière in Paris (Tournier-Lasserre et al., Stroke, 1991). Findings described in their collaborative efforts point to neuronal apoptosis as an important contributor in cortical atrophy and cognitive impairment in patients suffering from CADASIL (Gray et al., JNEN, 2007; Viswanathan et al., Stroke, 2006). Françoise Gray has served as the principal investigator of several grants funded by, among others, the Agence Nationale de Recherches sur le SIDA and Concerted Actions of the European Union. Topics of investigation include HIV neuropathology, neuronal damage in prion disease, fatal family insomnia, human transmissible spongiform encephalopathies and the pathology of septic shock. Dr. Gray teaches extensively in subjects such as neurology, forensic pathology, experimental and human neuropathology (infectious disease) and the molecular pathology of infectious disease.

(continued on page 4)



ISNV Highlight - Kelly Jordan-Sciutto, Ph.D.

Dianne Langford, Ph.D. • Philadelphia, PA

Dr. Kelly Jordan-Sciutto, an Assistant Professor in the Department of Pathology in the School of Dental Medicine at the University of Pennsylvania in Philadelphia is interested in neuronal response to neurodegenerative stimuli such as oxidative damage, misfolded proteins, and inflammation. Her laboratory investigates molecular mechanisms underlying neurodegeneration associated with neuroinflammation during HIV infection. Currently she is focusing her research efforts on the role of cell cycle proteins, the endogenous antioxidant response and unfolded protein response in human immunodeficiency virus (HIV) associated dementia (HAD). She explains, “As inflammation and oxidative stress play prominent roles in progression of non-infectious neurodegenerative diseases such as Alzheimer disease (AD) and Parkinson disease (PD), we often extend our findings in HAD to these diseases in the hopes of uncovering common mechanism and thereby, common therapeutic targets.” For example, she and others have shown that key regulators of cell cycle progression, Retinoblastoma susceptibility gene (pRb), E2F1, p53, and cyclin dependent kinase 5 regulatory subunit p35/p25 exhibit altered levels and patterns of expression in HAD, PD, and AD (Brion and Couck, Am J Pathol, 1995; Nakamura et al., ACTA Neurosci, 1997; Pei et al., Brain Res, 1998; Jordan-Sciutto et al., JNEN, 2002; Jordan-Sciutto et al., J Neurosci., 2002; Jordan-Sciutto et al., JNEN, 2003; Hoglinger et al., PNAS, 2007; Shimizu et al., Neuro Biol Dis, 2007; Wang et al., J NeuroChem, 2007).

Another very interesting line of investigation in her lab involves the endogenous antioxidant response and activation of the transcription factor, Nrf2. Recent studies from Dr. Jordan-Sciutto’s lab have shown that Nrf2 is aberrantly expressed in HAD and AD indicating it is not responding to oxidative stress in neurons of affected brain regions (Ramsey et al., JNEN 2007). Interestingly, Nrf2 does appear to be responding appropriately in neurons affected in PD (Ramsey et al., JNEN, 2007). Kelly adds, “While HAD, AD, and PD exhibit different pathologic features, theories as to their etiology share common molecular mechanisms including changes in the trophic factor environment, oxidative stress, and activation of CNS inflammatory components. We hypothesize that neuronal response to these neurodegenerative stimuli includes alterations in expression and/or activity of cell cycle proteins.” A third and convergence point for these two lines of research is the role of the unfolded protein response (also known as the endoplasmic reticulum stress response or integrated stress response) which activates Nrf2 and represses cell cycle progression, in HAD (Kaufman, Genes and Dev., 1999, and JCI, 2002; Kaufman et al., Nature Rev., 2002; Cullinan et al., MCB, 2003; Cullinan and Diehl, JBC, 2004).

(continued on page 4)



WELCOME TO SAN DIEGO (continued)

and inflammatory disease in the nervous system during the course of neurotropic virus infection and to enhance this knowledge acquisition by interfacing with experimental pathways ongoing in the study of other neuroinflammatory diseases and other neurologic infectious diseases.

The emergence of new forms of subtype B HIV-associated disease in the era of highly active antiretroviral therapy (HAART) in developed countries and neurologic disease caused by other HIV subtypes will be focal points of the meeting. The 8th Symposium will also address a number of issues impacting the inflammatory process including viral and host genetics, substance abuse, other CNS pathogens, the aging process, and innate as well as adaptive immune response pathways. The 8th Symposium is sponsored, in part, by the International Society for NeuroVirology (ISNV) and will (1) enhance cross-fertilization of basic/clinical concepts concerning prevention and treatment of neurologic disease caused by HIV and other viral and non-viral pathogens, (2) attract young investigators into these complementary and important multidisciplinary fields of investigation, and (3) stimulate collaborations with an international scope.

The 8th Symposium will also emphasize the integration of basic, translational, and clinical research to develop new strategies to prevent and/or diagnose and treat viral-induced neurologic disease. Major sponsorship of the meeting has been provided by a United States Public Health Service / National Institutes of Health R13 grant with funds received primarily from the National Institute of Mental Health, with additional support from the National Institute of Drug Abuse and the National Institute of Neurological Disorders and Stroke. Without this support, the Symposium would simply not be possible. As indicated below a number of sponsors also contributed generously to the 8th Symposium. A number of other significant events will occur at this years symposium, including the Paradigm builder lectureship delivered by Peter Palese entitled Influenza Virus Pandemics: Past and Future and the Neurological Infections Lectureship delivered by Karen Roos entitled Advancement in the Diagnosis and Management of CNS Bacterial, Fungal, and Tuberculous Infections. Finally, a Special Plenary Session has been organized and will be Chaired by one of our Pioneers in NeuroVirology, Michael Oldstone. Again, one of the major highlights will be the major focus on our Investigators-in-Training with two afternoon oral presentation sessions and countless outstanding poster presentations. Again, welcome to San Diego and we all hope this will be a memorable meeting.

ISNV Highlight - Françoise Gray, MD, PhD. (continued)

Among her many contributions to the scientific community, Dr. Gray has served on the editorial boards of numerous scientific journals including Brain Pathology, Journal of Neuropathology and Experimental Neurology, Neuropathology and Applied Neurobiology, Clinical Neuropathology, Annales de Pathologies, Neuropathology, La Revue Neurologique and Journal Watch Neurology. She is a member of many scientific societies including the International Society of Neuropathology of which she was President from 2003 to 2006, and, of course, the International Society of NeuroVirology.

Friends of ISNV Highlight - Antonio Giordano, MD, PhD and the SHRO (continued)

Journal of Cellular Biochemistry and the Journal of Cellular Physiology, for which he is Editor and Reviews Editor. Other professional activities include serving as a grant reviewer for the American Cancer Society and the NIH's National Cancer Institute, an external reviewer for evaluating research programs for the U.S. Food and Drug Administration, and an ad hoc reviewer for National Science Foundation and Veterans Administration grant programs. Over the past ten years, Dr. Giordano has been an invited lecturer at more than 200 scientific meetings throughout the United States and abroad. In addition to his work with the Sbarro Institute for Cancer Research and Molecular Medicine, Dr. Giordano has been appointed chiara fama Professor of Pathology at the University of Siena, and has trained more than 130 scientists and physician investigators from all over the world. Dr. Giordano has published over 250 articles in major scientific journals and holds eleven patents on his discoveries.

ISNV Highlight - Kelly Jordan-Sciutto, Ph.D. (continued)

A graduate of Thomas Jefferson University in Biochemistry and Molecular Biology, Dr. Jordan-Sciutto completed her post-doctoral training at the University of Pittsburgh in the Department of Pathology. Dr. Jordan-Sciutto teaches in the graduate school and the Dental School at UPENN where she also mentors students from all levels and serves on numerous graduate committees. Her laboratory is supported currently by two R01s for which she is the PI. Her publication record includes 37 peer-reviewed research articles, several editorials and book chapters. She is a member of several professional societies including the International Cell Death Society, The American Society for Cell Biology, Society for Neuroscience and the International Society for NeuroVirology. We look forward to seeing Dr. Jordan-Sciutto's work at the ISNV this year in San Diego where she and members from her lab will present data from four separate projects!

Contact the ISNV Administrative Office at:

Phone: 215-204-0680 • Fax: 215-204-0681

Email: mail@isnv.org • Web: www.isnv.org

ISNV Newsletter printed by



Center for
Scientific
Communication & Outreach



Drexel University College of Medicine