# International Society for NeuroVirology

May 2004

Editorial Board: Walter Atwood, Ph.D., Fred Krebs, Ph.D Steven Jacobson, Ph.D., Ehud Lavi, M.D.

# Passing the Torch

Brian Wigdahl, Ph.D. • Philadelphia, PA



I would like to take this opportunity to thank the Society membership and all the individuals that served as officers and members of the Board of Directors for their advice, assistance, and spirit of cooperation during the two three-year terms that I served as founding ISNV President. It was an extremely rewarding experience to help guide the ISNV during the formative stages. It has given me great pleasure to watch the Society membership grow to more than 325 during the 2003, and, under the new leadership of Drs. Kennedy and Fujinami, I anticipate the membership to swell to more than 400 scientists representing more than 30 countries.

Perhaps one of our most important objectives has been the development of an annual scientific forum for the exchange of cutting edge information in the area of neurovirology and related disciplines. The International Symposium on NeuroVirology and associated ISNV workshops have become the leading venue for basic and clinician scientists to communicate their most recent

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# Kennedy and Fujinami take the reigns as the newly elected President and Vice-President of the ISNV

Walter J. Atwood, Ph.D. • Providence, RI

Ehud Lavi, M.D. • Philadelphia, PA

Robert Fujinami, Ph.D., the

new Vice-President of the

NeuroVirology, brings to the

position a productive and rich

neuroimmunology research in

experimental animal models

of neurologic diseases. Dr.

Fujinami received his under-

graduate degree in 1972 from

International Society

Dr. Peter G.E. Kennedy, who was elected by his peers as the new President of the ISNV, was trained in Medicine at University College London University College Hospital Medical School where he received Atchison Scholarship for the outstanding student of his year prior to obtaining Bachelor's



Fujinami (left) and Kennedy

degrees in Medicine and Surgery. He continued his postgraduate clinical and research training in London and Glasgow, obtaining a Ph.D. and an M.D. by research. His Ph.D. thesis was completed in the laboratory of Dr. Martin Raff FRS and was titled "A study of cell-type specific the University of Utah and his Ph.D. (1977) in Immunology-Microbiology from Northwestern University in Chicago, with his thesis on experimental allergic encephalomyelitis (EAE). He then moved to the Scripps Institute for a postdoctoral Fellowship with Dr. Michael Oldstone,

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On April 20, 2004, Diane E. Griffin, M.D., Ph.D., Professor and Chair, Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, was elected to the National Academy of Sciences. The International Society of Neuro Virology congratulates Dr. Griffin on this remarkable achievement!

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- Passing the Torch
- ISNV Focus Dr. Peter G. E. Kennedy, ISNV President
- ISNV Focus Dr. Robert Fujinami, <u>ISNV</u> Vice-President
- VEEV and Bioterrorism
- New Director at the **NINDS**
- Sardinia 2004 Announcement

### Passing the Torch (continued from page 1)

experimental results. We have been extremely fortunate to obtain significant and consistent support from the National Institute for Mental Health and the National Institute for Neurological Disorders and Stroke. The Symposium has also received support from the National Cancer Institute, National Institute for Drug Abuse, and National Institute for Aging. Since 1998, funding from the National Institutes of Health and corporate sponsorship has enabled the Society to sponsor travel awards for more than 100 investigators-in-training to attend the annual meetings. More than half of these awards have facilitated the development of the next generation of outstanding women in science. We have also strived to provide equitable opportunities to all scientists with regard to underrepresented minority status, gender, special needs, and country of origin. This remains a high priority in all ISNV activities.

The field of neurovirology has enjoyed the outstanding leadership of many investigators over the past 50 years. During the past six years, the Society has honored a number of these individuals with the now annual Pioneer in NeuroVirology Award. These prestigious individuals include Drs. Richard Johnson, Volker ter Meulen, Neal Nathanson, and Michael Oldstone. Each of these individuals has made seminal contributions to our discipline. The Pioneer in NeuroVirology for 2004 will be announced at the 6th International Symposium on NeuroVirology to be held in Sardinia, Italy (September 10-14).

# "The strength of the ISNV lies in its membership" Brian Wigdahl

In addition to the annual ISNV Symposium and Workshops, the Society's Newsletter has also provided a vehicle for communication. We are now in the process of increasing the frequency of publication. The ISNV website has also played an important role in the dissemination of information relevant to the Society membership. The cornerstone our scientific communication has been the Journal of NeuroVirology (JNV). Under the leadership of Dr. Kamel Khalili (Editor-in-Chief) and the Editorial Board, JNV has become an outstanding subspeciality journal with great impact in the area of neurovirology and related disciplines.

As the first Past President of ISNV, I look forward to working with the new leadership as the Society continues to grow in stature.

### **Kennedy** (continued from page 1)

markers in neural cell cultures and their application to the study of demyelinating diseases." Dr. Kennedy's M.D. thesis was titled "Morphological and immunofluorescent observations in neural cell and BHK21/C13 cell cultures infected with Herpes Simplex Virus (HSV)." He was awarded a DSc degree in 1991, and also holds two Masters degrees in Philosophy. Dr. Kennedy has held numerous posts, including Research Fellow at the MRC Virology Unit in Glasgow; Senior Registrar in Neurology at the National Hospital for Nervous Diseases, Queen Square, London; Visiting Assistant Professor of Neurology at The Johns Hopkins University School of Medicine; and "New Blood" Senior Lecturer in Neurology and Virology at The University of Glasgow. Research recognition includes the BUPA Medical Foundation Research Award and the Linacre Medal of the Royal College of Physicians of London. He is a Fellow of the Royal Society of Edinburgh and a Founding Fellow of the Academy of Medical Sciences. Dr. Kennedy was also a Fogarty International Scholar-in-Residence at the National Institutes of Health in Bethesda. He is currently the Burton Chair of Neurology at the University of Glasgow, a post he has held since 1987.

In addition to his numerous administrative duties, Dr. Kennedy maintains an active and well-funded research lab. His major research interests are focused on the molecular pathogenesis of infectious diseases of the nervous system. His current research focuses on the molecular basis of Varicella-Zoster Virus latency in human ganglia. Dr. Kennedy also collaborates extensively with the University Veterinary School in studies of the neuropathogenesis of Human African Trypansosomiasis (sleeping sickness). During his career, Dr. Kennedy has published well over 100 primary papers that have served to advance our understanding of the neuropathogenesis of infectious disease.

#### Fujinami (continued from page 1)

who headed one of the largest and most productive neurovirology research groups. During that period, Drs. Fujinami and Oldstone introduced some of the early concepts of molecular mimicry in viral pathogenesis based on observations of measles viral infections.

Following a fellowship and a period as research associate, Dr. Fujinami joined the staff at the Scripps Institute as Assistant Professor. From 1985 to 1990, Dr. Fujinami held the position of Associate Professor of Pathology in the nearby Department of Pathology at the University of California in San Diego. The department was then headed by Peter Lampert, M.D., a pathologist with interests in neurovirology and a research program in virus-induced demyelination. In 1990, Dr. Fujinami had the opportunity to return to Salt Lake City, Utah, where he joined Richard Baringer, M.D., a neurovirologist who chaired the Department of Neurology at the University of Utah. As Professor of Neurology at the University of Utah, Dr. Fujinami's research endeavors focused primarily on the pathogenesis of the model system of Theiler's virus-induced demyelination. Dr. Fujinami's lab contributed to many aspects of this model, the most recent being the concept of virus priming for inflammatory demyelinating CNS disease triggered by a different viral infection. Over the years, Dr. Fujinami was successful in obtaining multiple NIH and National Multiple Sclerosis Society research grants, including the prestigious NMSS Harry M. Weaver Neuroscience Scholarship Award and the NIH Javits Neuroscience Scholar Award. Dr. Fujinami has contributed valuable concepts of autoimmunity and virusinduced demyelination to the field of neurovirology. As demonstrated by the number of researchers who have trained in his lab, Dr. Fujinami continues Dr. Oldstone's tradition of raising the next generation of neurovirologists.

## Venezuelan Equine Encephalitis Virus as an Agent of Terrorism

Major Michael Dobbs, M.D. • Lackland AFB, TX

Although there have been no reported uses of viruses as modern biological weapons, there is real potential for the use of viral pathogens as agents of bioterrorism, as suggested by the history of biological warfare. As late as the late 1980's, the Soviet Union had been developing viral pathogens as biological weapons. One pathogen in which they had particular interest was Venezuelan Equine Encephalitis Virus (VEEV), which is one of numerous RNA-containing viruses that cause a wide variety of mosquito-transmitted diseases.

While several arboviral encephalitic agents might be exploited as weapons, there are several factors that make VEEV a likely choice as a bioterrorism agent. First, VEEV, which is an alphavirus that causes an epidemic zoonosis normally limited to the tropical and subtropical Americas, has high infectivity coupled with a low infectious dose. Second, there is no specific treatment for the disease caused by VEEV infection. Finally, very few people have been vaccinated against infection by the virus.

Immediate recognition of the involvement of VEEV in a bioterrorism attack may be difficult. In nature, Venezuelan Equine Encephalitis (VEE) epidemics are easily recognizable by the large numbers of equines succumbing to the disease. However, since a deliberate aerosol release would likely occur indoors or in areas remote from livestock, dead equines may not be a useful barometer for recognition of an attack with VEEV. The most suggestive indicator of a deliberate VEEV release would be a human case occurring anywhere outside of the tropical/subtropical Western Hemisphere. Such a sentinel event would require an immediate and detailed investigation.

Identification of VEEV as a bioterrorism agent and appropriate responses to such an attack may also be impacted by the time course of VEEV-associated disease. Covert release of VEEV will not have an immediate effect on public health because of the incubation period of one to six days. VEEV normally causes a bimodal illness in humans (Fig. 1), with an initial severe flu-like illness in nearly everyone exposed, followed several days later by potentially deadly encephalitis in a few patients (1). The overall human mortality rate in a natural epidemic is less than 1% (2). However, attacks involving VEEV will likely be carried out using aerosolized viral particles, since the use of infected vectors may be highly unpredictable and logistically much more difficult to accomplish. Studies of VEEV infection using animal models suggests that aerosolized VEEV is highly neurotropic and accesses the central nervous system through the olfactory epithelium (3). In attacks involving aerosolized viral particles, it is reasonable to expect increased numbers of encephalitis cases following the initial exposure (Fig. 2).

Preventative and post-exposure options are limited. Vaccines, which have been shown in limited studies to have protective efficacy (4), are available for laboratory personnel at high risk of exposure. Treatment of the disease subsequent to infection is limited to supportive care. In severe cases, prophylactic, anticonvulsant drugs should be considered. Pegylated alpha-

interferon has resulted in improved survival in mice (5), but the implications of these results for humans are unclear. More research needs to be done to find effective therapies for this and other viral encephalitides, especially in light of the potential for the use of VEEV and other viral pathogens as agents of bioterrorism.

#### References

- 1. Ellison DH. Handbook of chemical and biological warfare agents. CRC Press, Boca Raton, FL; 2000.
- 2. Paredes A, Alwell-Warda K, Weaver SC, Chiu W, Watowich SJ. Structure of isolated nucelocapsids from Venezuelan equine encephalitis virus and implications for assembly and disassembly of enveloped virus. J Virol 77:659-64, 2003.
- 3. Steele KE, Davis KJ, Stephan K, Kell W, Vogel P, Hart MK. Comparative neurovirulence and tissue tropism of wild-type and attenuated strains of Venezuelan equine encephalitis virus administered by aerosol in C3H/HeN and BALB/c mice. Vet Pathol 35:386-97, 1998.
- 4. Bronze MS, Huycke MM, Machado LJ, Voskuhl GW, Greenfield RA. Viral agents as biological weapons and agents of bioterrorism. Am J Med Sci 323:316-25, 2002.
- 5. Lukaszewski RA, Brooks TJ. Pegylated alpha interferon is an effective treatment for virulent Venezuelan equine encephalitis virus and has profound effects on the host immune response to infection. J Virol 74:5006-15, 2000.

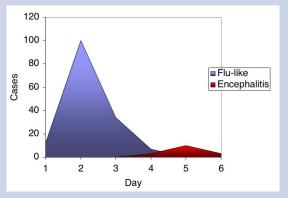


Fig. 1. Illustrated here is a typical epidemic curve for a point-source outbreak, as is usual for VEEV. The flu-like cases (blue) would be followed days later by a few cases of fulminant encephalitis (red).

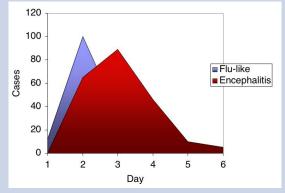


Fig. 2. A possible point-source outbreak curve for a deliberate aerosolized VEEV release. Because aerosolized virus may be more neurotropic, more cases of encephalitis (red) would be seen, and encephalitis cases would present earlier than in a natural epidemic.

# Story C. Landis, Ph.D., Appointed New Director of the National Institute of Neurological Disorders and Stroke

Steven Jacobson, Ph.D. • Bethesda, MD

On September 1, 2003, Elias Zerhouni, M.D., director of the National Institutes of Health (NIH), announced the appointment of Story C. Landis, Ph.D., as director of the National Institute of Neurological Disorders and Stroke (NINDS).

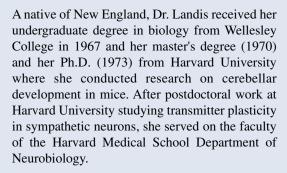
As the new NINDS Director, Dr. Landis will oversee an annual budget of \$1.5 billion and a staff of more than 900 scientists, physician-scientists, and administrators. The Institute supports research by investigators in public and private institutions across the country, as well as by scientists working in its intramural laboratories and branches in Bethesda, Maryland. Since 1950, the Institute has been at the forefront of U.S. efforts in brain research, with studies in areas ranging from the structure and function of single brain cells to research on the causes, prevention, diagnosis, and treatment of neurological disorders and, most

recently, translational research that is bridging the gap. The Institute's mission is to reduce the burden of neurological disease - a burden borne by every age group all over the world.

Dr. Landis said she was "delighted to have been chosen to lead an NIH Institute with an outstanding staff, whose investigators have a wonderful history of accomplishments in basic and clinical neurology. This is a particularly exciting time in neuroscience with many opportunities for rapid translation of scientific discovery into new diagnostics and therapeutics. I look forward to developing strong collaborations between the NINDS, the other NIH institutes that fund neuroscience research, and our most important partners, patient and professional advocacy groups."

Dr. Landis joined the NINDS in 1995 as Scientific Director and worked with then-Institute Director Zach W. Hall, Ph.D., to coordinate and re-engineer the Institute's intramural research programs. Between 1999 and 2000, under the leadership of NINDS Director Gerald D. Fischbach, M.D., she led the movement, together with NIMH Scientific Director Robert

Desimone, Ph.D., to bring some sense of unity and common purpose to 200 laboratories from eleven different NIH Institutes, all of which conduct leading edge clinical and basic neuroscience research.



In 1985, she joined the faculty of Case Western Reserve University School of Medicine in

Cleveland, Ohio, where she held many academic positions, including Associate Professor of Pharmacology, Professor and Director of the Center on Neurosciences, and Chair of the Department of Neurosciences, a department she was instrumental in establishing. Under her leadership, Case Western's neuroscience department achieved worldwide acclaim and a reputation for excellence.

Throughout her research career, Dr. Landis has made many fundamental contributions to the understanding of developmental interactions required for synapse formation. She has garnered many honors and awards and is an elected fellow of the Academy of Arts and Sciences, the American Association for the Advancement of Science, and the American Neurological Association. In 2002, she was named the President-Elect of the Society for Neuroscience.

The NINDS is a component of the National Institutes of Health within the Department of Health and Human Services and is the nation's primary supporter of biomedical research on the brain and nervous system.



# 6th International Symposium on NeuroVirology

# **HIV Neuroprotection Workshop**

September 10 - 14, 2004 • Sardinia, Italy

Conference Chairs:

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For more information, visit www.isnv.org/sardinia2004 and www.isnv.org/hiv-neuro

