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Volker ter Meulen named Pioneer in NeuroVirology for 2000

KAMEL KHALILI, Ph.D. • PHILADELPHIA, PA

The International Society for NeuroVirology has announced Volker ter Meulen as the recipient of the 2000 ISNV Pioneer in Neuro-Virology Award. The award was presented to Dr. ter Meulen at the Third International Symposium on Neuro-Virology held in September 2000.

Dr. ter Meulen's contributions to the field of neurovirology span a period of more than thirty years in which his research has been directed toward the study of virus persistence in the CNS. His studies have focused on viruses in either animal models or human diseases such as measles virus, coronavirus, and more recently, simian immunodeficiency virus. Specifically, his research has targeted acute measles encephalitis, measles inclusion body encephalitis, and subacute sclerosing panencephalitis. His seminal findings have greatly contributed to our current understanding of virus persistence and pathogenesis in the CNS. In addition, his work has been instrumental in determining the etiology of other neurological syndromes associated with viral infections. His studies on measles virus infection in the CNS have contributed to our understanding of the mechanism of persistent viral infection and, in particular, the manner in which viruses are able to escape the immune response. To pursue the mechanisms of viral neuropathogenesis, Dr. ter Meulen developed an animal model to examine human samples. Prior to the development of advanced molecular biology and immunological techniques, Dr. ter Meulen



studied viral homology, gene expression, and mutations. Through his studies he was able to demonstrate how measles and coronavirus infections are able to induce MHC class I and II expression and initiate an autoimmune response. One of the important

implications of these findings was the notion that viral infections are able to trigger autoimmune responses. More recently, Dr. ter Meulen has expanded his studies to include work on retroviruses, particularly HIV-1 and SIV.

Dr. ter Meulen received his M.D. from the University of Göttingen in 1960. Following an internship at the University of Göttingen, he completed a fellowship in Virology at Children's Hospital of Philadelphia under the direction of Dr. Werner Henle. He then returned to Germany to complete a residency in Pediatrics at the Universitäts-Kinderklinik in Göttingen. Dr. ter Meulen returned to the United States as a visiting scientist at the Wistar Institute in Philadelphia where he worked on measles neuropathogenesis. In 1968, Dr. ter Meulen accepted the position of Assistant Professor in the Departments of Pediatrics & Microbiology at the University of Göttingen. He quickly rose through academic ranks attaining the title

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of Professor and Chairman of the Institute of Virology and Immunobiology at the University of Würzburg in 1975. From 1983 to 1985 he served as Dean of the Faculty of Medicine at the University of Würzburg. Since 1993, Dr. ter Meulen has been the Chairman of the Research Centre for Infectious Diseases at the University of Würzburg. Dr. ter Meulen remains an active and important neurovirologist. He has published more than 400 papers in leading international journals and has received many awards and honors including the prestigious Max Planck Research Prize. He continues to make numerous contributions to the scientific community through his service on various committees throughout Europe and the world, including the World Health Organization. Dr. ter Meulen has been very generous with his time and knowledge through training postdoctoral fellows and students. He is a committed and dedicated researcher whose contributions have made a considerable impact on the field of neurovirology.

Message from the President

BRIAN WIGDAHL, Ph.D. • HERSHEY, PA



Brian Wigdahl Dr. Lynn Pulliam (Chair of the Organizing Committee for the 3rd International Symposium on NeuroVirology) provided an overview of the Scientific Program and Objectives for the 2000 Symposium in her introductory remarks to more than 250 Symposium participants from around the world. We have been extremely pleased with the level of interest and excitement about the Symposium. This event has clearly become a major focal point for dissemination of research ideas in the area of neurovirology. We are very pleased to acknowledge the generous and essential support of the National Institute for Neurological Disorders and Stroke as well as the National Institute of Mental Health. The quality of our Symposium has been greatly enhanced by their involvement. We would also like to acknowledge additional Symposium support from The Pennsylvania State University and Temple University as well as support from the Journal of NeuroVirology, Pharmacia & Upjohn, Inc., Advanced Bioscience Resources, Inc., Medivacs, Inc., and Centaur Pharmaceuticals, Inc. The Board of Directors and Editorial Board of the International Society for NeuroVirology and the Journal of NeuroVirology is very proud of the high quality of the Symposium Speakers and the breadth and quality of the participants. The success of the Annual Symposium and an expanding ISNV Membership from around the world will continue to enhance our efforts to understand the pathogenesis of neurotropic viral diseases and to develop strategies to prevent and treat these often fatal processes.

NIAID and NINDS Panel Discusses Emerging Neurovirologic Diseases at 3rd International Symposium on NeuroVirology

STEVEN JACOBSON, Ph.D. • BETHESDA, MD



Steven Jacobson In conjunction with the 3rd International Symposium on NeuroVirology held September 14-16 in San Francisco, the National Institute of Allergy and Infectious Diseases and the National Institute of Neurological Disorders and Stroke sponsored a Blue-Ribbon Advisory Panel that convened to identify key scientific issues and research opportunities for future NIH support in the area of emerging neurovirologic diseases. During the course of this one-day meeting, participants met to assess the state of knowledge of neurovirology and relevant resources and technologies; identify questions that should be addressed in basic and clinical investigation, and to discuss proposed areas and mechanisms for research and resource allocation. The meeting was organized to allow

maximum time for discussion and achievement of consensus. Selected presentations were used to provide an overview of critical aspects of the field and a framework for dialogue and synthesis. Topics included: Overview of Neurologic/Neuropsychiatric Disease Due to Viral Infection; Causation: What is required to implicate a virus (or other infectious agent) as a factor or cofactor in pathogenesis of disease?; Infrastructure Issues: Databases and Sample Repositories; Pathogen Discovery; Pathogenesis; and Clinical Intervention. The meeting was organized by Dr. Ian Lipkin, Department of Anatomy and Neurobiology, University of California, Irvine; Dr. Michael Buchmeier, Department of Neuropharmacology, The Scripps Research Institute; and Dr. Steven Jacobson, Viral Immunology Section, Neuroimmunology Branch, NINDS, NIH. Inquiries regarding this meeting may be directed to any one of these individuals.

Nipah Virus: A Newly Emergent Deadly Paramyxovirus with an Extended Host Range that Includes Humans

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An outbreak of severe febrile encephalitis associated with human deaths was reported in Peninsular Malaysia beginning in late September of 1998. The outbreak was first recognized near Ipoh, a city in the northern state of Perak. Associated with respiratory illness in pigs, and was initially attributed to Japanese encephalitis. By February 1999, a similar disease in pigs and humans was recognized in other regions of Malaysia and was associated with the movement of a large number of pigs from Ipoh southward into the new outbreak areas. In March 1999, a cluster of 11 cases of respiratory and encephalitis illnesses was noted in Singapore in abattoir workers who handled pigs from the outbreak regions in Malaysia. The outbreak in Singapore ended when the importation of pigs from Malaysia was prohibited. The outbreak in Malaysia ceased when over one million pigs were culled from the outbreak and immediately surrounding areas. A total of 265 cases of encephalitis, including 105 deaths, were associated with the outbreak in Malaysia.

The virus, named Nipah virus after the village in which the first case death occurred, was determined to be a paramyxovirus that is related to Hendra virus, another recently emerged paramyxovirus. The virus is comprised of a single-stranded RNA genome (18,000 nucleotides) of negative polarity. The nucleocapsid structures are approximately 1.6 μm in length and 21 nm in diameter and the virus appears to assemble and bud from the plasma membrane. The assembled virions measure 500-700 nm in diameter, are enveloped, and appear to contain surface projections consistent with the transmembrane glycoproteins of the family Paramyxoviridae. The gene order of the Nipah virus is consistent with that of the family Paramyxoviridae and there are two genes encoding the fusion and attachment proteins. Nipah is both genetically and antigenically related to Hendra virus. Phylogenetic analysis suggests that these viruses form a new genus within the Paramyxovirinae subfamily.

Nipah virus was determined to be the etiologic agent of the outbreaks in Malaysia and Singapore. Isolation or

serologic testing confirmed Nipah virus infection in all cases from Singapore and over 75% of the cases from Malaysia. The most notable illness in pigs implicated in transmitting the virus to humans was respiratory and included a loud and distinctive cough. Although serologic studies found evidence of Nipah virus infection in most of the pigs on farms with infected humans, only a minority of these pigs were noted to be ill with only a minimal (~5%) increase in pig deaths. Serologic studies also indicated that Nipah virus infection occurred in dogs, cats, two polo ponies, and in bats.



Two key features of this outbreak were the fatal encephalitis and the nearly universal history of infected humans and other animals, including cats and dogs, in direct contact with pigs.

Pathologic studies of infected human and pig tissues provided plausible explanations for these two features of the outbreak. Autopsy studies of humans suggested that the primary pathology was a multi-organ vasculitis associated with infection of endothelial cells. Infection was most prominent in the central nervous system, where a diffuse vasculitis was noted in the cerebral cortex and brain stem with extension to parenchymal tissue. Eosinophilic, mainly intracytoplasmic, viral inclusions were observed in the affected neurons and other parenchymal cells. Intense immunostaining of endothelial cells and dead and dying parenchymal cells was noted in the central nervous system. These studies demonstrated that Nipah virus infection in humans can cause widespread central nervous system pathology consistent with a severe encephalitis.

Pathologic examination of pigs revealed extensive involvement of the respiratory tract. In the lungs, a giant-cell pneumonia with characteristic multi-nucleated syncytial cells was noted. By immunohistochemistry, Nipah virus antigens were demonstrated in syncytial cells in the lungs and epithelial cells lining the upper airway passages.

see Nipah Virus

The "Featured Brief" section of the newsletter highlights an area of international importance that the editors feel deserves special attention. An update of current activity and information on a "featured" topic should help keep members aware of fast paced studies and new results. The Editors are always interested in your ideas for future articles and brief comments on its topics.

1st Pan-Am Neurovirology Symposium

J. ROBERTO TRUJILLO, M.D., Sc.D. • BOSTON, MA



The purpose of the First Pan-American Symposium on Neurovirology is to bring together medical scientists from the United States, Canada, and Latin America to share knowledge with respect to the relatively new field of neurovirology. This is the first meeting of the The Pan-American Society of Neurovirology, which was established to understand the impact of viral infections on the nervous system in the Americas. The meeting will take place from November 13 to 15, 2000, at the Princes Hotel, Acapulco, Mexico. This symposium is a scientific component of the Neuroscience 2000 Congress organized in collaboration with the Mexican Society of Neurology (November 10-18, 2000). The meeting will cover a broad range of topics in the field of neurovirology and will include workshops on the cutting-edge tools of molecular biology. The meeting will feature outstanding speakers in the fields of virology, neurology, neuroscience, and psychiatry.

President: J Roberto Trujillo, M.D., Sc.D.

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from Nipah Virus

Abundant viral antigen was observed in intraluminal necrotic debris in the upper and lower airways. In a small number of pigs, there was prominent central nervous system pathology with meningeal inflammatory infiltrates, and viral antigen was detected focally in inflammatory cells as well as within the nuclei of rare parenchymal cells. Nipah antigen was also detected in kidneys as focal staining in renal tubular epithelial cells. The presence of extensive infection in the upper and lower airways suggests that the respiratory secretions from infected pigs are likely to be a rich source of infectious virus. The finding of neutralizing antibodies to Nipah virus in two species of fruit bats (*Pteropus vampyrus* and *Pteropus hypomelanous*) and the results implicating fruit bats as a reservoir for Hendra virus led us to suspect a similar reservoir for Nipah virus. Recently, Nipah virus was reported to be isolated from bat urine of *Pteropus* sp. in Malaysia. If such findings can be confirmed, these large fruit bats might provide both a reservoir and the source of Nipah virus outbreak.

Specialized Neuroscience Research Programs (SNRPs) and NINDS

SHANNON GARNETT, Ph.D., • BETHESDA, MD

The National Institute of Neurological Disorders and Stroke (NINDS)—in collaboration with the National Center for Research Resources and the Office for Research on Minority Health—supports a new, innovative funding mechanism called Specialized Neuroscience Research Programs (SNRPs). Dr. Al Gordon is the Director of the NINDS Office of Special Programs in Neuroscience. The purpose of the SNRPs is to augment and strengthen the research capabilities of faculty, students, and fellows at minority institutions by supporting the development of new or the enhancement of ongoing basic and clinical neuroscience research programs, and by developing the necessary infrastructures of these programs. This mechanism represents a long-term strategy to prepare future neuroscience research and health professionals who can assist the NINDS in reducing disease disparities of populations at increased risk for disorders of the nervous system. Additionally, the NINDS supports a SNRP in Health Disparities: HIV and the Nervous System to encourage research collaborations between established investigators, investigators at minority institutions, and health care providers to better deliver the benefits of research to all Americans as described by Dr. Joana Rosario, a program director in the NINDS Office of Special Programs. Institutions that develop successful research programs under this initiative will receive additional support to help them develop more intensive and larger research studies aimed at reducing the national burden of HIV and AIDS. Five institutions received SNRP awards in 1999 (University of Hawaii, University of Puerto Rico, Universidad Central del Caribe, University of Texas St. Antonio, and Howard University), and three additional awards are planned for this year.

10th Int'l Conf. on Human Retrovirology HTLV & Related Viruses

The conference is scheduled for June 25-29, 2001 at Trinity College in Dublin, Ireland and is being organized by The International Retrovirology Association - HTLV and Related Diseases in collaboration with the University College, Dublin, Ireland. For more detailed information contact Professor William Hall, University College Dublin, Bellfield, Dublin 4 (william.hall@ucd.ie) or visit the web site at www.htlvconference.com.

