ISNV
Oct 2010
Special Issue
International Society for NeuroVirology
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Susan Weiss gives the 2010 Bill Narayan Lectureship

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Dr. Susan R. Weiss, Professor of Microbiology and Associate Dean for Postdoctoral Research Training at the University of Pennsylvania School of Medicine, will deliver the 2010 Bill Narayan Lectureship. Dr. Weiss received a BA in Biology from Brandeis University. After completing graduate studies at Harvard School of Medicine on paramyxovirus transcription and four years of post-doctoral training, in retrovirus molecular biology at the University of California in San Francisco, Dr. Weiss joined the UPENN Faculty in 1980. With the guidance of her colleagues, Drs. Neal Nathanson and Don Gilden, she developed an interest and research program in coronavirus pathogenesis, and became a leader in that field. Using murine coronavirus, mouse hepatitis virus (MHV), infection of its natural host, Dr. Weiss' research has provided the scientific community with a greater understanding of the viral and host determinants of tropism and neurovirulence.

Murine coronavirus strains induce disease in several organ systems of mice, including the central nervous system (CNS) and the liver. The outcome of MHV infection is determined by a combination of viral genes and host cell response. Infection with neurotropic strains causes acute encephalitis, and in survivors, chronic demyelination, the latter of which serves as an animal model for multiple sclerosis. Dr. Weiss describes her long-term research goal as the elucidation of viral and cellular determinants of tropism and pathogenesis in both the brain and the liver. Towards this end, her group has developed a well-characterized animal model and has contributed to the development of two reverse genetic systems with which to manipulate the viral genome.

The highly neurovirulent JHM strain spreads rapidly thoughout the CNS inducing a minimal T-cell response, resulting in lack of viral clearance and mortality of all infected mice, even when very low levels of virus are administered. The more neuroattenuated A59 strain spreads less extensively in the CNS and induces a robust T-cell response, resulting in viral clearance; surviving mice develop a chronic demyelinating disease. A chimeric virus,

expressing the JHM spike within the background of A59, like JHM, spreads rapidly in the CNS but, also like A59, induces a robust CD8 T-cell response. Thus, multiple genes contribute to the high neurovirulence of JHM. On the other hand, JHM, unlike A59, can induce lethal CNS disease in the absence of the only known MHV receptor, CEACAM1a; this mechanism likely contributes to the extensive viral spread in neurons observed during JHM infection, despite the low level of CEACAM1a expression in the CNS, especially in neurons. There may also be a neuron-specific mechanism and/or an additional neuronal receptor that enhances the spread of JHM in the CNS. In this context, two mechanisms likely contribute to the very high neurovirulence of JHM: (1) JHM infects and spreads more efficiently in the CNS, due in part to CEACAM1a-independent spread, and (2) JHM elicits a weak antiviral T-cell response resulting from an inability to prime a CD8 T-cell response in the CNS.

In addition to the crucial role of the T-cell response, the type I interferon (IFN-α/β) response is essential for protection from MHV. This is demonstrated by the uniformly rapid death of IFN receptor knockout mice, infected with low doses of either A59 or JHM. Paradoxically, infection of cell lines such as murine L2 and human 293T cells induces only a low level of IFN-β mRNA, but no detectable IFN-β protein, and replication in these cells is not inhibited by pretreatment with IFN-β. However, in primary cell types such as pDCs and macrophages, IFN is induced by MHV infection and an antiviral state is established. MHV induction of type I IFN depends primarily on MDA5 in macrophages. The CNS expresses a much lower basal level of IFN signaling molecules than the liver, and this may contribute to permissiveness for MHV infection in the CNS despite the very low CEACAM1a receptor expression. Cell types such as neurons and astrocytes fail to produce IFN following infection, and in vivo, likely depend on IFN produced by pDCs and macrophages for protection from MHV. Thus, MHV induction of IFN-α/β and the ability to induce an antiviral state in response to IFN is both organ and cell-type dependent. IFN-induced protection from MHV pathogenesis in the CNS likely requires the orchestrated activities of several cell types; however, the cell types involved in limiting MHV replication may be different in the immune privileged CNS.

Request for Nominations for Bill Narayan Lectureship Award

The 11th symposium will be held in New York, New York, 2012

International Society for NeuroVirology ISNV LectureShip Series

The International Society for NeuroVirology will accept nominations for the 11th International Symposium on NeuroVirology in 2012. Please send all inquiries and nominations to mail@isnv.org

The Bill Narayan Lectureship is dedicated to the study of viral pathogenesis and the neurovirology of lentiviruses. Dr. Narayan started his career as Dr. Richard T. Johnson's first post-doctoral fellow in the laboratory of NeuroVirology at Johns Hopkins School of Medicine in 1970. From 1972 through 1993, he developed his research and was promoted at Johns Hopkins to Professor in the Division of Comparative Medicine and founded the Retrovirus Biology Laboratories in 1988. Since 1993, Dr. Narayan had served as Chair of the Department of Microbiology, Molecular Genetics, and Immunology at the University of Kansas Medical Center, Kansas City, KS, USA. He also served as the Marion Merrell Dow Foundation Distinguished Professor and Director of the Marion Merrell Dow Laboratory of Viral Pathogenesis at the University of Kansas Medical Center. Bill studied the pathogenesis of lentiviruses before the emergence of HIV, and his studies predicted the neuropathogenesis of HIV, the inability of antibody to control lentiviruses, antigenic variation within the infected host, and the difficulty in protecting the host with vaccine strategies. He had done all this before HIV was identified. When HIV was identified as the cause of AIDS, Bill made a conscious decision to study the pathogenesis of the simian immunodeficiency virus in the macaque model. His research provided the foundation for the early studies of the pathogenesis of the human immunodeficiency virus and its effects on the immune and nervous systems. His long-term contributions established the SIV model for studies of AIDS and CNS pathogenesis. In the final stages of his career, Dr. Narayan focused major efforts on the development of a vaccine against HIV-1 using the simian/human immunodeficiency virus (SHIV) macaque model of AIDS. His contributions in SIV research are considerable, spanning pathogenesis, neuropathogenesis, and the development of a therapeutic SIV vaccine. All of these accomplishments pale in comparison to his role as mentor and his ability to develop independent scientists. He trained over 40 scientists whom he taught to think critically about pathogenesis and become leaders in their fields. He always respected the training and background of his mentees and sought their ideas. He mentored by making you a trusted colleague and friend.

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ISNV Newsletter printed by the Center for Scientific Communication and Outreach: Director, Michael Nonnemacher, Ph.D.