

1999 Pioneer in NeuroVirology: Richard T Johnson, MD



Dr Richard Johnson was presented with the first annual Pioneer in NeuroVirology Award by the International Society for Neurovirology this summer at the Gordon Conference on Neurovirology. Dick Johnson is recognized as one of the founding fathers of neurovirology. In addition, Dick Johnson has trained a large number of the leaders in the field of virus pathogenesis and viral immunology, this article will highlight his important role in training.

Dr Richard Johnson's interest in the pathogenesis of viral diseases and viral infections of the central nervous system began in the 1960s when he was in the Department of Viral Diseases at Walter Reed Army Institute of Research. He worked with Dr Edward Buescher, a virologist, and characterized the pathogenesis of enterovirus infections and the effects in the central nervous system. He went on to the Massachusetts General Hospital where he trained in neurology. Dick Johnson's first faculty position was in the Neurology Department at Case Western Reserve University School of Medicine (1964–1969). However, the majority of Dick's academic career was on the faculty of the Johns

Hopkins University School of Medicine as the Dwight D Eisenhower Professor of Neurology, a position he held from 1969 until his appointment as Neurologist-in-Chief and director of the Department of Neurology in 1988. He served in this position until 1997, when he retired. He currently splits his time between editing *Annals of Neurology* and serving as the Director of the National Neuroscience Institute of Singapore. Both his clinical and basic research work over the past 30 years have focused on infections of the nervous system. Dr Johnson has been the leader in the synthesis of the fields of virology and neurology. One of his important roles in these fields has been the postgraduate training of MDs, PhDs and DVMs as leaders in biomedical research. Among the 50 or more fellows that he has trained eight are currently chairs of departments at major medical institutions.

Dr Johnson began his tradition of training in 1967 at Case Western Reserve in Cleveland. His first fellow was Dr Kenneth Johnson who worked on California encephalitis and virus induced hydrocephalus; Dr K Johnson is currently the Chair of Neurology at the University of Maryland School of Medicine. After being recruited to Johns Hopkins University School of Medicine in 1969 by Dr Guy McKhann, Dick assembled a group of faculty and fellows with expertise in immunology, pathology, virology and ultrastructure. The faculty involved in this group were Dr Robert Herndon (neurologist and electron microscopist) and Dr Leslie Weiner (neurologist and current chair of the Department of Neurology, University of Southern California Medical School). The first fellows to join the group had expertise in pathology, virology and immunology: Opendra (Bill) Narayan, DVM who just completed his PhD studying influenza virus, Diane Griffin, MD had completed her PhD in Immunology, Dale MacFarland studied immunological models of encephalitis during his residency training and Howard Lipton, MD, a resident in Neurology had field experience in infectious diseases.

Henry MacFarland and Diane Griffin undertook studies of Sindbus virus and the role of immunological factors in the pathogenesis of the disease. Diane also began studies on measles virus infections during her fellowship. Bill Narayan's research was focused on animal virus pathogenesis and he studied Bluetongue virus in sheep and later, visna virus, a lentivirus infection in sheep. Howard Lipton studied the pathogenesis of Baltimore rat virus, now known to be a hantavirus. Dick's efforts

were focused on training fellows to learn to do independent research, and so each fellow's project involved a different virus and required that the fellows established the *in vivo* or *in vitro* system and developed the reagents required for the studies. Research focused on the overall viral pathogenesis with particular interest in the involvement of the CNS. Because the fellowship training provided broad research experiences, it was excellent preparation for establishing independent laboratories and obtaining grant funding. Dick's fellows have been particularly successful as independent research scientists.

It may not be necessary to point out that the first group of Dick Johnson's fellows are leaders in virology and immunology. Henry MacFarland is the Laboratory Chief of the Neuroimmunology Branch at NINDS, the National Institutes of Health and is known for his innovative studies characterizing the status of disease in Multiple Sclerosis (MS) patients with neuroimaging techniques. Diane Griffin is renowned for her immunological studies on Sindbus virus and measles virus, and is Chair of the Department of Molecular Microbiology and Immunology at the Johns Hopkins University School of Public Health. Bill Narayan has been a leader in lentivirus pathogenesis, first with studies of visna virus and CAEV and then using the simian immunodeficiency virus-macaque system as a model of AIDS, he is Chair of Microbiology at the University of Kansas Medical School. Howard Lipton is at Northwestern University where he has established a dynamic research group studying Tyler's virus pathogenesis.

The next group of fellows that joined Dick in 1972 included Larry Becker, MD, currently Professor and Chairman of the Department of Neuropathology at the University of Toronto School of Medicine, Ljiljana Kostovic, MD, Professor of Anatomy, University of Zagreb Medical School, Jack Burks, MD, former president of the Rocky Mountain Multiple Sclerosis Center and Professor of Neurology at the University of Colorado School of Medicine.

I am proud to be a member of this illustrious group of trainees, joining Dick Johnson's laboratory as a fellow in 1975. One of my lasting memories of this time is gathering as a group in Dick's office every Monday morning at 8.30 a.m. to discuss our individual research projects. It was where I learned to think about virus pathogenesis and the experimental approaches used in animal model and *in vitro* systems. The lessons I learned in those meetings have provided me with the framework for molecular pathogenesis studies of lentiviruses. Each of Dick's fellows was given a great deal of his time and direction, this gave each of us an enormous start on the road to independent research.

While I was training the other fellows in the laboratory were Raymond Roos, MD, John Greenlee,

MD, Mary Lou Oster-Granite, PhD, Maria Mazlo, MD, Benjamin Brooks, MD and Burk Jubelt, MD. It was an exciting time, we were all involved in research on different virus systems and we all had very different backgrounds and experience. John Greenlee was working on papovaviruses, using a hamster model to study the induction of tumors by the human papovavirus, BK. Mary Lou Oster-Granite also studied the papovaviruses characterizing ultrastructural changes caused by these viruses in cultured cells. Ben Brooks focused his research on a mouse retrovirus that caused infections and spongiform changes in the CNS. Burk Jubelt studied the pathogenesis and CNS involvement in mouse adapted poliovirus. I worked with Dick and Bill Narayan on an unusual retrovirus that did not harbor an oncogene nor cause neoplasia in infected animals; visna virus caused a multi-organ disease as well as infections in the CNS and this system provided an excellent model for Multiple Sclerosis. One of the really amazing results of being mentored by Dick Johnson is that each of us during this period (1970–1978) worked on newly developed virus models and many of us have continued to study these systems throughout our careers. I remember many late night discussions at the tissue culture hood with Ben Brooks about this time in Dick Johnson's laboratory and how we would look back on this time in the future. Ben always maintained that this was the 'golden period' for us and the laboratory, in terms of the varied research that was being done, the faculty (Bill Narayan, Diane Griffin, Jerry Wolinsky and Dick Johnson) who were part of the group and the fellows who were training together. Indeed I remember it as a critical time in my career development.

Dick Johnson has trained over 40 fellows since 1969, and it would be impossible to note all of them in this short article, however, there is a chronological list at the end so that everyone is included. Particularly notable is the number of Neurologists Dick Johnson has trained: Micheline McCarthy, MD, PhD, Patricia Coyle, MD, Alan Seay, MD, Gunther Schwendemann, MD, Walter Royal III, MD, Peter GE Kennedy, MD, PhD, Alan Jackson, MD, Thiravat Hemachudha, MD, William Tyor, MD, Martin Westarp, MD, Dana Gabuzda, MD, David Irani, MD, John Corboy, MD, Christopher Power, MD, Stephen Wesseling, MD and Justin McArthur, MD. The other remarkable thing is that most of Dick's fellows are still working in the areas of neurovirology. Among Dick Johnson's trainees there are four current Neurology department chairs and eight chairs of other academic departments.

With the advent of the AIDS epidemic, a new CNS disease emerged that was caused by HIV-1 infection of the nervous system. Dick Johnson was involved early on in the clinical evaluation of the disease and its outcome, in research efforts and in training the leaders in the NeuroAIDS field. Howard Gendelman

joined the research training program and worked closely with Dick and Bill Narayan on developing sensitive *in situ* hybridization techniques to examine replication of lentiviruses *in vivo* and *in vitro*, this training contributed to Dr Gendelman's continued interest and involvement in HIV-1 research. Steve Wesselingh, MD examined the role of cytokines in the CNS and showed an important correlation between the intracerebral TNF- α levels and AIDS Dementia. William Tyor, MD with Dick Johnson, Diane Griffin and Richard Markham, MD, PhD developed a SCID mouse model to study aspects of the CNS infection in this small animal model. Justin McArthur, MD worked closely with Dick on the clinical aspects of HIV infections in the CNS and has taken over many of the leadership roles in NeuroAIDS at Johns Hopkins since Dick retired.

Dick Johnson's research has had an enormous impact on how viral infections are studied and has pioneered an entirely new area of research, virus infections of the nervous system. Clearly his research has had a major impact on academic medicine. In addition, Dick's mentoring of the next several generations of virologists, neurologists, immunologists and neurovirologist will carry these areas into the next millennium. In speaking with Dick recently, he told me when he set up his laboratory at Johns Hopkins one of his major goals was to provide the setting to train fellows. It is clear that he was enormously successful in achieving that goal.

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<i>Postdoctoral Fellows</i>	<i>Period of Training</i>
Opendra Narayan, DVM, PhD	1970–1972
Howard L Lipton, MD	1970–1972
Henry F McFarland, MD	1970–1972
Diane E Griffin, MD, PhD	1970–1973
Laurence E Becker, MD	1972–1974
Ljiljana Kostovic, MD	1972–1973
Larry E Davis, MD	1973–1975

Jack S Burks, MD	1973–1975
Raymond P Roos, MD	1974–1976
John E Greenlee, MD	1974–1976
Mary Lou Oster-Granite, PhD	1974–1976
Maria Mazlo, MD	1975–1976
Janice E Clements, PhD	1975–1978
Benjamin R Brooks, MD	1976–1979
Burk Jubelt, MD	1976–1979
Jeffrey Swarz, PhD	1976–1979
Robert L Hirsch, PhD	1977–1979
Micheline McCarthy, PhD, MD	1977–1979
Patricia Coyle, MD	1978–1980
Alan Seay, MD	1978–1981
Bjorn Nexo, PhD	1979
Stephen Buell, PhD	1979–1980
Alfred Server, MD, PhD	1979–1981
Foroozan Mokhtarian, PhD	1979–1982
Mahin Park, PhD	1979–1980
E Gunther Schwendemann, MD	1980–1981
Suzanne Kennedy-Stoskopf, DVM, PhD	1980–1983
Jeff Stanley, MD	1981–1984
Howard Gendelman, MD	1982–1985
Thomas Moench, MD	1982–1985
Walter Royal III, MD	1983–1985
Peter GE Kennedy, MD, PhD	1984–1985
Victor Tamashiro, MD	1984–1986
Alan C Jackson, MD	1984–1987
Yin-Chang Yang, MD	1985–1986
Thiravat Hemachudha, MD	1985–1986
Kathryn Carbone, MD	1985–1988
Christine Zink, DVM, PhD	1985–1988
William Tyor, MD	1986–1988
Alexander Dromerick, MD	1968–1987
Guillermo van Weillink, MD	1987–1988
William Boggs, MD	1987
Martin E Westarp, MD	1987–1988
Dana Gabuzda, MD	1987–1989
David Irani, MD	1988–1990
Pamela Tucker, MD	1988–1991
Nikki Baumrind, PhD	1989–1991
Brian Ward, MD	1988–1991
Eithne McMahon, MD	1988–1992
John Corboy, MD	1989–1992
Beth Levine, MD	1990–1992
Judith Ryon, MD	1990
Christopher Power, MD	1990–1993
Stephen Wesselingh, MD	1991–1993
Lisa Esolen, MD	1991