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Donald H. Gilden Receives Pioneer in NeuroVirology Award for 2007

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Dr. Donald H. Gilden is Professor of Neurology and Microbiology and Chairman of the Department of Neurology at the University of Colorado School of Medicine. He has excelled as a clinician, teacher and researcher. He has published more than 270 papers, reviews, and book chapters.

Dr. Gilden's scientific contributions to neuroscience began early during his fellowship years at Johns Hopkins, where he analyzed the pathogenesis of acute lymphocytic choriomeningitis virus (LCMV) infection in mice. Contrary to the widely held notion at the time that LCMV antiviral immune complexes were responsible for disease in all organs, including the brain, Dr. Gilden showed that acute lymphocytic choriomeningitis (LCM) in brain was in fact cell-mediated. In an elegant series of experiments, he infected mice with LCMV, treated those mice with cyclophosphamide, which abrogated disease, and transferred LCMV-sensitized immunocytes to these immunosuppressed LCMV-carriers; the syngeneic recipients developed acute LCM in brain. This now-classic work actually provided a model for the studies of Doherty and Zinkernagel, which riveted attention on the importance of histocompatibility antigens in cell-cell recognition, work for which those investigators received the Nobel Prize. Dr. Gilden then showed that LCMV produced cerebellar hypoplasia in neonatal rats, thus providing an experimental model for developmental CNS abnormalities produced by virus infection, which were previously thought to be exclusively genetic. In the 1970s, Dr. Gilden devoted considerable effort toward the isolation of a virus from tissues derived from individuals who had suffered from multiple sclerosis (MS) using tissue culture explant techniques. Although these studies did not find a viral cause of MS, they constituted a complete and detailed body of work for the application of these methods to a human disease of suspected viral etiology.

Despite more than 100 years of speculation that varicella zoster virus (VZV) was latent in human ganglia, virus could not be found using standard techniques of explantation of human ganglion cells *in vitro*, or by cocultivation or cell fusion of ganglionic cells with indicator cells. Using molecular biological methods, Dr. Gilden was the first to detect VZV DNA in normal human ganglia. After proving VZV latency, Dr. Gilden directed studies on the physical state of viral nucleic acid and gene expression in latently infected human ganglia, leading to several milestones in VZV research, including the first detection of the entire viral genome in human ganglia along the entire neuraxis; the first demonstration of the circular configuration of latent VZV DNA; the first demonstration of its highly variable abundance; the first identification of five VZV transcripts during latency, and finally the demonstration that VZV was latent exclusively in neurons of human ganglia. Dr. Gilden's studies on VZV latency provided experimental evidence that shingles (rash and pain in a restricted dermatome usually lasting 4-6 weeks) is due to VZV reactivation and not new infection. His work also explained universal susceptibility to such reactivation and why shingles develops anywhere on the body. His nearly 30 years of work on VZV has led the field in basic science research on VZV latency and has had profound clinical implications for human disease.

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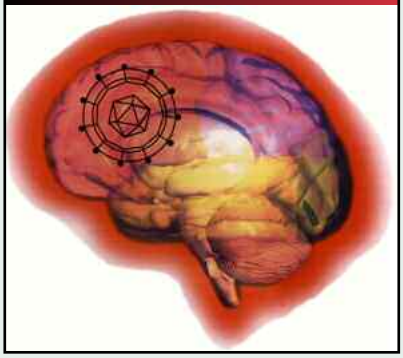
Many patients with shingles experience pain that persists for months to years, a syndrome called postherpetic neuralgia (PHN). Because ganglia cannot be studied during the life of the patient and because PHN is not fatal, Dr. Gilden analyzed blood mononuclear cells and detected VZV-specific protein and DNA in these cells in many patients with PHN, but not in blood mononuclear cells of age- and gender-matched shingles patients who did not develop PHN. Dr. Gilden's detection of more widespread infection provided the first rationale for antiviral therapy, which has now shown efficacy in a series of PHN patients. In addition to Dr. Gilden's contributions to the understanding of VZV latency and PHN, he discovered that VZV "encephalitis" is actually a vasculopathy with virus production primarily in cerebral arteries rather than brain cells. From laboratory to bedside, Dr. Gilden showed that the spectrum of VZV vasculopathy is considerable, with unifocal vasculopathy predominant in immunocompetent individuals, while multifocal vasculopathy occurs mostly in immunocompromised individuals. He showed that rash is not required for diagnosis and that virologically-verifiable VZV vasculopathy may develop as late as 6 months after zoster (shingles) and still be treated successfully. Importantly, Dr. Gilden also showed that the detection of anti-VZV IgG in the CSF is a significantly more sensitive indicator of VZV vasculopathy than detection of VZV DNA by PCR.

Dr. Gilden remains active in the field of MS research. He has developed a cadre of investigators who have identified clonally expanded plasma cells in the brain and cerebral spinal fluid (CSF) of patients with MS and subacute sclerosing panencephalitis (SSPE). Using single-cell RT-PCR, investigators working in the Gilden laboratory have identified over-represented heavy- and light-chain immunoglobulin sequences, which have been used to produce recombinant monoclonal antibodies. In SSPE, such antibodies produced from brain or CSF were directed against measles virus, the cause of SSPE. Parallel studies in MS have identified clonal populations of plasma cells that are antigen-driven. These MS antibodies have not yet identified an antigen unique to MS, but are not directed against normal or diseased brain white matter, nor any white matter proteins (MBP, PLP, MOG, and MAG). Investigators in the Gilden laboratory appear on track towards identifying a low-abundance, novel antigen that is likely to be the trigger, if not the cause, of MS.

Nearly 22 years ago, Dr. Gilden became Chairman of a small academic Department of Neurology at the University of Colorado. Since that time, the Department has tripled in size, due mainly to Dr. Gilden's efforts in rigorously identifying and recruiting outstanding clinician-educators and clinician-scientists. In 1991, Dr. Gilden received the Alumni Award for Distinguished Service from the University of Chicago School of Medicine. In 1994, he was elected to the Association of American Physicians. For the past 12 years, he has been elected by fellow neurologists as one of the Best Doctors in America. In 2003, he was elected to Fellowship in the American Association for the Advancement of Science. In 2006, he was elected to the Johns Hopkins Society of Scholars. In 2007, he was awarded honorary membership in the American Neurological Association. He has generously served in multiple professional and scientific societies and on numerous editorial boards, and on NIH and National Multiple Sclerosis Society study sections. Dr. Gilden continues to receive active research support from the NIH, and in an age of increasing specialization, his work represents an extraordinary integration of cutting-edge molecular technology and clinical medicine.

2009 Pioneer In Neurovirology Award



REQUEST FOR NOMINATIONS

Awardee to be announced at the 9th International Symposium on NeuroVirology to be held in 2009.

Nominations should be forwarded to:

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