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Guest Editorial

The biology of JC virus and progressive multifocal leukoencephalopathy

It has been 30 years since the original isolation of the human polyomavirus JCV from brain tissue of a PML patient whose initials, JC, now bear the name of the virus. Throughout much of that time, JCV and PML have been relegated to what best is described as a "back of the textbook" topic, only of concern after the more prominent virus associated CNS infectious diseases have been discussed. There are several reasons for this. JCV had been a difficult viral agent to manipulate for laboratory study and PML had been a rare disease in immune compromised patients. Although the population worldwide becomes infected early in life with JCV, the presence of antibody to JCV is neither diagnostic for PML nor prognostic for treatment. For almost half of those 30 years, the number of investigators and clinicians who worked on JCV and PML formed a small community of scientists whose measured progress was recorded in just a few, select journals. In the mid-1980s, all that began to change; and that change has continued at an ever increasing pace. The reasons for a JCV/PML revolution are simple enough: AIDS and technology.

As it has been documented throughout the United States and Europe, the incidence of PML remains high in AIDS patients, from 5% to 8% in most studies. PML also can be the defining illness for AIDS in an HIV-1 infected patient and is more frequently considered in a differential diagnosis for leukoencephalopathy. There have been more PML patients diagnosed in the past several years than in the previous several decades. What has assisted the recognition of PML in no small measure have been technical advances in molecular methods from nucleotide probe development to DNA amplification procedures. This has greatly accelerated the experimentation of the complex gene regulation of JCV in cell culture studies and also allowed highly sensitive and specific detection of viral products in brain and CSF samples. It is now possible, and routine, to track and quantitate JCV genomic DNA or proteins throughout the course of infection from lymphoid tissues to kidney epithelium to peripheral lymphocytes and into the brain. Diagnosis of PML has been greatly enhanced by use of JCV DNA detection, and quantitative measurement of the DNA holds promise for risk assessment and therapeutic response. These advances are already being expedited by trials of the Neurologic AIDS Research Consortium (NARC).

Recognizing the rapid accumulation of data and in-depth understanding of JCV pathogenesis leading to PML, basic and clinical scientists met for a 2-day workshop to exchange information, share ideas, and plan for future studies on the molecular aspects of JCV biology and for new therapeutic avenues for treatment of PML patients. Under the sponsorship of the NARC with support of the National Institute of Neurological Disorders and Stroke, a group of investigators, equally divided from laboratories and hospitals, gathered to discuss data on the state of the art of this field. The Workshop on the Biology of JCV and PML was the first time that such a conference was held in this area and the first time that basic and clinical scientists met for the sole purpose of updating each other on the major issues and challenges of understanding the process of a viral induced demyelinating disease.

The research reports in this special issue of the Journal highlight that meeting and provide details of knowledge now available on JCV, the progress in conducting clinical trials, and the difficulties still ahead when full knowledge of JCV and PML will give rise to effective treatment paradigms derived from the fundamental understanding of JCV pathogenesis of the human nervous system.

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