Journal of NeuroVirology, 10(suppl. 2): 29, 2004

ISSN: 1355-0284 print / 1538-2443 online
DOI: 10.1080/13550280490469725

Taylor & Francis
Taylor & Francis Group

Human polyomaviruses and autoimmunity to components of chromatin

U Moens and OP Rekvig

Department of Biochemistry, Faculty of Medicine, University of Tromsø, Tromsø, Norway

The presence of antibodies against nuclear components, including dsDNA and histones, serves as diagnostic markers for systemic lupus erythematosus (SLE) and may be involved in disease development. The etiology of these autoimmune responses is still largely unknown. One pathway has, however, been linked to polyomavirus infections in an experimental and natural context. The polyomaviruses BK (BKV) and JC (JCV) establish a latent infection in the majority of the normal human population. Reactivation of BKV and JCV, as determined by presence of viral sequences in urine or transient antibody production against large T-antigen, is rarely encountered in healthy individuals. Intermittent or chronic BKV and JCV reactivation occurs frequently in individuals with perturbed immune conditions, including SLE patients. A prerequisite for reactivation is expression of the early viral protein large T-antigen, a DNA-binding protein necessary for both viral DNA replication and gene expression. Our studies have shown that BKV and/or JCV initiate autoimmunity to nucleosomes in animals and humans by a process where large T-antigen binds host cell chromatin, thereby rendering this complex immunogenic. The large T-antigen-chromatin complex may function as a hapten-carrier model with potential to stimulate the immune system to produce anti-chromatin antibodies, including pathogenic anti-dsDNA and anti-histone antibodies. Sequence analyses of the transcriptional control regions of BKV and JCV in urine of SLE patients revealed no major differences with those described in the healthy human population, arguing against SLE-specific strains. The basis for BKV/JVC reactivation and the mechanism for anti-DNA antibody-mediated nephritis in SLE patients remain unsolved.