Serological and Molecular Detection of HHV-8 in Brazilian Populations

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Little is known about human herpesvirus 8 (HHV-8) distribution in Brazil. We used indirect immunofluorescence serological assays to determine HHV-8 seroprevalence in two Amerindian tribes from the Amazon region, and blood donors and Kaposi's sarcoma (KS) patients from the Campinas/SP (Southeastern region). Anti-HHV-8 antibodies were detected in 56.8% of the Amerindians (558/982), in all ages (0-81 years old) and both sexes. In these populations, high prevalence in children younger than 2 years old (44.4%) and children from 2 to 9 years old (35.0%) suggests non-sexual routes of HHV-8 transmission, through vertical transmission or contact to contaminated secretions. HHV-8 seroprevalence in blood donors from Campinas/SP was low (2.8%) and all positive cases were male (9/319) in the fourth and fifth decades of life. Curiously, these individuals were negative to routine serological tests applied in blood banks. Every KS patient assessed in our study was male, with average age of 37 years (27 to 79 years) and anti-HHV-8 positive assays in all cases.

In order to determine HHV-8 molecular prevalence, we analyzed DNA from three Amerindian tribes from the Amazon region, KS patients from Campinas/SP and HIV patients from Salvador/BA (Northeastern region). We used Nested-PCR to amplify HHV-8 ORF-26 region by molecular screening. Every ORF-26 amplified sample was also amplified to hypervariable ORF-K1 region for HHV-8 genotyping. We analyzed 384 DNA samples from Amerindian tribes and detected HHV-8 sequences in 3.8% (13/384). KS patients had all DNA samples from skin biopsies and 45.5% from peripheral blood (PBMC) amplified. DNA samples from 148 HIV positive patients were analyzed and HHV-8 sequences were detected in 4% of cases (6/148). Almost all positive DNA samples were amplified to ORF-K1 and determined HHV-8 subtypes.

Molecular techniques for amplification and sequencing of two fragments (VR1 and VR2) from ORF-K1 region made possible to build up phylogenetic trees and determine HHV-8 main viral subtypes (A, B, C, D and E) and its variants. Patients with KS from Campinas had subtypes A, B and C detected, with greater frequency of subtype C. Subtypes A and E were detected in Amazon Amerindians. This study is the first to perform genotyping in samples of HIV positive patients from Salvador, detecting subtype B and an unclassified subtype. Thus, it was possible to determine that HHV-8 subtypes A, B, C and E are present in Brazilian populations.
As Brazil is a large country with variable population, culture and different geographical characteristics, more HHV-8 epidemiological studies are necessary to establish possible regional differences.

This study was supported by grants from the Conselho Nacional de Pesquisa (CNPq) and Fundação de Apoio à Pesquisa na Bahia (FAPESB).

Innate Immune Immunity and Viral Therapy of Cancer

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Activation of host innate immune responses following virus infection is largely mediated by viral dsRNA, the mechanisms of which remain to be fully determined. We have recently reported that murine embryonic fibroblasts (MEFs) lacking the death adaptor molecule FADD are defective in double-stranded RNA (dsRNA)-activated antiviral gene expression, including Type I interferon (IFN), and thus predisposed to virus infection. The dsRNA signaling pathway incorporating FADD was found to be largely independent of Toll-like Receptor (TLR)-3, tumour-necrosis factor (TNF) receptor-associated factor 6 (TRAF6) and the dsRNA-dependent protein kinase, PKR, though obligated TBK1 activation of IRF3. The requirement for FADD in innate immune responses is evocative of the *imd* pathway in Drosophila, which involves an *imd*/dFADD complex that responds to bacteria