Retrovirology

BioMed Central

Oral presentation

Characterization of specific HHV-6 and cell cycle genes implicated in virus-mediated G1/S cell-cycle arrest of glial precursors

David J Mock*[1], Pauline Chugh[2], Baek Kim[2], Christoph Pröschel[3], Jöerg Dietrich[3], Frederick Strathmann[4], Benjamin M Blumberg[1] and Margot Mayer-Pröschel[3]

Address: [1]Department of Neurology, University of Rochester School of Medicine and Dentistry, 601 Elmwood Avenue Rochester, New York, 14642, USA, [2]Department of Microbiology and Immunology, University of Rochester School of Medicine and Dentistry, 601 Elmwood Avenue Rochester, New York, 14642, USA, [3]Department of Biomedical Genetics, University of Rochester School of Medicine and Dentistry, 601 Elmwood Avenue Rochester, New York, 14642, USA and [4]Department of Pathology, University of Rochester School of Medicine and Dentistry, 601 Elmwood Avenue Rochester, New York, 14642, USA

* Corresponding author

from 2006 International Meeting of The Institute of Human Virology
Baltimore, USA. 17–21 November, 2006

Published: 21 December 2006

Retrovirology 2006, **3**(Suppl 1):S65 doi:10.1186/1742-4690-3-S1-S65

Human herpesvirus 6 (HHV-6), a common resident virus of the human central nervous system (CNS), has been implicated in both acute and chronic inflammatory-demyelinating diseases. HHV-6 persists within the human CNS and has been described to infect mature oligodendrocytes and astrocytes. We recently demonstrated that HHV-6 infects human glial precursor cells, the ancestors of myelin producing oligodendrocytes, in vitro. Productive infection was demonstrated by both electron microscopy and expression of viral gene transcripts and proteins. Infection led to impairment of cell replication but not increased cell death. Infected cells showed decreased proliferation as measured by BrdU uptake and demonstrated strong G1/S-phase inhibition by FACS. We now present evidence detailing both specific viral and cell cycle genes inducing cellular G1/S cell cycle arrest. In parallel with human cells, the well characterized rodent oligodendroglial progenitor cell (OPC) system was used. Restricted infection of the murine cells was demonstrated by quantitative PCR, EM, and RT-PCR, and IFA for viral late proteins but, intriguingly, reproduced the G1/S arrest seen after productive virus infection of human progenitors. Restricted infection of murine OPCs was also found to be sufficient to induce the activation of DNA damage pathways previously reported by our group in human glial progenitors (ISNV 2004) and after productive infection in human lymphocytes (Oster et al. 2005). IFA and immunoblot again demonstrated expression of phospho-ATM, CHK-2, and p53 in infected murine precursors and two viral IE proteins were sufficient to induce G1/S arrest. Virus-induced cell-cycle arrest was accompanied by GalC+ differentiation with corresponding loss of the OPC pool as had been previously seen in the human precursors. Enhanced GFP-expressing murine OPCs have been created that can be readily infected with ALEXA-632-labeled HHV-6, allowing both sorting for infected cells and their identification in evaluating repair in demyelinated mice. In light of recent observations that repair of CNS remyelination is dependent on the generation of mature oligodendrocytes from the glial precursor cell pool, these findings may have broad implications for both the ineffective repair seen in human demyelinating diseases and the disruption of normal glial differentiation.