Abstract:

BACKGROUND: HIV can reside in the brain for many years. While astrocytes are known to tolerate long-term HIV infection, the potential of other neural cell types to harbour HIV is unclear. OBJECTIVE: To investigate whether HIV can persist in neural progenitor cell populations. DESIGN: A multipotent human neural stem cell line (HNSC.100) was used to compare HIV infection in neural progenitor and astrocyte cell populations. METHODS: Expression of cellular genes/proteins was analysed by real-time reverse transcriptase PCR, Western blot, immunocytochemistry and flow cytometry. Morphological properties of cells were measured by quantitative fluorescent image analysis. Virus release by cells exposed to HIV-1IIIB was monitored by enzyme-linked immunosorbent assay for Gag. Proviral copy numbers were determined by real-time PCR and early HIV transcripts by reverse transcriptase PCR. Rev activity was determined with a fluorescent-based reporter assay. RESULTS: Progenitor populations differed from astrocyte populations by showing much lower glial fibrillary acidic protein (GFAP) production, higher cell-surface expression of the CXCR4 chemokine receptor, higher Rev activity and distinct cell morphologies. HIV-exposed progenitor cultures released moderate amounts of virus for over 2 months and continued to display cell-associated HIV markers (proviral DNA, early HIV transcripts) during the entire observation period.
Differentiation of HIV-infected progenitor cells to astrocytes was associated with transient activation of virus production. Long-term HIV infection of progenitor populations led to upregulation of GFAP and changes in cell morphology. CONCLUSION: These studies suggest that neural progenitor populations can contribute to the reservoir for HIV in the brain and undergo changes as a consequence of HIV persistence.