HIV-1 Vpr Causes Synaptodendritic Damage in Neurons

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ABSTRACT

HIV weakens the immune system by infecting and destroying T-cells, leaving the body vulnerable to infection and the development of AIDS. Conventional treatments for HIV, such as combined anti-retroviral therapy (cART), fail to prevent the development of HIV-associated neurocognitive disorder (HAND). Neurological dysfunction has been directly related to the invasion of HIV in the central nervous system (CNS). HIV produces neurotoxic proteins, such as the Viral Protein R (Vpr), which contribute to HAND. Astrocytes are the most abundant cells in the brain and an important HIV target. We hypothesize that astrocytes expressing Vpr will cause neuronal damage in our co-culture system. Primary astrocytes were transfected with Vpr plasmid or control (pEGFP or mock) using electroporation. Astrocytes were then co-cultured with cortical neurons. At 48 and 72 hours we collected the primary astrocytes to confirm the Vpr expression via western blot analysis. We then measured structural damage in the neurons using immunofluorescence for cytoskeletal (MAP2, f-actin) and synaptic (synaptophysin) damage. Preliminary results showed strong staining of filamentous actin and MAP2 with weak detection of synaptophysin. The positive control for neurotoxicity (2.8μM acrylamide) showed substantial damage to the cellular structure. Results for Vpr expression are pending. After confirming that the immunofluorescence assays are working with our controls, we expect to detect any synaptodendritic damage in the neurons caused by Vpr in our upcoming experiments.

Key Words: synaptodendritic, neurocognitive, synaptophysin, MAP2, cART

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