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Retroviral Infection of Human Neurospheres and Use of Stem Cell EVs to Repair Cellular Damage

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HIV-1 remains an incurable infection and HIV-associated neurocognitive disorders are reported to affect at least 50% of infected individuals despite cART treatment. Recently, neurospheres derived from iPSCs have been used to model the effects of neurotropic viruses. Here, we report the generation of neurospheres from iPSC-derived neural progenitor cells (1). Our data suggests these cultures contain microglia-like cells that are permissive to retroviral infection, as well as the induction of cytokines and reversal with Cannabidiol. However, repair of infected cells requires additional treatments. Stem cells have broad therapeutic potential and stem cell therapy has been evaluated for CNS repair. While the exact mechanisms are unknown, it is believed that extracellular vesicles (EVs) mediate many of their functional effects. Because of their small size, stability, and low immunogenicity, EVs hold high therapeutic potential, especially for CNS pathologies since they can cross the blood-brain-barrier (2, 3). Here, we also report the isolation of high yields of EVs from iPSCs and mesenchymal stem cells. Our EV characterization includes phenotypic (size, tetraspanin expression), biochemical (protein, cytokine, RNA), and functional analysis (3,4). Consistent with the literature, our data suggests that stem cell EVs may modulate neuroprotective and anti-inflammatory properties in damaged and/or infected CNS cells (1, 4). Collectively, this data demonstrates the feasibility of NPC-derived neurospheres for modeling HIV-1 infection and highlights the potential of stem cell EVs for rescuing cellular damage induced by HIV-1 infection.

References:
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