Role of Autophagy on HIV Tat-Induced Intracellular Calcium Release in Murine Astrocytes

Maytin, Amanda

Astrocytes, the most abundant cell type in the central nervous system (CNS), have the vital role of keeping homeostasis in the brain. HIV infects the CNS early after primary infection and causes neurological complications. When HIV infects astrocytes, virions and viral proteins signal the release of inflammatory cytokines and metabolic compounds, such as calcium, which can be further aggravated by opiate use, such as morphine. Earlier studies have shown that calcium release by astrocytes is enhanced by HIV and that excess amounts of calcium can be toxic to neuronal cells in the CNS. Although the effects of HIV on astrocytic functions are known, the exact mechanism that leads to astrocytic dysfunction is unknown. The autophagy pathway is a catabolic process that rids of unnecessary cytoplasmic material in cells. Earlier studies have shown that imbalances in the autophagy pathway can cause neurodegeneration such as Alzheimer's and Parkinson's disease. Therefore, we explored whether imbalances in autophagy modulates HIV-induced calcium release in astrocytes. Astrocytes from wild type (WT+/+) mice and autophagy deficient mutant (Atg6+/-) mice were treated with HIV protein Tat and/or morphine. Intracellular calcium was measured in murine astrocytes labeled with fura-2AM. Ratio metric calcium measurement was acquired at 340/380 nm excitation and 510 nm emission wavelengths using Zeiss inverted fluorescent microscope with environmental control (37°C, 95% humidity, 5% CO2). Our studies showed that decreased levels of autophagy resulted in lowered levels of intracellular calcium in astrocytes. These results suggest that autophagy can serve as a potential therapeutic target to treat HIV-induced neurocognitive disorders.

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