Ferroptosis Sensitivity of HIV-Uninfected vs. HIV-Infected Human Microglia

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An estimated 30-50% of people with HIV experience HAND (HIV-associated neurocognitive disorder). HAND may be influenced by ferroptosis, i.e., iron-regulated cell death linked to oxidative stress and lipid peroxidation. Ferroptosis is associated with cognitive deterioration in other degenerative diseases like Alzheimer's disease. We investigated possible associations between HIV infection and ferroptosis in microglia and the development of HAND. To investigate whether HIV infection is associated with ferroptosis-induced cell death in microglia, we compared quantities of four ferroptosis-related proteins in HIV latently infected (GFP-), actively infected (GFP+), and HIV uninfected microglia. GFP (Green Fluorescent Protein) indicated active HIV infection. We serially diluted HIV- and GFP- microglia using erastin (a ferroptosis inducer) and used automated cell counters to plot proportions of live cells vs exposure time. We measured ferroptosis in HIV-, GFP-, and GFP+ microglia using varying concentrations of erastin and ferrostatin-1 (a ferroptosis inhibitor/control). We used enzyme-linked immunosorbent assays (ELISAs) to determine quantities of four different ferroptosis-associated proteins in HIV-, GFP, and GFP+ microglia. HIV- and HIV+/GFP- microglia experienced similar survival rates in the serial dilution with erastin. ELISA results suggested that HIV+/GFP+ microglia had increased quantities of the proteins FTH1 (ferritin heavy-chain 1) and SLC3A2 (co-factor for SLC7A11) compared to HIV+/GFP- cells, which may protect GFP+ cells from ferroptosis. HIV+ and HIV- microglia have suggested differences in rates of ferroptosis as reflected in quantities of the proteins FTH1 and SLC3A2.

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