CNS is a site of HIV persistence which can lead to virologic failure

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HIV infection persists despite antiretroviral therapy (ART) due to cellular reservoirs and most often results in rebound of drug sensitive virus if therapy is interrupted. The central nervous system (CNS) may serve as one anatomical site for the cellular HIV reservoir due to lowered ART penetration and possible production of virus from long lived cells such as tissue resident macrophages. Here, we asked whether virus from individuals showing CNS escape, where HIV is suppressed below the limit of detection in the blood but detectable in the cerebrospinal fluid (CSF), is derived from macrophage origin cells or persists but does not evolve due to lowered ART penetration. We assayed cellular source by detecting cell surface markers on the HIV envelope. We observed surface markers consistent with a T cell viral origin. We also measured the concentrations of antiretroviral drugs in the CSF and blood and observed a dramatic median reduction in the concentration of the first line ART agent efavirenz and to a lesser extent emtricitabine and tenofovir. To examine whether this reduction in drug penetration was sufficient for replication of drug sensitive virus, we performed in vitro evolution at drug concentrations found in the individuals with CSF escape. ART levels were sufficiently high to lead either evolution of drug resistance or decline in viremia. These observations argue that the CNS may be a source of drug resistant virus but unlikely to be a reservoir for drug sensitive HIV.

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