Liver Macrophages and HIV-1 Persistence

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Abstract

Background: Cellular reservoirs of HIV-1 infection that persist despite combination antiretroviral therapy (cART) are a major target of cure strategies. The tissue macrophage (TRM) niche may represent a reservoir of HIV-1 infection. We hypothesized that liver macrophages (LM) in human liver transplant recipients (HLT) may harbor HIV-1 that is resistant to cART.

Methods: From a cohort of 24 unrelated HLT recipients who were cART-suppressed at liver explantation, liver explants from patients with cART-detected HIV-1 proviral DNA (LT01: 2.4 cp/10^6 cells; LT02: 4.9 cp/10^6 cells). Reporter cells treated with LM supernatants were tested periodically for the presence of viral RNA. To assess their role in vivo, LT01 and LT02 LM were maintained ex vivo for 36 and 95 days, respectively, with or without cART.

Results: LT01 and LT02 LM were purified from liver explants taken from HIV-1 infected persons with uncontrolled (n=1) and cART-suppressed viremia could transmit infectious HIV-1 after a prolonged duration; therefore, LM may represent an important reservoir of HIV-1 infection and potential impediment to cure.

Conclusions: T cell count, cART status, and plasma HIV-1 RNA levels did not correlate with HIV-1 RNA levels in LM. These findings suggest that liver macrophages (LM) may serve as a reservoir of HIV-1 infection that is resistant to cART.

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Introduction

Clinical evidence has revealed that HIV-1 cure is possible. However, long-lived tissue macrophages of HIV-1 which exist in all patients may play a major role in HIV-1 persistence.