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Cell-intrinsic HIV-1 immune responses in conventional dendritic cells from HIV-1 elite controllers

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Background: Recent data suggest that conventional dendritic cells (cDC) are able to mount cell-intrinsic immune responses against HIV-1. However, in the majority of infected individuals, such immune activity is blocked by the host proteins Samhd1 and Trex1 that reduce the accumulation of early HIV-1 replication products. Elite controllers (EC) are able to control HIV-1 replication in the absence of treatment, but immune defense mechanisms in these patients are incompletely understood. Here, we investigated cell-intrinsic immune responses to HIV-1 in cDC from these patients.

Methods: PBMC from EC, untreated chronic progressors (CP), HAART-treated and HIV-1 negative subjects were ex vivo infected with HIV-1. Cellular expression of viral replication products, type I interferons, Samhd1 and Trex1 were analyzed by qPCR.

Results: Paradoxically, we observed the highest susceptibility to HIV-1 infection in cDC from HIV-1 negative persons, while cDC from EC and CP only very weakly supported HIV-1 replication. Yet, reasons for reduced susceptibility to HIV-1 in CP and EC were different: In CP, HIV-1 replication was blocked at the level of early reverse transcription, likely as a result of high-level Samdh1 expression. In EC, reverse transcription was unaltered, and inhibition of HIV replication mostly occurred at the level of viral integration. Functionally, these altered patterns of viral replication dynamics in cDC from EC were associated with increased activation and secretion of type I interferons.

Conclusion: Our data suggest specific alterations of HIV-1 replication patterns in cDC from EC that enable the generation of cell-intrinsic HIV-1 immune responses, while simultaneously blocking productive HIV-1 replication.