OPEN ACCESS Freely available online

HIV: Current Research

ISSN: 2572-0805

Opinion Article

HIV Cure: Stable Persistence of Integrated Proviruses within CD4 T Cells during Antiretroviral Therapy

Arsalan Grace*

Department of Medicine and Health Science, University of Bost, Lashkar Gah, Afghanistan

DESCRIPTION

The specific function of CD4 T cell turnover in Human Immunodeficiency Virus (HIV) persistence during Antiretroviral Treatment (ART) has yet to be determined. This study directly measured cellular turnover by heavy water labelling in resting CD4 T cell subpopulations from 24 HIV-infected ART-suppressed and 6 HIV-uninfected individuals, HIV reservoir size by integrated HIV-DNA (intDNA) and cell-associated HIV-RNA (caRNA), and HIV reservoir clonality by proviral integration site sequencing. ART-suppressed people showed identical fractional replacement rates in all subpopulations, but lower absolute proliferation rates in all subpopulations except Effector Memory T cells (TEM), and lower plasma IL-7 levels (p=0.0004) compared to HIV-negatives. The median half-life of CD4 T cells decreased with cell differentiation from naive to TEM cells (3 years to 3 months, p0.001).TEM exhibited the quickest replacement rates, the greatest intDNA and caRNA enrichment, and the most clonal proviral growth. Clonal proviruses found in less mature subpopulations were found to be more enlarged in TEM, suggesting that they were retained through cell differentiation. Lower levels of intDNA, caRNA, and fractional replacement rates were related with earlier ART commencement. In conclusion, circulating integrated HIV proviruses appear to be maintained *via* clonal expansion as well as cell differentiation into effector cells with quicker replacement rates, as well as sluggish turnover of immature CD4 subpopulations.

The persistent survival of integrated proviruses within CD4 T cells throughout antiretroviral treatment is the greatest impediment to an HIV cure. Although ART suppresses active viral replication, replication-competent virus reservoirs exist in latently infected cells, and viral rebound occurs when ART is stopped.

Homeostatic processes guiding the maintenance of a varied CD4 T cell repertoire are hypothesized to impact the cellular makeup of the HIV reservoir. The number and location of the CD4 T cell population are determined by the generation of new progenitor cells, cell maturation, trafficking, homeostasis, and antigen-driven proliferation. Although less typically infected than more mature subpopulations, naive and stem-cell memory CD4 T cells may support long-term viral persistence due to their renewal characteristics and extended lifespan. *Via* unknown processes, more developed memory populations are enriched for HIV proviruses. Homeostatic cytokines (such as interleukin-7 or IL-7) enhance thymopoiesis and the survival of progenitor cells (such as naive and central memory cells), whereas antigenic stimulation and other cytokines (such as IL-15) stimulate the growth of highly differentiated cells.

Considering the importance of memory cell homeostasis in reservoir maintenance, investigations of T cell proliferation, differentiation, and death in HIV illness are required. Most previous research has concentrated on the turnover of bulk CD8 and CD4 T cell populations as determined by radioisotope. Untreated chronic HIV infection has been linked to shorter half-lives in subpopulations of the bulk CD4 T cell population, as well as reduced production rates, which return to normal when ART is initiated. A biphasic pattern in the memory/effector cell population, reflecting shorter-lived and longer-lived subpopulations, and a low-level proliferation rate in the longer-lived subpopulation, attributable to naive CD4 T cells, have been identified.

CONCLUSION

The validation of novel phenotypic markers that characterize different maturational phases of CD4 T cell subpopulations now allows to define the turnover of distinct subpopulations and investigate the association between such turnover and HIV persistence during ART. Due to the fact that HIV proviruses integrate into numerous distinct places in the cellular genome, integration site analysis may be utilized to identify cells that have clonally propagated from a single infected progenitor cell that has the same integration site. Long-term ART-mediated viral suppression appears to select for genetically-identical HIV variants *in vivo*, and specific HIV integration sites (often in genes involved in cell proliferation and survival) have been linked to clonal expansion and persistence of infected cells in the periphery during effective ART, with up to 40% of distinct integrants clonally expanding and persisting longitudinally.

Correspondence to: Arsalan Grace, Department of Medicine and Health Science, University of Bost, Lashkar Gah, Afghanistan, E-mail: graceh38@yahoo.com

Received: 14-Feb-2023, Manuscript No. HICR-23-23294; **Editor assigned:** 16-Feb-2023, PreQC No. HICR-23-23294 (PQ); **Reviewed:** 07-Mar-2023, QC No. HICR-23-23294; **Revised:** 15-Mar-2023, Manuscript No. HICR-23-23294 (R); **Published:** 24-Mar-2023, DOI: 10.35248/2572-0805.23.8.223

Citation: Grace A (2023) HIV Cure: Stable Persistence of Integrated Proviruses within CD4 T Cells during Antiretroviral Therapy. HIV Curr Res. 8:223.