[SHORT TALK AND POSTER]

PERSISTENCE OF REPLICATION COMPETENT HIV-1 RESERVOIRS UNDER ART IN CENTRAL MEMORY TH17 CELLS

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BACKGROUND: Persistence of HIV reservoirs in a small fraction of central memory (CM) CD4+ T-cells is a major barrier against eradication under ART. We previously demonstrated that CD4+ T-cells expressing the Th17 marker CCR6 are highly permissive to HIV replication *in vitro* and that *retinoic acid* (RA) increases both imprinting for gut-homing and HIV integration/replication in these cells. Thus, we investigated the contribution of CM Th17 cells to HIV persistence under ART and used different strategies including RA to reverse HIV latency.

METHODS: Leukapheresis from 12 ART-treated HIV-infected subjects with undetectable plasma viral load and median CD4 counts of 520 cells/µl were available for this study. CM (CD45RA-CCR7+) CD4+ T-cells expressing or not CCR6 were sorted by flow cytometry. Cells were stimulated with CD3/CD28 Abs and IL-2 and/or RA for 10 days. Integrated HIV-DNA was quantified by nested real-time PCR *ex vivo* and upon culture. Quantification of intracellular HIV-p24 expression and levels of HIV-p24 and HIV-RNA in cell culture supernatants revealed HIV reactivation.

RESULTS: CCR6+ T-cells with CM phenotypes and Th17 polarization profile harbored the highest integrated HIV-DNA levels. HIV reservoir reactivation was induced upon TCR triggering and amplified by RA, even in subjects with undetectable integrated HIV-DNA.

CONCLUSIONS: CM Th17 contribute to the persistence of replication competent HIV reservoirs under ART. Understanding molecular mechanisms of HIV latency in Th17 cells is critical for the design of new cell-specific therapeutic strategies aimed at viral eradication and mucosal immunity restoration.