Peripheral Blood CCR4+CCR6+ and CXCR3+CCR6+ CD4+ T-Cells are Highly Permissive to HIV-1 Infection

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Helper T-Cell Lineage Specification
A New Understanding of CD4+ T-Cell Functional Heterogeneity

Zhou L et al., Immunity, 2009
Chemokine Receptors are Markers for CD4+ T-Cells with Distinct Lineage Commitment and Antigenic Specificity

- **CXCR3** regulates cell migration into inflamed tissues including the gut
- **CCR4** regulates cell migration into skin tissues
- **CCR6** mediates cell homing into the GALT

⇒ The permissiveness to HIV infection of these four memory CD4+ T-cell subsets remains unknown

**Acosta-Rodriguez et al., Nat. Immunol., 2007**
CCR4, CXCR3 and CCR6 Identify CD4+ T-Cells Subsets Expressing Cytokines and Transcription Factors Specific for Th17, Th2, Th1Th17, and Th1 Lineages

Mann-Whitney test

Expression of the HIV Coreceptors CCR5 and CXCR4 on CD4+ T-Cells Expressing CCR4, CXCR3 and/or CCR6

Mann-Whitney test

CCR4+CCR6+ (Th17) et CXCR3+CCR6+ (Th1Th17) T-Cells are Highly Permissive to R5 and X4 HIV Replication

Altered Heterogeneity of CD4+ T-Cells in HIV-Infected Patients Despite CD4 Count Normalization under ART

Preferential Permissiveness to HIV-DNA Integration and Depletion of Memory CCR6+ T-Cells in HIV-Infected Patients

Mann-Whitney test

Expression of the Gut-Homing Integrin $\beta 7$ on CD4+ T-Cell Subsets Expressing CCR4, CXCR3 and/or CCR6

Mann-Whitney test
Conclusions and Significance

Infiltration of CCR6+ Th17 and Th1Th17 cells into sites of HIV replication in vivo (e.g., gut, vaginal mucosa, lymph nodes, and brain)
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