Follicular Helper T Cells Serve as the Major CD4 T-Cell Compartment for HIV-1 Infection, Replication and Production

1. ABSTRACT

Background. Follicular helper T (TFH) cells are the primary autocrine components for follicular generation of the immune response and for HIV replication and spreading. TFH cell helper cells (TH cells) reside within the germinal center (GCs) and are specialized in providing B-cell help, especially the transcription factor BCL-6, the chemokine receptor CXCR5, FOXP3 and PD-1. Recently, studies have shown an expansion of TFH cells in HIV and Simian Immunodeficiency Virus (SIV) infections, and that TH cells are beneficial for HIV infection. However, limited data are available on the HIV infection of TH cells and their role as a potential reservoir for HIV.

Methods. We investigated the distribution of SIV-specific and HIV-infected TH cells within different populations of memory CD4 T-cells from lymph nodes of 23 subjects with chronic HIV infection with CD4 T-cell count >400 per mm$^3$ and plasma HIV RNA levels <5000 copies per mL, from 14 subjects with undetectable plasma HIV RNA copies per mL after 72 weeks of ART, from 3 subjects with nonprogressive HIV disease, i.e. long-term non progressors (LTNPs) and from 3 subjects with nonprogressive HIV disease (P<0.05) of CD4 T-cells harboring HIV DNA, it was the most efficient in supporting productive HIV infection and replication.

Conclusions. These results demonstrate that TH cell populations contained the highest percentage of HIV-infected cells and was the most efficient in supporting virus replication and production.

2. MATERIALS & METHODS

Phenotypic and functional analysis of CD4 T-cell populations including cytokine production and proliferation of lymph node mononuclear cells from chronically HIV-infected memory subjects prior to and after ART and from healthy subjects were assessed using flow cytometry. Cells were stained with a panel of antibodies including CD45RA, CD3, CD4, CD8, CXCR5, PD-1, ICOS and BCL-6.

3. RESULTS

4. CONCLUSIONS

Our findings show that TH cells:

1. are defined by a high expression level of CXCR5 and PD-1 as such BCL-6
2. support the production of Igs from GC-B cells
3. are expanded during the viremic phase
4. are enriched in HIV-specific CD4 T cells
5. are enriched in HIV infected cells during the viremic phase of HIV infection
6. are the most efficient cells in supporting virus replication and production.

Taken together, these results show that THF cells are a cellular compartment of HIV infection, replication and production.

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