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P16-31. Skewed HIV-1-specific CD4+ Th2 helper cell contribution in progressive HIV-1 infection

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Background

CD4+ T helper cells play a crucial role in the orchestration of the immune system. While CD4+ Th1 responses provide important helper signals to the survival and maturation of CD8+ T cells, CD4+ Th2 responses are involved in B cell maturation and antibody class switching. However, very little is known about the role and contribution of HIV-1-specific CD4+ T helper responses to the control of viral replication. Here we show that the presence of Gag-specific CD4+ Th1 responses and Th2 responses against Env are associated with viral control, while changes in this pattern are associated with disease progression.

Methods

We cross-sectionally screened 21 subjects with chronic HIV-1 infection (>10,000 copies/mL) and 15 elite controllers (<50 copies/mL) for HIV-1-specific CD4+ T helper responses by flow cytometry before and after cultivation in helper subset polarizing conditions (Th1: IFNγ/IL12; Th2: IL4/anti-IFNγ; Th17: anti-IL4/anti-IFNγ/TGFβ/IL6).

Results

HIV-1-specific CD4+ T helper responses were detected in similar frequencies in chronic HIV-1 infection and elite controllers. However, we observed in HIV-1 elite controllers significantly more CD4+ T cell responses consisting of a Th1 (IFNγ+/IL2+) CD4+ T cell phenotype. These responses were predominantly directed against the HIV-1 Gag protein. In contrast, in subjects with chronic-progressive HIV-1 infection Th1 responses were directed against envelope in a higher frequency ($p < 0.02$). Interestingly, while the HIV-1-specific Th2 responses in elite controllers were preferentially directed against envelope, we observed a skewed over-representation of Th2 responses against Gag in subjects with chronic-progressive HIV-1 infection. These responses were also associated with higher activation levels.

Conclusion

Our data suggest that the presence of a distinct CD4+ T helper cell pattern is associated with viral control. The presence of Gag-specific Th1 responses and Env-specific Th2 responses suggests a potential important role for the helper signals for B and T cell responses. This finding might be highly important for vaccine design.