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INFECTIOUS DISEASE

CASE STUDY

IL-15 promotes activation and expansion of CD8+ T cells in HIV-1 infection

Younes SA, et al. *Journal of Clinical Immunology*. 2016;126(7):2745-2756.
JULY 2016

WHY IMMUNOSEQ?

Clonality metric allows differentiation of antigen driven expansion versus non-specific bystander expansion

Enables tracking of clones between samples and sorted subsets of cells

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CASE STUDY: IL-15 promotes activation and expansion of CD8⁺ T cells in HIV-1 infection—
Younes SA, et al. Journal of Clinical Immunology. 2016;126(7):2745-2756.

BACKGROUND

Increased CD8⁺ T cells in circulation is linked to increased morbidity and mortality risk in HIV-1 infected patients. HIV-1-specific expansion is present in early infection, but the drivers for increased CD8⁺ T-cell numbers in chronic untreated infection is not fully elucidated. Recent data shows that increased cycling in CD4⁺ T cells to be due to bystander activation rather than antigen specific means. Here, the authors explore that hypothesis for the CD8⁺ T-cell population.

AIM

- Determine if CD8⁺ (T-cell) cycling in untreated HIV-1 infection is antigen driven or a bystander effect.
- Elucidate driving mechanism of CD8⁺ T-cell expansion in these patients.

METHODS

Sorted memory and cycling CD8⁺ T cells from 3 HLA-A*02:01 HIV-1 infected, untreated patients and 3 healthy controls were sequenced.

1. Cycling and non cycling CD8⁺ T cells sorted from untreated HIV-1 infected patients and healthy controls.
2. DNA extracted from sorted cells and sequenced using the human TCRB immunoSEQ assay.
3. Compared clonality and sequence overlap between the two populations in each patient or control.

RESULTS

- In both HIV-1 infected patients and controls, the cycling cell repertoires resembled the non-cycling CD8⁺ memory T-cell repertoire.
- Diversity and clonality of the memory CD8⁺ T cells were not significantly different between cycling and non-cycling cell subsets or between patients and controls.
- Expansion and activation of CD8⁺ T cells derived from the blood of healthy controls can be induced *in vitro* through addition of IL-15, which is present at increased levels in lymph nodes of untreated HIV-1 infected patients.

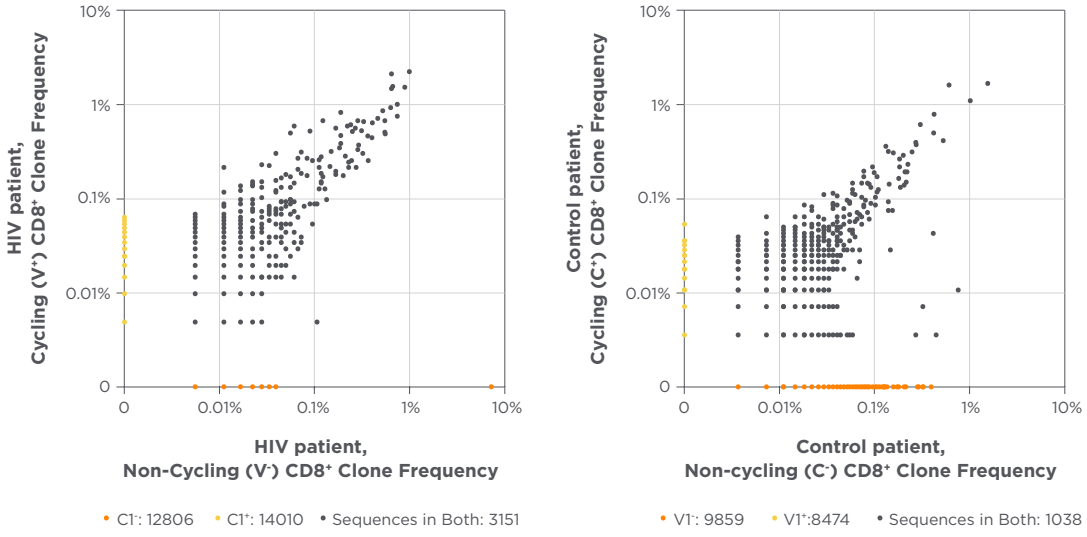

Figure 1. Scatterplots of clone sequences between the cycling and non-cycling memory CD8⁺ T cells in an HIV patient and a control show very similar overlap patterns, indicating the cycling population is representative of the non cycling population, rather than a contracted, antigen specific subset.

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CONCLUSIONS

$CD8^+$ T-cell activation and expansion in untreated HIV-1 infected patients is a bystander effect and is driven by increased IL-15 expression

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