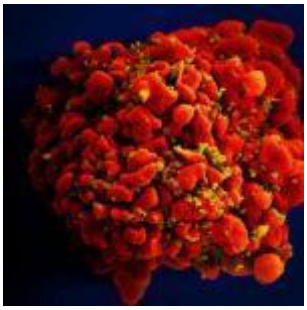
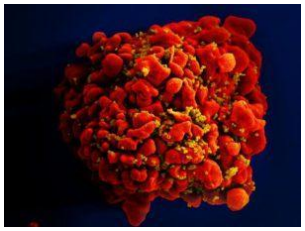
Non-cytotoxic function of HIV-specific rectal CD8+T cells





T cell (red) infected with HIV particles (yellow) (Public Health Image Library, NIAID, Image ID:18143)

The gastrointestinal mucosa is a major site of HIV transmission and pathogenesis. CD8 T cells play a major role in viral immunity against HIV infection. However, the exact functional role of CD8+ T cells in the gastrointestinal mucosa has not been well defined. Studies have shown poor cytotoxic potential of gastrointestinal CD8+ T cells, illustrated by lower levels of perforin and granzyme (Gzm) B expression compared to CD8+ T cells in the blood.

Researchers from California, aimed to fully explore and

compare rectal (proxy for gastrointestinal mucosa) and blood CD8+ T cell cytotoxic molecules (Gzm A, B,K and perforin) co-expression patterns. As well as illustrate differences in co-expression patterns between ART naïve, HIV controllers, and ART-treated HIV infected individual with no gastrointestinal tract inflammatory condition.

As shown by other levels, Kiniry *et al.* observed lower expression of perforin and GzmB in rectal CD8+ T cells compared to blood CD8+ T cells in HIV infected individuals. Surprisingly, levels of Gzm A and K expression in CD8+ T cells were similar between rectal and blood CD8+ T cells in HIV infected individuals. Individuals with detectable viral load (ART naïve and controller) were observed to have increased levels of Gzm A, B and K expression by rectal CD8+ T cells, compared to ART treated HIV infected and HIV seronegative individuals. Suggesting that HIV infection results in upregulation of cytotoxic effectors, in viral load dependent mechanism.

Kiniry *et al.* observed an inverse relationship between cytotoxic function and ability to produce cytokine in HIV (Gag)-specific CD8 T cells. Where Gag-specific CD8+ T cells predominantly produced cytokine (MIP1-β) rather than express cytotoxic molecules perforin and GzmB. Moderate expression of Gzm A and K by Gag-specific CD8+ T cells, further illustrate a predominant non-cytotoxic function of rectal residing HIV-specific CD8+ T cells. As Gzm A and K have been shown to have non-cytotoxic functions, that include induction of pro-inflammatory responses.

In summary, Kiniry *et al.* showed that despite total CD8+ T cells being able to express cytotoxic molecules, HIV-(Gag)-specific CD8 T cell have poor cytotoxic potential and express high levels of cytokine with moderate expression of inflammatory cytotoxic molecules Gzm A and K.

Journal Article: Kiniry *et al.*, 2018. Differential Expression

of CD8+ T Cell Cytotoxic Effector Molecules in Blood and Gastrointestinal Mucosa in HIV-1 Infection. Journal of Immunology.

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