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

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.


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