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Poster presentation

P16-32. Antigen exposure regulates the balance between proliferating and cytotoxic subsets of virus-specific CD8 T-cells

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Background

Cytotoxicity and proliferation are key functions of CD8 T-cells whose relationship remains unclear. We recently showed that perforin, more than GrmB, and unlike GrmA and K, is correlated with cytotoxicity. CD127 (IL-7Ra) has been suggested as a marker of proliferation capacity. Here we investigated the relationship between cytotoxicity and proliferation in different viral infections.

Methods

Virus-specific CD8 T-cell responses (n = 74) including CMV, EBV, Flu and HIV-1 were characterized using tetramer complexes or peptide stimulation and analyzed for proliferation capacity, expression of CD127 and perforin. CCR7, CD45RA, PD-1 and CD57 were used to assess T-cell differentiation/exhaustion. Simultaneous expression of IFNγ, IL-2, TNFα and perforin was analysed by polychromatic flow cytometry.

Results

We first confirmed the association between CD127 expression and proliferation capacity ($P < 0.01$) in virus-specific CD8 T-cell responses. Combined expression of perforin and CD127 revealed the existence of three populations of CD8 T-cells: CD127+perforin-, CD127-perforin- and CD127-perforin+ which were mostly CD45RA-CCR7+, CD45RA-CCR7- and CD45RA+CCR7- CD8 T-cells, respectively. CD127-perforin+ was CD57+, whereas CD127-perforin- had higher PD-1 expression ($P < 0.002$). Furthermore, CD127+perforin- represented the large majority (90%) of Flu-specific CD8 T-cells; CD127-perforin- were the majority (64%) of EBV-specific CD8 T-cells; and CD127-perforin+ were dominant for CMV-specific CD8 T-cells (43%). HIV-specific CD8 T-cells were mostly CD127-perforin-. These differences were significant (all $P < 0.002$). Of note, we observed a negative correlation between perforin and CD127 expression in virus-specific CD8 T-cells ($P < 0.001$). Consistently, ICS on CMV-specific CD8 T-cells confirmed the lack of co-expression of perforin and IL-2, which is known to correlate with proliferation. Finally, changes in antigen exposure in vitro, or in vivo during primary HIV-1 infection, modulated CD127 expression, as previously showed for perforin.

Conclusion

Proliferative (CD127+/IL-2-secreting) and cytotoxic (perforin+) CD8 T-cells are distinct T-cell subsets that are at different stages of differentiation. The balance between proliferation and cytotoxic capacity appears to be influenced by antigen exposure.