Retrovirology

Poster presentation

P01-05. Rapid perforin upregulation dominates the HIV-specific CD8 T cell response during acute HIV-infection

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Background

Recent dogma suggests that CD8 T cell ''polyfunctionality'' is essential for control of HIV, however none of the commonly measured functions are likely responsible for clearing infected target cells. During acute HIV infection, when HIV-specific CD8 T cells are thought to resolve peak viremia, an effector response has not been formally demonstrated.

Methods

PBMC from 23 acutely infected HIV patients were stimulated with pools of overlapping peptides encompassing all HIV open reading frames. A panel of antibodies directed against cell surface and intracellular entities was employed to stain for HIV-specific CD8 T cells by flow cytometry. Functionality was assessed by the ability to upregulate perforin, IFN-γ, IL-2, TNF-α, MIP-1β, and CD107a simultaneously.

Results

Nineteen of 23 (82.6%) subjects mounted an HIV-specific CD8 T cell response of at least 3 functions against a minimum 1 peptide pool, however none of the cells were capable of performing all functions. While MIP-1β and CD107a were ubiquitous functions, and TNF-α and IFN-γ were consistently expressed, IL-2 production was rarely observed. In contrast, the majority of subjects (17/19; 89.5%) demonstrated a pronounced ability to upregulate perforin upon HIV-specific stimulation. Even in the absence of highly polyfunctional responses perforin upregulation was reliably detected; 16/17 (94.1%) perforin responders displayed a strong perforin+degranulation+ subset. The HIV-specific CD8 T cells capable of perforin upregulation were largely effector (CCR7-CD45RO-) or effector memory (CCR7-CD45RO+), and most of these cells co-expressed CD57.

Conclusion

Rather than the absolute number of functions an HIV-specific CD8 T cell can perform, it is the quality of the functions that correlates to potential control HIV replication. Being that rapid perforin upregulation is a direct marker of *in vivo* cytotoxicity, its prevalence during acute HIV infection, even in concert with only degranulation, provides compelling evidence for a critical role of CD8 T cells in the control of acute HIV infection.