HIV-1 Tat affects the programming and functionality of human CD8$^+$ T cells by modulating the expression of T-box transcription factors

Fabio Sforza, Francesco Nicoli, Eleonora Gallerani, Valentina Finessi, Eva Reali, Aurelio Cafaro, Antonella Caputo, Barbara Ensoli and Riccardo Gavioli

Objective: HIV infection is characterized by several immune dysfunctions of both CD8$^+$ and CD4$^+$ T cells as hyperactivation, impairment of functionality and expansion of memory T cells. CD8$^+$ T-cell dysfunctions have been associated with increased expression of T-bet, Eomesdermin and pro-inflammatory cytokines, and with down-regulation of CD127. The HIV-1 trans-activator of transcription (Tat) protein, which is released by infected cells and detected in tissues of HIV-positive individuals, is known to contribute to the dysregulation of CD4$^+$ T cells; however, its effects on CD8$^+$ T cells have not been investigated. Thus, in this study, we sought to address whether Tat may affect CD8$^+$ T-cell functionality and programming.

Methods: CD8$^+$ T cells were activated by T-cell receptor engagement in the presence or absence of Tat. Cytokine production, killing capacity, surface phenotype and expression of transcription factors important for T-cell programming were evaluated.

Results: *Tat* favors the secretion of interleukin-2, interferon-γ and granzyme B in CD8$^+$ T cells. Behind this functional modulation we observed that Tat increases the expression of T-bet, Eomesdermin, Blimp-1, Bcl-6 and Bcl-2 in activated but not in unstimulated CD8$^+$ T lymphocytes. This effect is associated with the down-regulation of CD127 and the up-regulation of CD27.

Conclusion: Tat deeply alters the programming and functionality of CD8$^+$ T lymphocytes.