Retrovirology

Poster presentation

P16-25. HIV specific CTL from elite controllers have a unique survival advantage

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Background

Understanding how elite controllers (EC), patients controlling virus without antiretroviral therapy (ART), differ from those with chronic disease is an area of intense investigation. HIV Gag specific (sp) cytotoxic T lymphocytes (CTL) play a dominant role in this control. Unfortunately, most HIV sp CTL are primed for apoptosis. We hypothesize that EC up-regulate survival factors allowing them to resist apoptosis.

Methods

We examined pro- and anti-apoptotic factors in HIV Gag specific CTL in EC (viral load (VL) < 50 off ART), successfully treated (ST) (VL < 50 on ART), and untreated viremics (V). Using flow cytometry based assays, we performed cross-sectional and longitudinal analysis of pro-apoptotic (cleaved caspase-3) vs. anti-apoptotic (Bcl-2) markers in HIV specific CD8 T cells examining spontaneous cell death.

Results

VL only partially drives expression of cleaved caspase-3 (CC3). $CC3^{hi}$ HIV sp CTL in EC were not only lower compared to V (2.3 vs. 13%, respectively) but also lower than ST (5.4%) ($p < 0.05$). Bcl-2 trended towards higher levels in HIV sp CTL of EC and ST compared to V. Combining these makers we found differences in $CC3^{hi}$/$Bcl\text{-}2^{lo}$ HIV sp CTL with the greatest number of HIV sp CTL at risk of apoptosis in viremics (6.5%), followed by ST (2.1%) and EC (0.80%) ($p < 0.05$). In a longitudinal analysis pre and post ART we found decreases in both $CC3^{hi}$ HIV sp CTL and $CC3^{hi}$/$Bcl\text{-}2^{lo}$ CTL after successful treatment. $CC3^{hi}$/$Bcl\text{-}2^{lo}$ populations represent cells at greatest risk of undergoing apoptosis and this phenotype appears to be only partially reversible with ART.

Conclusion

EC have a survival advantage over patients with chronic disease even when treated with ART. Elucidating pro- and anti-apoptotic factors contributing to the survival of CTL in EC including costimulatory signaling necessary to generate these CTL capable of resisting apoptosis is paramount to development of effective HIV-1 vaccines.