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Poster presentation

P16-28. The first year: early correlates of long-term HIV progression

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Background

SIV studies reveal dramatic, systemic destruction of CD4+ T-cells in acute disease; this, and early levels of central memory (T_{CM}) subsets predict progression to death independently of viral load. Similar data are not available for HIV, because samples from early disease are rare and long, untreated follow-up is usually not possible. We analyzed a large cohort of confirmed seroconverters to test whether T-cell and viral dynamics in early disease predict long-term progression.

Methods

Samples from 466 untreated, early infection individuals (median = 225 days), with substantial follow-up (median = 4 years), were studied using two 13-color flow cytometry panels, including: A) CD45RO, CD27, CD28, CCR5, CCR7, CD127, CD57, and Ki-67 (unstimulated) and B) IFNγ, IL2, TNFα, CD154, CD107a, CD45RO, CD27, CCR7, and CD57 (after stimulation with HIV antigens). We also measured cell-associated viral load (CAVL) in various CD4+ T-cell subsets. We correlated T-cell subset representation, CAVL, and the magnitude, quality, and phenotype of HIV-specific T cells with disease progression.

Results

T_{CM} levels at the earliest HIV+ visit did not predict long-term outcome. However, the following were associated with slow progression: high levels of long-lived cells (naive or CD127+ memory CD8), low Ki-67 expression, and low CAVL during the first 7.5 months. Notably, CAVL was present in naive cells. Also, no single T-cell function (e.g. IFNγ) had predictive value; however, rapid progressors (AIDS < 4.6 years) had "higher" levels of polyfunctional CD4+ T-cells in early disease than AIDS-free subjects. Finally, cytokine responses to Gag and Env differed dramatically.

Conclusion

These results suggest: 1) early depletion of precursor cells, mediated by proliferation/differentiation, is a poor prognostic factor independent of antigen load, 2) Ki-67 measurements can inform early treatment decisions, and 3) the quality of the T-cell response to HIV early in disease impacts long-term progression. These data inform experimental design in vaccine trials that test efficacy after breakthrough infections.