Retrovirology

Poster presentation

P16-21. Altered T cell homeostasis and activation in HIV-1 elite suppressors with low CD4+ T-cell counts

KC Groves*[1], D Bibby[2], A Isaksen[2], J Deayton[3], J Anderson[4], C Orkin[2], AJ Stagg[3] and Á McKnight[3]

Address: [1]Institute of Cell and Molecular Science, Barts and The London School of Medicine and Dentistry, London, UK, [2]Barts and the London NHS Trust, London, UK, [3]ICMS, Barts and The London School of Medicine and Dentistry, London, UK and [4]Homerton University Hospital NHS Foundation Trust, London, UK

* Corresponding author

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Background

HIV-1 elite-suppressors (ES) maintain low viral-load (VL) without therapy and classically maintain normal CD4+counts. We have identified a rare subset with falling CD4+counts (discord-ES). Disease progression in these patients may result from a viral influence on T-cell homeostasis and activation, rather than a direct consequence of virus-replication. Therefore, we compared T-cell homeostatsis and activation in discord-ES and typical-ES.

Methods

Fresh whole blood samples were obtained from 8 discord-ES (VL<2000 copies/ml >1 year, CD4+count <450 × 10^6/L), 12 typical-ES (VL<2000 copies/ml >1 year, CD4+count >450 × 10^6/L), 5 progressors (VL>5000 copies/ml, CD4+count <450 × 10^6/L) and 5 uninfected individuals. Using multiparameter flow-cytometry we quantified naïve and memory T-cell subsets based on expression of CD45RA/RO and CD62L, and assessed activation based on co-expression of CD38 and HLA-DR.

Results

Blood from discord-ES contained fewer naïve ($CD45RA^+62L^+$) $CD4^+$ T-cells than blood from typical-ES (median 80[IQR 52–121] versus 277[218–401]; p = 0.001). This lower number of naive T-cells represented a lower proportion of total $CD4^+$ T-cells. Numbers of naive $CD4^+$ T-cells in discord-ES did not differ significantly from those in progressors and were reduced (p = 0.002) compared with uninfected controls. A similar pattern was observed with regard to numbers of $CD4^+$ central-memory ($CD45RO^+CD62L^+$) and effector-memory ($CD45RO^+CD62L^-$) populations. Both activated and resting naive $CD4^+$ T-cells were reduced in number in discord-ES, but activated cells constituted an increased proportion of the naive $CD4^+$ pool compared with typical-ES (p = 0.003).

Conclusion

$CD4^+$ T-cell subsets and their activation in discord-ES are distinct from those in typical-ES and indistinguishable from those in progressors, suggesting that $CD4^+$ T-cell decline is more closely associated with perturbations in T-cell activation than with VL. The increased proportion of activated naïve $CD4^+$ T-cells against a backdrop of declining numbers of these cells in discord-ES may suggest that activation contributes to progressive cell-loss despite only low-level viral-replication. However, impaired T-cell production or sequestration to non-blood compartments may also contribute.