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Oral presentation

HIV infection destabilizes a targeted subset of the gamma/delta T cell repertoire

Andrew M Hebbeler, Nadia Propp, Cristiana Cairo, Jean-Saville Cummings, Charles Davis, Robert R Redfield and C David Pauza*

Address: Institute of Human Virology, University of Maryland, Baltimore, Maryland 21201, USA
* Corresponding author

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The mature gamma/delta T cell receptor repertoire arises by a process of positive selection and amplification of cells expressing the Vg2Vd2 TCR, with further skewing to TCR with the Vg2-Jg1.2 rearrangement. Once formed, the Vg2 repertoire is stable in healthy adults showing more than 50% sequence conservation over intervals of up to 7 years. The Vg2-Jg1.2 chains are among the most conserved elements in healthy individuals and even the balance among naïve and memory cell types is maintained. This situation is altered by HIV infection. We showed previously that HIV disease was associated with the targeted loss of cells expressing the Vg2-Jg1.2 rearrangement. In longitudinal studies with specimens from the MACS cohort, we showed that peripheral blood Vg2Vd2 T cell has a high frequency of staining with the vital dye 7-AAD, in most specimens the Vg2Vd2 T cells were twice as likely to be 7-AAD positive compared with CD4+ T cells. The lower viability of circulating Vg2Vd2 T cells was reflected in the repertoire characteristics. We observed a high degree of repertoire conservation in HIV+ individuals, with values consistent with the lower range found in healthy adults. However, stability was confined largely to Vg2 cells with rearrangements using J segments other than Jg1.2. In most cases, any Jg1.2 sequences that were found in HIV+ individuals were not seen in subsequent specimens collected at 6 monthly intervals. The pattern of instability among only the Vg2-Jg1.2+ cells, shows that the effect of HIV on repertoire is a process of rapid turnover among cells that may be reacting to viral antigens while cells without known responses to HIV (Vg2 with all other Jg rearrangements) are relatively unaffected. Even in this population of cells that are not susceptible to direct infection, owing to the lack of CD4 receptor, depletion is confined to the virus reactive cells.