Retrovirology

Oral presentation

Loss and Recovery of Vg2Vd2 T cells in HIV/AIDS

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HIV infection results in an early and profound loss of Vg2Vd2 T cells, and this is the only T cell receptor-specific depletion that is common to all individuals with HIV/AIDS. A similar pattern of Vg2Vd2 T cell depletion occurs in mycobacterium infection and during malaria. We hypothesize that the loss of Vg2Vd2 T cells, irrespective of the primary cause for this loss, results in disease acceleration during HIV+ tuberculosis or HIV+ malaria coinfections and also leads to increased incidence of cancer in the context of HIV/AIDS.

Using a macaque model for mycobacterium infection, we demonstrated the dynamics of Vg2Vd2 responses to infection with attenuated M. bovis (BCG). In this study, we confirmed that activation-induced cell death is the mechanism for Vg2Vd2 T cell depletion in vivo, and confirmed this with in vitro studies using human T cells. In vitro studies with human PBMC allowed us to understand the specificity of T cell receptor recognition of human lymphomas. Using AIDS-related and non-AIDS related B NHL, we defined the T cell receptor structures required for tumor recognition and showed they are indeed, missing in HIV-infected individuals. Lastly, we evaluated longitudinal specimens from HIV-infected individuals receiving HAART and showed that recovery of the Vg2 repertoire was occurring by the use of previously rare sequences that survived initial HIV-mediated depletion and were expanded during the treatment interval. Importantly, repertoire recovery occurred in the absence of new cell synthesis, consistent with observations on CD4 and CD8 T cell repertoire and changes during HIV infection and treatment.

The Vg2Vd2 T cell subset is an example of indirect or bystander cell killing during HIV infection, and its impact on immunity to seemingly unrelated pathogens. Destruction of Vg2Vd2 T cells and the critical elimination of the Vg2-Jg1.2 expressing subset, likely accounts for the mutual acceleration of HIV, malaria and tuberculosis diseases, and may explain the specific of enhanced risk for AIDS-related neoplasia. We continue efforts to comprehend this unusual T cell subset both as a model for the impact of HIV in host immunity, and to define new targets for immunomodulatory therapy.