

Impact of HIV Infection on the T Cell Repertoire

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Abstract

As individuals infected with HIV progress to AIDS, they lose CD4+ T cells, and this decline is well-correlated with their risk of opportunistic infections. The "holes in the repertoire" hypothesis posits that this decline in T cell numbers is accompanied by a loss of T cell diversity, and that this loss of diversity is a major cause of AIDS-related immunodeficiency. The sheer magnitude of the T cell receptor repertoire has made it impossible to test this hypothesis with existing methods. We have devised a new method, called AmpliCot, which harnesses the principles of DNA reassociation kinetics to measure the sequence diversity of PCR products. AmpliCot is able to measure a wide dynamic range of T cell receptor diversity in a high-throughput manner. Preliminary studies with AmpliCot suggest that HIV infection is associated with a loss of T cell receptor diversity, particularly in memory/effector lymphocyte populations. A better understanding of the effects of HIV infection on T cell receptor diversity may help inform clinical decisions about when best to begin antiretroviral therapy and help evaluate the potential benefit of adjunctive immunologic agents.