Yiding Yang, Department of Microbiology, University of Tennessee, Knoxville, TN, USA
Vitaly V. Ganusov, Department of Mathematics, Department of Microbiology, University of Tennessee, Knoxville, TN, USA

Kinetics of CD8+ T Cell Responses during Primary HIV-1 Infection

Despite numerous studies involving mathematical modeling of CD8+ T cell responses to HIV, we lack understanding of basic principles in T cell immunology: how T cell responses to different epitopes of HIV are generated; how many responses there are; what role of the viral load in T cell kinetics is and whether T cells specific to different viral epitopes compete during the infection. Using recently published data from a cohort of HIV-infected patients that were followed from the onset of symptoms into the chronic phase, we address some of these questions. On average in a given patient there is 10 CD8+ T cell responses specific to different viral epitopes. Surprisingly, the number of HIV-specific CD8+ T cell responses (breadth of the response) changes very little from the earliest measurement to the chronic phase suggesting that most if not all T cell responses are generated in primary infection. Using a simple mathematical model for the kinetics of CD8+ T cell response, we find that majority of epitope-specific CD8+ T cells expand at the rate less than 0.1 day^{-1} or double in size in more than 7 days (60%, median is 0.07 day^{-1}) and most of acute responses peak before 100 days post symptoms. There is a strong positive correlation between the estimated precursor frequency and maximum value of epitope-specific CD8+ T cells reached during infection, and a strong negative correlation between the precursor frequency and the rate of expansion of epitope-specific T cells; the latter suggests intra-clonal competition between epitope-specific T cells. Finally, we find that although many CD8+ T cell populations expand and contract in unison, in many cases (around 18%) there is evidence of competition between T cell responses such as change in magnitude of one response leads to a decrease in another response. These results provide basic immunological details on the kinetics of CD8+ T cell responses to HIV, and also provide evidence that some but not all HIV-specific T cell responses compete during the infection.