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Prediction of the control of HIV infection

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Statement of the Problem: After 37 years of HIV studies, we still do not understand why most HIV patients cannot clear infection, why a small fraction of individuals can control HIV infection spontaneously or post-treatment, and why some of these lucky individuals maintain control longer than the others. All we know is the empiric statistical correlation of control with some HLA subtypes.

Methodology & Theoretical Orientation: To shed light on this enigma, based on the available data in the literature, I have developed a model of the adaptive immune response that explains the diverse outcome of HIV infection from the variation in a few critical immunological parameters that can be measured in advance in an individual. The model includes 5 compartments of immune cells and the dual activation of CD8 T cells directly by antigen in MHC-I context and by helper cells.

Findings: The outcome of infection in an individual is decided by the arms race between the proliferation of helper CD4 Th1 cells enabling effective control of the virus and the virus infecting CD4 T cells and employing CD8 T cells to suppress the helper cells. Computer simulation predicts four parameter regions in the plane of the functional avidities of CD8 T cells and CD4 T cells, which correspond to the cohorts of patients with high viremia, spontaneous control, long-term post-treatment control, and short-term control. The model predicts that CD4 T cells in controllers must be very avid, while the avidity of CD8 T cells should be modest, which predictions agree with the clinical observations. Whether a patient maintains a spontaneous of post-treatment control is decided by the infectivity ratio between the target CD4 T cells and their virus-specific activated subset. Simulation predicts a broad region of transient control is discovered, which explains the variable stability of HIV control in different controllers. The predictions are fit to the available data on CD4 T cell avidity to demonstrate the segregation between patient cohorts.

Conclusion & Significance: The number of potential post-treatment patients may be much larger than currently observed. The broad region of transient controllers predicted by the model explains why some patients maintain control longer than the others. The present study offers a mathematical model of the helper-dependent immune response that explains the differences between the HIV patient cohorts from the variation in several critical immunological parameters of the adaptive response.

Biography

Igor M Rouzine, has done his PhD in Theoretical Physics, has been working in virological departments for 25 years developing models of virus evolution, host-virus interaction, and immune response. He has pioneered the analytic method of traveling wave predicting the asexual evolution of a large number of linked loci and the evolution with rare recombination, as well as the immune models with the dual response to helper cells and infected cells.