Viral and immune system co-evolution

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Pathogens and the immune system play an intricate evolutionary game, where pathogens employ various means to evade immune detection, and the host selects B and T cell clones with higher and higher affinities to pathogens determinants. We here discuss multiple aspects of this two sided evolutionary game.

One common evasion strategy is the removal of CD8+ cytotoxic T-lymphocyte (CTL) epitopes. We use a combination of multiple bioinformatic tools and large amount of genomic data to compute the epitope repertoire presented by over 1,300 pathogens in many HLA alleles, and study escape mutation in viruses and bacteria. We show that viral proteins in general have a higher epitope density than human proteins. This difference is due to a good fit of the human MHC molecules to the typical amino acid usage of viruses. Among different viruses, viruses infecting humans present less epitopes than non-human viruses. This selection is not at the amino acid usage level, but through the removal of specific epitopes. Within a single virus, not all proteins express the same epitopes density. Proteins expressed early in the viral life cycle have a lower epitope density than late proteins. Such a difference is not observed in non-human viruses. The removal of early epitopes and the targeting of the cellular immune response to late viral proteins, allow the virus a time interval to propagate before its host cells are destroyed by T cells. The accumulation of escape mutation is limited by the complexity of the virus, where large and complex viruses fail to adapt rapidly enough to the immune response.

The parallel evolution of the immune response occurs at the level of MHC selection in the population and B and T cell clone selection in a host. We analyze high-throughput sequences of B and T cells to show clear selection mechanisms affecting the repertoire and its response to external threats.