SFB 680

Molecular Basis of Evolutionary Innovations

Molekulare Grundlagen evolutionärer Innovationen

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Identifying coevolutionary patterns in HLA molecules: Insights into host-pathogen coevolution

The antigenic peptide, major histocompatibility complex molecule (MHC; also called human leukocyte antigen, HLA), coreceptor CD8, or CD4 and T-cell receptor (TCR) function as a complex to initiate effectors' mechanisms of the immune system. The tight functional and physical interaction among these molecules may have involved strong coevolution links among domains within and between proteins. Despite the importance of unraveling such dependencies to understand the arms race of host–pathogen interaction, no previous studies have aimed at achieving such an objective. Here, we perform an exhaustive coevolution analysis and show that indeed such dependencies are strongly shaping the evolution and probably the function of these molecules. We identify intramolecular coevolution in HLA class I and II at domains important for their immune activity. Most of the amino acid sites identified to be coevolving in HLAI have been also detected to undergo positive Darwinian selection highlighting therefore their adaptive value. We also identify coevolution among antigen-binding pockets (P1-P9) and among these and TCR-binding sites. Conversely to HLAI, coevolution is weaker in HLAII. Our results support that such coevolutionary patterns are due to selective pressures of host–pathogen coevolution and cooperative binding of TCRs, antigenic peptides, and CD8/CD4 to HLAI and HLAII.

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Institute for Genetics, Seminar Room, 4th floor

Host: Michael Lässig

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