Alloreactive TCRpMHC Complexes: Conformation Analysis

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The key actors in the cell-cell interactions of the adaptive immune response are the major histocompatibility complex (MHC) molecule and the T cell antigen receptor (TCR). The former (in humans also known as human leukocyte antigen – HLA) is found on antigen presenting cells and serves as extraction tool to bring antigens in the intercellular space for recognition by the T cells through the TCR.

T cells are selected for recognition of certain pMHC complexes, but often alloreact with foreign HLA, presenting different allopeptides, sometimes subject to extensive polymorphism and with disparate peptide sequences. Understanding mechanisms behind this phenomenon is of great theoretical and practical importance. We study two MHC molecules with a single-aminioacid polymorphism to the original (alloreactive) complex (LC13 TCR in complex with HLA B*4405 bound to EEYLQAFTY – a self peptide from the ABCD3 protein) and significantly different binding affinities, resp. immunogenicity, in the context of molecular mimicry hypothesis [1]. We use molecular dynamics (MD) to get insights into the TCRpMHC interaction and investigate these complexes from a structural point of view, augmenting the crisp-clustering analysis of their semi-rigid domains.

References

[1] W. A. Macdonald et al., *T Cell Allorecognition via Molecular Mimicry*, Immunity **31** 897–908, 2009.