"The molecular mechanism of peptide exchange by MHC class II proteins"

The presentation of peptide-MHCII complexes (pMHCII) for surveillance by T cells is a well-known immunological concept in vertebrates, yet the underlying dynamics of antigen exchange remain elusive. We have used a combination of X-ray crystallography, NMR spectroscopy and molecular modeling to define two major exchange pathways: The kinetic stability of a pMHCII’s ground state defines its propensity for intrinsic peptide exchange, while the population of a rare, intermediate conformation correlates with the propensity of the HLA-DM-catalyzed pathway. Helix-destabilizing mutants designed based on our model shift the exchange behavior towards the HLA-DM-catalyzed pathway and further allow us to conceptualize how allelic variation can shape an individual’s MHC restricted immune response. The findings will be discussed in the context of autoimmunity and cancer immunotherapy.

References:

Date & time: Thursday, October 13, 2016 at 05:00 pm
Location: Lecture Hall Y44-H-11, UZH Irchel
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