MS02-2-2 Autoimmunity and molecular recognition in type I diabetes
#MS02-2-2

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Abstract
The NY4.1 T-cell clone was originally isolated from pancreatic islet-infiltrating lymphocytes from non-obese diabetic (NOD) mice. We have recently shown that the NY4.1 T cell receptor (4.1-TCR) recognizes pancreatic beta cell-derived hybrid insulin peptides (HIPs) in the context of the Major Histocompatibility Complex class II (pMHCII) molecule I-Ag7. In TCR-transgenic NOD mice, recognition of these peptide-MHCII (pMHCII) complexes triggers the activation and recruitment of NY4.1-CD4+ T cells into pancreatic islets, leading to rapid destruction of pancreatic beta cells and overt type 1 diabetes within the first few weeks of life.
We present the crystal structure of a HIP peptide/I-Ag7 complex at 1.80 Å resolution, as well as the structure of this pMHCII bound to the 4.1-TCR at 2.6 Å resolution. Comparison of the two structures reveals a previously unrecognized mode of interaction between a pMHCII and its cognate TCR, whereby TCR engagement entails exquisite conformational motions in I-Ag7 and the HIP that are essential for stable binding.
This observation suggests that some pMHCII complexes are malleable and that some TCRs trigger conformational motions on their cognate pMHCIIs to optimize binding.

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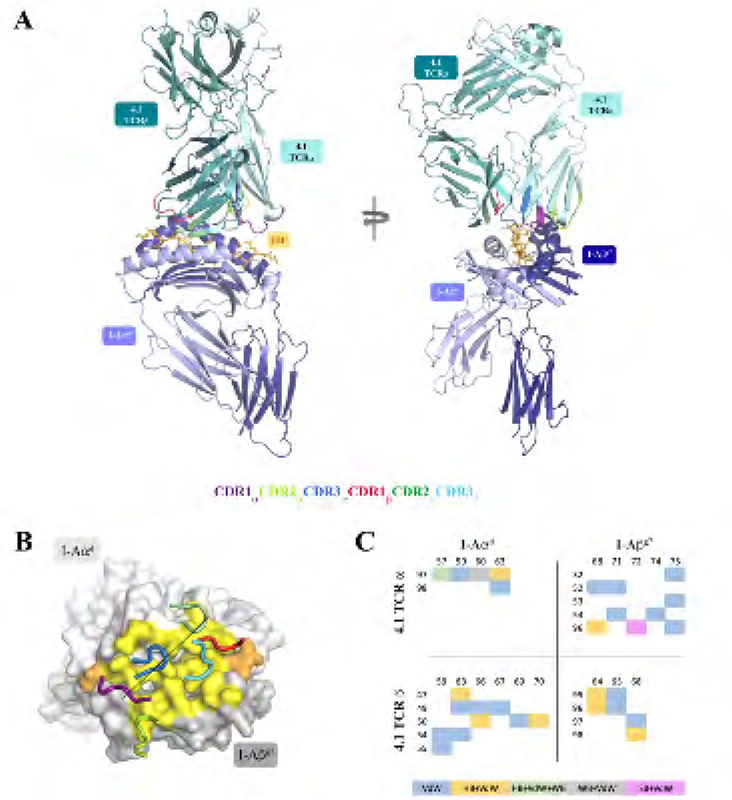
Structure of the 4.1-TCR:HIP39/I-Ag7 complex.



Structural plasticity of both I-Ag7 and peptide co