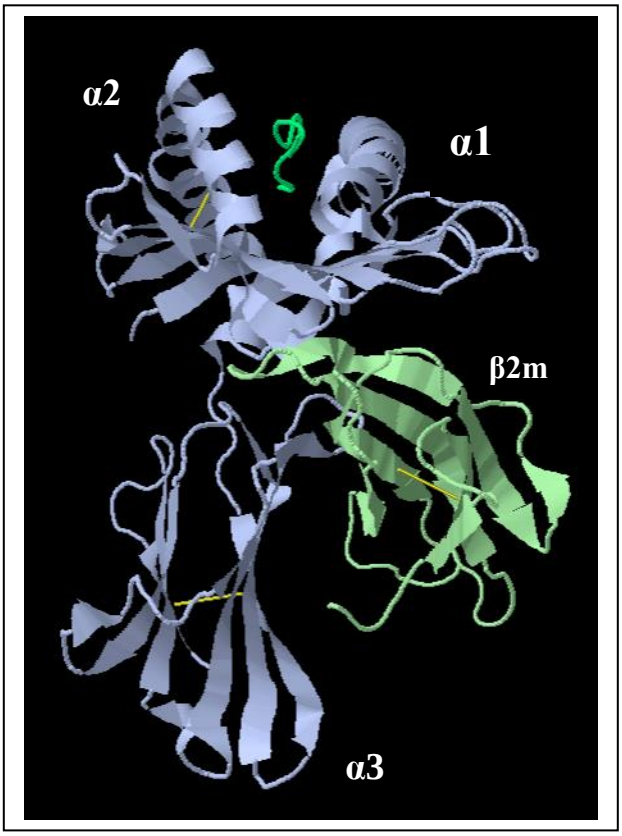
VISIBLE MHC

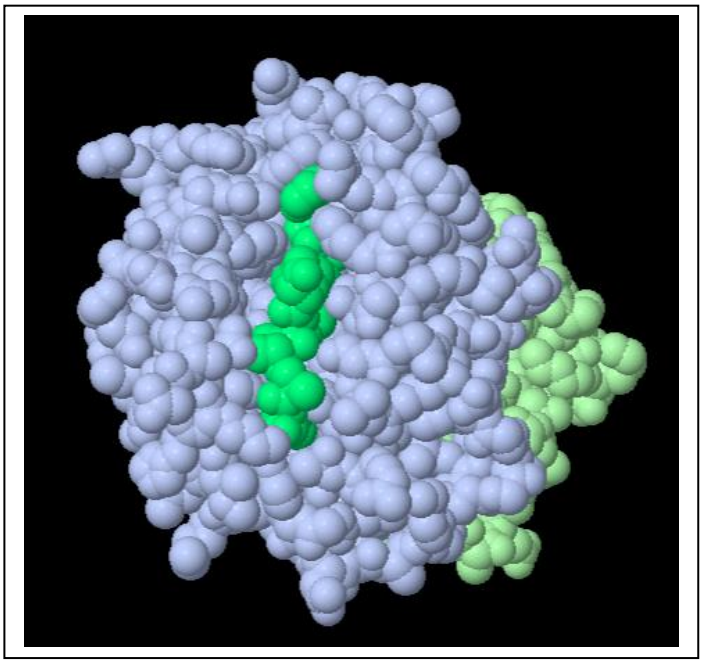


Protein Data Bank is a source of fabulously useful structures. This is the extracellular domain of an **MHC Class I** molecule, seen from the side. The main chain is in purple: at upper right is the alpha-1 domain; at the upper left, the alpha-2 domain; and below, the membrane-proximal alpha-3. In pale green ribbons is β_2-microglobulin, which is invariant, stabilizes the folding of the alpha chain, is not inserted into the plasma membrane, and is not coded for within the MHC. The floating green string at the top is the antigenic peptide. It's not floating at all except in this stick view; its ends are making contacts with the MHC.

PDB file 1VAB.

Here's the CTL cell's view. In Class I molecules the groove is closed on both ends, so that peptides must fit entirely within the groove; they are usually 7 to 10 amino acids long. Typically peptide-MHC anchor points are at the far ends of the peptide. (Compare the space-fill view of Class II on the next page.)

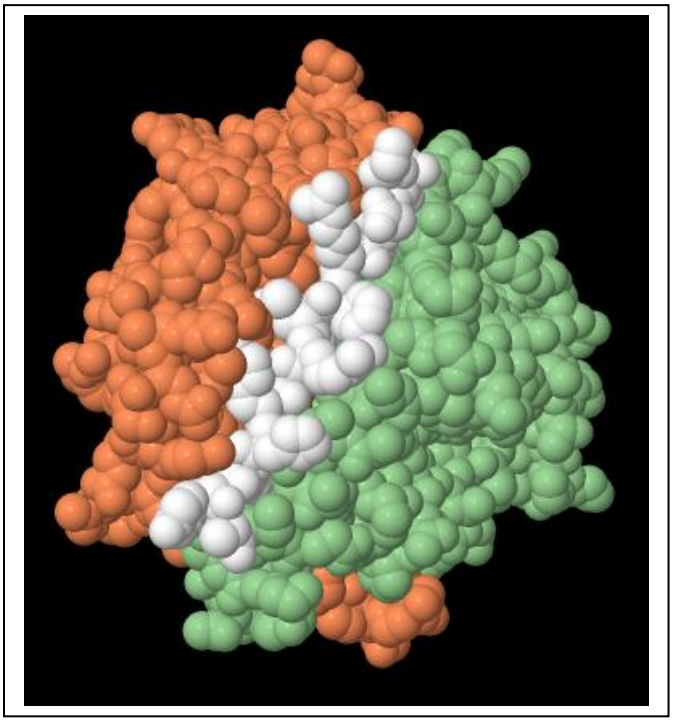
PDB file 1VAB.



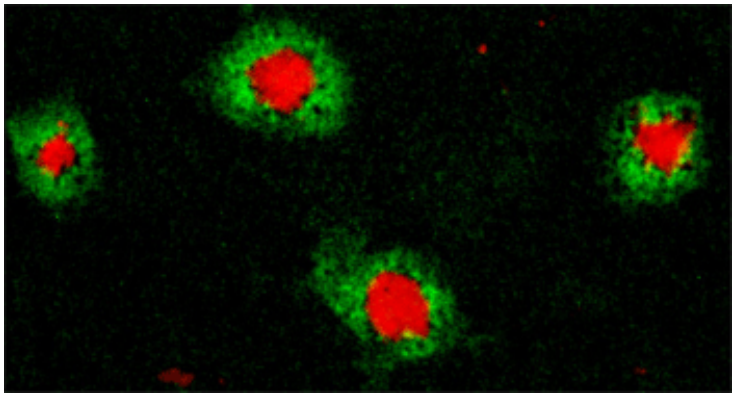
This is **MHC Class II**. It has two chains, alpha and beta. The alpha-1 and beta-1 domains jointly form the cleft in which the white antigenic peptide sits. Alpha-2 and beta-2 domains below are membrane-proximal, attached to the transmembrane stretches which are not shown here.

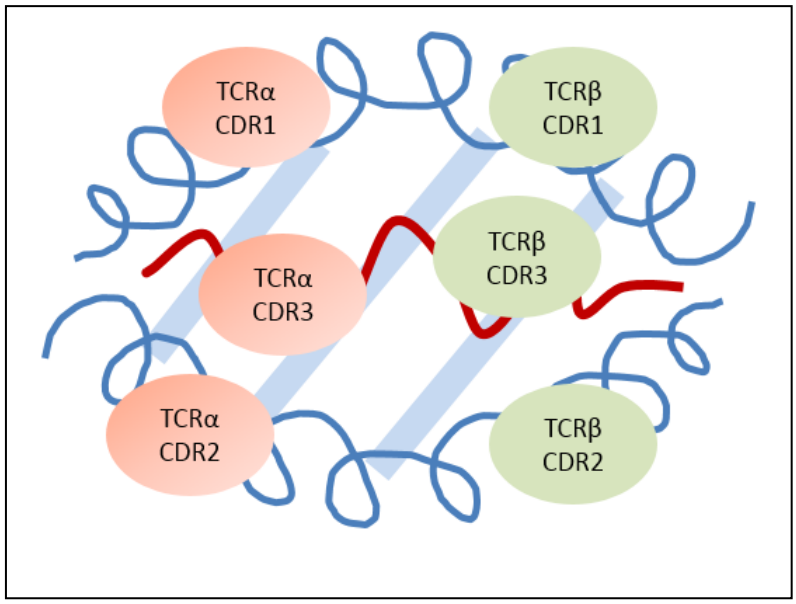
PDB file 4OV5.

This is the Th cell's view of a loaded MHC Class II. Peptides associating with Class II are longer, commonly 14 amino acid residues or more, and drape over the cleft. There are several anchor points along the length of the peptide. Residues in the groove make hydrogen-bond contacts with main-chain atoms of the peptide; this forces the peptide to assume a kinked orientation. Although MHC can bind a lot of different peptides, which ones do depends on the side chains of their anchor residues; they must fit into pockets in the MHC groove. This explains why certain peptides (gliadin, insulin) fit in HLA-DQ8 or –DQ2 but hardly any other alleles. PDB file 4OV5.



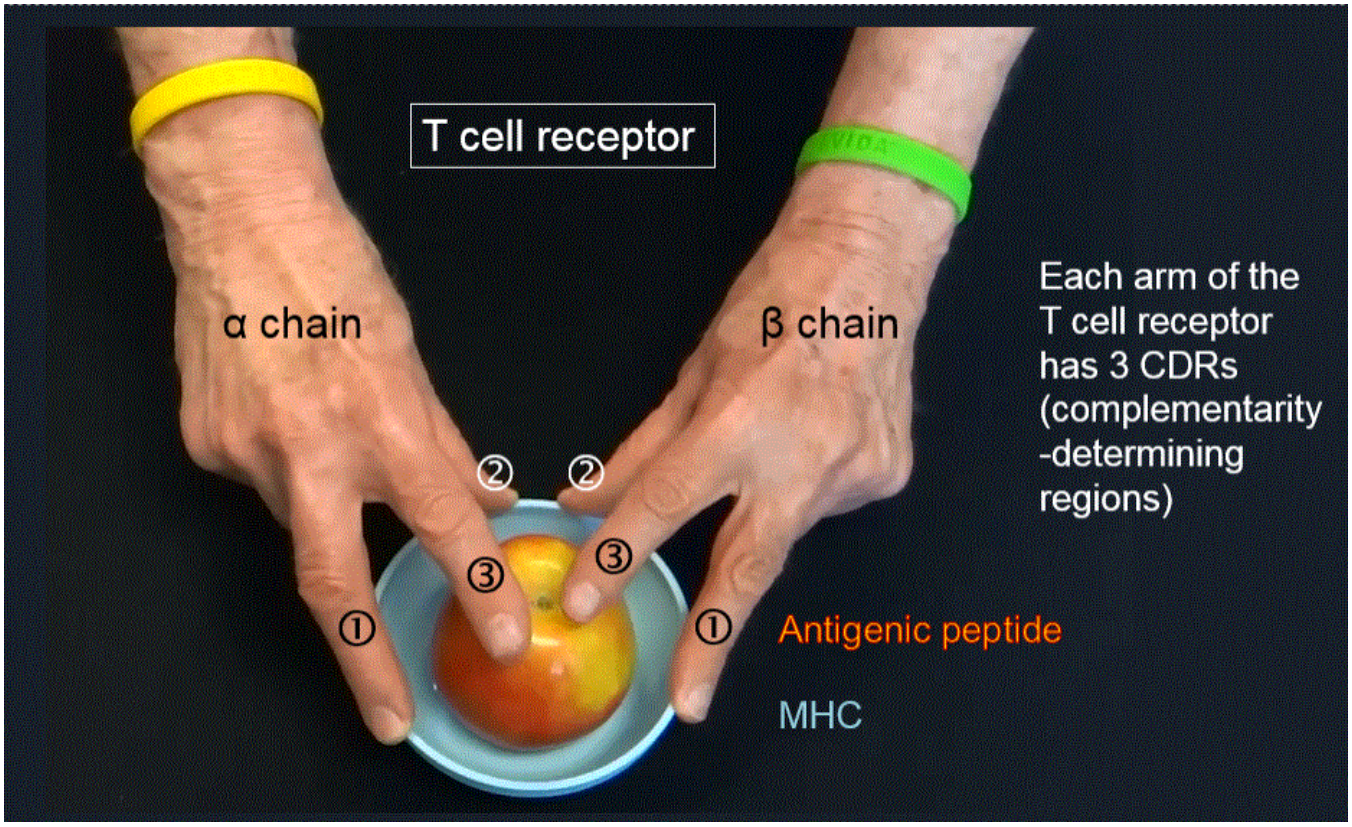
Pucker Up: An antigen-presenting cell's view of the "**immunological synapses**" of 4 T cells. The T cell receptors (stained red) are clustered in the centers of the synapse, and accessory adhesion molecules (in green) surround them.[1]





Typical footprints of the 3 TCRα and 3 TCRβ CDRs on a Class I MHC groove with a contained peptide. The highly-variable CDR 3s are most likely to engage amino acid residues on the peptide.

[1] Kaizuka, Y. et al. 2007. Mechanisms for segregating T cell receptor and adhesion molecules during immunological synapse formation in Jurkat T cells. PNAS 104:**20296-20301**



Another way to visualize the TCR. Typically the CDRs 1 and 2 of both the alpha and beta chains engage amino acids on the MHC molecule, while the two CDR 3s engage the contained peptide. Because CDR 3s are the most highly variable (as they are in antibodies) it makes sense that they look at antigenic peptides, of which there are potentially nearly infinite numbers.