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Crystal Structure of Staphylococcal Enterotoxin I in Complex with a Human MHC II Molecule. R. Guan^{1,2}, M.M. Fernández¹, E.L. Malchiodi¹, R.A. Mariuzza¹, ¹Center for Advanced Research in Biotechnology, Univ. of Maryland Biotechnology Inst., Rockville, MD 20850, ²Laboratory of Molecular Biology, National Inst. of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892.

Superantigens (SAGs) are immunostimulatory and disease-causing proteins of bacterial or viral origin that can be presented by MHC II molecules to T cell receptors. Staphylococcal enterotoxin I (SEI), a SAG belonging to the Zn²⁺ SAG family, binds MHC II molecules through a Zn²⁺ containing high affinity site. We determined the crystal structure of SEI in complex with HLA-DR1, an MHC II molecule, loaded with an influenza hemagglutinin (HA) peptide. SEI and DR1/HA bury a much smaller surface area but have a higher shape correlation compared with other SAG-MHC/peptide complexes. Most of the interactions between SEI and DR1/HA are with the β chain of DR1 and there is no interaction with the α chain. Zn²⁺, which plays important role in stabilizing the SEI and DR1 complex, is coordinated by residues H169, H207 and D209 from SEI and H81 from DR1 β chain. SEI makes less contacts with HA than that in other SAG-MHC/peptide complexes, by forming only one side chain H-bond with Kp-1 at the N-terminal of HA, which indicates that SEI binds DR1 irrespective of peptide sequence.