TIFR Centre for Interdisciplinary Sciences, Narsingi, Hyderabad 500075

Seminar

T cell antigens: Selection, presentation and recognition

Dhruv Sethi

Dana-Farber Cancer Institute, Harvard Medical School, Boston

Abstract: Antigen presenting cells (APCs) present peptide antigens displayed on HLA (Human Leucocyte Antigen; MHC in mouse) for recognition by T cells. HLA-DR molecules bind antigenic peptides in an endosomal compartment, where a non-classical molecule HLA-DM plays a critical role in the peptide selection process. Mechanistic details of the interaction between HLA-DR and the catalytic HLA-DM have been long sought after and had proven elusive. The structure of the HLA-DR – HLA-DM complex shows major rearrangements in the peptide binding groove. This conformational change creates a rapid and stringent selection process for the highest-affinity binders. Post antigen selection and loading, HLA molecules migrate to the surface of the APCs and are recognized by cognate TCR (T cell receptors) on T cells. The rules of TCR – peptide-HLA recognition are, however, broken during the recognition of self peptide antigens by TCRs during autoimmunity. The crystal structure of a TCR – self peptide-HLA complex from a patient of Multiple Sclerosis revealed aberrant binding of the TCR to the self peptide and novel interactions between the TCR and the HLA molecule. Structural characterization of additional complexes of the autoreactive TCR with pathogen derived peptides bound to HLA revealed the role of altered binding topologies in cross-reactivity and autoimmunity.

***Date*: Tuesday, February 05th 2013**

***Time*: 11:30AM (Tea/Coffee at 11:15AM)**

***Venue*: Conference Hall, TCIS**

All are cordially invited