

Cognate peptide-MHC complexes are expressed as tightly apposed nanoclusters in virus-infected cells to allow TCR crosslinking

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Abstract— Antigenic T cell stimulation requires interaction between the TCR of the T cell and cognate peptide-MHC molecules presented by the APC. Although studies with TCR-specific Abs and soluble peptide-MHC ligands have shown that the TCR needs to be crosslinked by two or more ligands to induce T cell stimulation, it is not understood how several MHC molecules loaded with the cognate antigenic peptide can produce crosslinking under physiological conditions. We show at the molecular level that large clusters of cognate peptide-MHC are formed at the surface of murine professional and nonprofessional APCs upon virus infection and that these clusters impinge on the stimulatory capacity of the APC. These clusters are formed by tight apposition of cognate peptide-MHC complexes in a configuration that is compatible with simultaneous engagement of two or more TCRs. This suggests that physiological expression of Ag allows formation of multivalent ligands for the TCR that permit TCR crosslinking and T cell activation.

Index Terms—

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