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A window of opportunity for cooperativity in the T cell receptor

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Abstract-

The T-cell antigen receptor (TCR) is pre-organised in oligomers, known as nanoclusters. Nanoclusters could provide a framework for inter-TCR cooperativity upon peptide antigen-major histocompatibility complex (pMHC) binding. Here we have used soluble pMHC oligomers in search for cooperativity effects along the plasma membrane plane. We find that initial binding events favour subsequent pMHC binding to additional TCRs, during a narrow temporal window. This behaviour can be explained by a 3-state model of TCR transition from Resting to Active, to a final Inhibited state. By disrupting nanoclusters and hampering the Active conformation, we show that TCR cooperativity is consistent with TCR nanoclusters adopting the Active state in a coordinated manner. Preferential binding of pMHC to the Active TCR at the immunological synapse suggests that there is a transient time frame for signal amplification in the TCR, allowing the T cells to keep track of antigen quantity and binding time.

Index Terms-

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