

KAPIL GUPTA

Pathology

Role of Co-receptor in modulating the membrane organization of T cell receptors on CD8⁺ T cells.

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The characteristic features of the adaptive immune response include both, antigenic specificity, and the enhanced biological response of activated and memory T cells compared to the naïve T cells. While much research has focused on the antigen specificity of the T cell response, it has only recently become apparent that enhanced sensitivity of activated T cells is in part controlled by TCR organisation and enhanced TCR cross-linking. Here we demonstrate that CD8 controls TCR cross-linking and modulates T cell signalling. Desialylation of the terminal carbohydrate residues of naïve T cells affects TCR membrane organization in a CD8 dependant fashion. This leads to an increase in overall binding avidity without affecting TCR-MHC specificity. The avidity for peptide-MHC-Ig was up to 50 fold greater in desialyated cells as compared to naïve cells. The biological consequences of this increase in avidity are enhanced TCR signalling leading to the acceleration and amplification of the proliferative T cell response. In summary these findings support a novel role for CD8 in controlling TCR cross-linking and thereby T cell activation and antigenic sensitivity.