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Oral presentation

Ligation of CD28 Alone by its Natural Ligand, CD86, Induces Lipid Raft Polarization in Human CD4 T-cells

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Background

Stimulation of naïve CD4 T-cells with anti-CD3/CD28-coated beads leads to polarization of lipid rafts (LRs). Since neither stimulus alone can polarize LRs, it has been postulated that a major role of costimulation is to facilitate LR aggregation. CD86 is upregulated or expressed aberrantly on immune cells in many autoimmune and infectious diseases, including HIV-1 infection.

Methods

To ligate CD28, we used an Ig fusion with extracellular domain of CD86 bound to magnetic beads, or K562 cells expressing CD86. Cell-bead conjugates were plated onto coverslips, stained with anti-GM1 or choleratoxin B, and LR polarization was visualized by digital immunofluorescence microscopy.

Results

Ligation of CD28 by natural ligand, but not antibody, induced polarization of LRs at the cell-bead interface, in absence of TCR ligation. This correlated with activation of Vav-1, increased IC calcium and translocation of NFkB p65, but did not result in proliferation or cytokine production. Using DNA microarrays, we detected induction of a subset of genes, including the Egr1 family of transcription factors. Engagement of CTLA-4 blocked CD86Ig induction of LR polarization and new transcription.

Conclusion

Lipid raft polarization can occur without TCR triggering, driven solely by CD28/CD86. HIV virions preferentially incorporate CD86 into their membranes and lipid rafts facilitate HIV entry. These virions have been shown to trigger NFkB activation in a CD86-dependent manner. The heightened immune activation in HIV infection enhances CD86 expression, which could induce LR polarization between infected cells and resting T-cells, permitting virological synapse formation and HIV entry. The ability of CD86 to induce LR may in part explain susceptibility of resting T-cells to HIV infection.