SUPERANTIGENIC ACTIVATION OF T LYMPHOCYTES AND ENDOTHELIAL CELLS: A MECHANISM FOR SUPERANTIGEN-INDUCED VASCULITIS

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Introduction: Superantigens (SAgs) are potent stimulators of T cells bearing specific Vβ T cell receptors (TCR), and although controversial, may have a pathogenetic role in Kawasaki disease (KD) and other childhood systemic vasculitides. We examined a novel mechanism of SAg-induced T cell/endothelial cell activation, and specifically investigated the hypothesis that the endothelial cell may operate as a "non-professional" SAg-presenting cell for T cells bearing specific Vβ TCRs.

Methods: To assess the ability of the endothelial cell to present SAg to T cells, human umbilical vein endothelial cells (HUVECs) with and without pretreatment with γ-interferon (to upregulate MHC Class II) were co-cultured for 4 hours in the presence or absence of purified allogeneic T cells with SEB, or TSST-1. After staining of the co-cultured cells with fluorescent conjugated monoclonal antibodies, flow cytometric analysis was performed on the HUVECs and T cells to examine surface expression of endothelial cell activation markers (cell adhesion molecules), Vβ-specific T cell activation (CD69), and Vβ-specific T cell adherence to the endothelial cell monolayer in vitro.

Results: Co-culture of purified T cells (CD3+, <0.8% expressing HLA-DR) with HLA-DR expressing HUVECs and TSST-1 or SEB resulted in Vβ-restricted CD4 and CD8 activation as determined by surface expression of the T cell activation marker CD69 (Vβ2 activation for TSST-1; Vβ3 and 12 activation for SEB). Additionally, there was CD4 T cell (but not CD8 T cell) Vβ-restricted adherence at 4 hours to the HUVEC monolayer. ICAM-1 and E-selectin expression was upregulated only on the HLA-DR expressing HUVECs following exposure to TSST-1 or SEB in the presence of CD3+ T cells.

Conclusion: In vitro, in the presence of the Th-1 cytokine γ-interferon, the endothelial cell becomes a competent SAg-presenting cell. This results in massive T cell activation and CD4 adherence to the endothelium, consequently resulting in endothelial cell activation. If this mechanism is operational in Kawasaki disease or other childhood vasculitides, it may be possible to block SAg-mediated vascular injury with SAg-peptide antagonists, providing a novel, specific, and potentially nontoxic therapy.