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HTLV-I Tax Protein Induces the Secretion of ThI Cytokines and β -Chemokines from Dendritic Cells

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HTLV-1-associated myelopathy/tropical spastic paraparesis is characterized by highly stimulated immune response that includes elevated levels of inflammatory cytokines/ chemokines, and oligoclonal expansion of Tax-specific CD8+ cytotoxic T lymphocytes in the cerebrospinal fluid. Studies have shown that the HTLV-1 transactivator protein Tax is available for immune recognition by antigen presenting cells such as dendritic cells. In this study, we have shown that the treatment of monocyte-derived dendritic cells (MDDCs) with extracellular Tax induces the secretion of Th1 cytokines (IL-12, and TNF- α) and β chemokines (MIP-I\alpha, MIP-I\beta, and RANTES). A significant dose-dependent increase was observed with IL-12 (5-, 7-, and 24-fold) and TNF- α (5-, 6-, and 9.6-fold) with Tax treatment for 24 hr at concentrations of 0.1, 1, and 10 mg/ ml, respectively. All three chemokines exhibited both dose- and time-dependent increase in the presence of Tax. More specifically, after 24 hr treatment with Tax (0.1, 1 and 10 µg/ml), MIP-1a was induced by 3.7-, 5.3-, and 6fold, MIP-1b by 2-, 3.7-, and 3.7-fold, and RANTES by 7-, 8-, and 20-fold, respectively. The mRNA expression of these cytokines/chemokines was confirmed by real time PCR and was in direct correlation with observations regarding their protein expression.