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Umbilical Cord Tissue-Derived Mesenchymal Stem Cells Inhibit T Cell Response to Peptide

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Mesenchymal stem cells (MSC) have been shown to possess immunomodulatory properties that highlight their potential as a cellular therapy for autoimmune disease. We propose to examine the *in vitro* potential of stem cells derived from umbilical cord tissue to suppress the effector functions of human auto-reactive T cells. While the mechanism(s) of suppression of T cell function are not fully understood, it has been hypothesized that MSC-derived immunosuppressive soluble factors and cell-to-cell contact are important. We developed an *in vitro* culture assay to assess the effects of umbilical cord derived MSC (TC-MSC) on T cell function. Various doses of low-passage TC-MSCs were adhered to collagen-coated 96 well plates or in the lower chamber wells of transwell plates. HLA-matched EBV transformed B cells were pulsed +/- with appropriate autoantigenic peptide and cultured with adherent MSC or in the upper transwell chambers with the appropriate T cell clone. After 48 hours, cells were stained for CD4 and stained intracellularly for IFN- γ and analyzed by flow cytometry. We observed decreased T cell effector function with MSC co-culture and this was partially restored by separation of MSC and T cell+B cell+peptide in the transwell. We examined if prostaglandin E2 derived from the MSC also contributed to decreased T cell effector function. The inclusion of a COX-2 inhibitor in the culture system led to partially restored T cell effector function. We conclude that TC-MSC-derived soluble factor(s) and TC-MSC:T cell contact both contribute to the TC-MSC's immunosuppressive effects. Primary TC-MSC isolates (with no prior cell culture) will also be tested in this system to determine if they possess similar immunosuppressive effects as adherent, cultured TC-MSC. These studies will pinpoint the functional mechanisms of the TC-MSC immunomodulatory properties on T cell effector function and may suggest avenues of enhancing MSC function in the treatment of autoimmune disease.
