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

Megan DeNicola
University of Massachusetts Medical School


Creative Commons License

This work is licensed under a Creative Commons Attribution-Noncommercial-Share Alike 3.0 License. This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Center for Clinical and Translational Science Research Retreat by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
Umbilical Cord Tissue-Derived Mesenchymal Stem Cells Inhibit T Cell Response to Peptide

Megan DeNicola¹, Robert Briddell², Kate Falcon-Girard³, William Fodor⁴, Morey Kraus³, and Sally C. Kent¹

¹Diabetes Center of Excellence, Department of Medicine, University of Massachusetts Medical School, Worcester, MA, 01605, ²ViaCord Processing Laboratory, Hebron, KY, 41048, ³ViaCord-PerkinElmer, Cambridge MA, 02142, and ⁴Cell Therapy Group, Madison, CT, 06443,

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.