Placenta-Derived Multipotent Cells Exhibit Immunosuppressive Properties That Are Enhanced in the Presence of Interferon-{gamma}

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Abstract

Several types of nonhematopoietic stem cells, including bone marrow mesenchymal stem cells (BMMSCs) and embryonic stem cells, have been shown to have immunosuppressive properties. We show that human placenta-derived multipotent cells (PDMCs), which are isolated from a source without ethical concern and harbor multilineage differentiation potential, have strong immunosuppressive properties. PDMCs suppress both mitogen-induced and allogeneic lymphocyte proliferation in both CD4 and CD8 populations. The immunosuppression seen with PDMCs was significantly stronger than that with BMMSCs. Both PDMCs and BMMSCs express indoleamine 2,3-dioxygenase, but only PDMCs are positive for intracellular human leukocyte antigen-G (HLA). Mechanistically, suppression of lymphocyte reactivity by PDMCs is not due to cell death but to decreased cell proliferation and increased numbers of regulatory T cells. Addition of neutralizing antibodies to interleukin-10 and transforming growth factor (TGF)-beta partially restored lymphocyte proliferation. Unlike BMMSCs, PDMCs treated with interferon-gamma for 3 days only very minimally upregulated HLA-DR. On the contrary, PD-L1, a cell surface marker that plays an inhibitory role in T-cell activation, was upregulated and TGF-beta expression was seen. The immunosuppressive properties of PDMCs, along with their multilineage differentiation potential, ease of accessibility, and abundant cell numbers, may render these cells as good potential sources for future therapeutic applications.