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Mesenchymal stem cells from chronic pancreatitis patients prolongs mice and human islet survival

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Mesenchymal stem/stromal cells (MSCs) have tissue repair abilities and immunoregulatory effect. We investigated whether MSCs derived from chronic pancreatitis (CP) patients are suitable for use in cell therapy. We first compared MSCs from CP patients with those from healthy donors. We found that cell surface markers, ability of colony formation and multi lineage differentiation abilities were similar between healthy MSCs (H-MSCs) and CP-MSCs. Gene profile study indicated 4 out of 84 human MSC-related genes were differentially expressed in CP-MSCs in comparison with healthy MSCs, among which growth differentiation factor 6 (GDF6), hepatocyte growth factor (HGF) were downregulated, whereas transforming growth factor (TGF) ?3 and matrix metalloproteinase-2 (MMP2) were upregulated. CPMSCs displayed great potential of inhibition of T cells proliferation to the same extent as healthy MSCs, with even higher indoleamine 2, 3-dioxygenase (IDO) expression upon IFN-? stimulation. The protective effects of MSCs on hypoxiainduced ? cell death are also comparable between CP-MSCs and H-MSCs. We further tested the protective effects of MSC in a marginal mass mouse islet transplantation model, and found that co-transplantation of islets with CP-MSCs improved islet survival and function after transplantation. The effects are in part mediated by paracrine secretion of insulin-like growth factor-1 (IGF-1), suppression of inflammation, and promotion of angiogenesis. In addition, in a pilot clinical trial, co-transplantation of patient islets with autologous MSCs showed safety and primary efficacy. Therefore our rodent and clinical trial data demonstrated that CP-MSCs have the potential to be used as a synergistic therapy to enhance the efficacy of islet transplantation.

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