Immunomodulatory Effects of Engineered hTERT-MSCs Overexpressing IDO1 Gene against Xenogeneic Rat Peripheral Blood Mononuclear Cells

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Background: Mesenchymal stem cells (MSCs) exhibit amenable immunoregulatory properties mainly through their paracrine effects. Some of the factors involved in this process include indoleamine 2,3-dioxygenase (IDO), prostaglandin-E2 (PGE2), and nitric oxide (NO). IDO1 is the rate limiting enzyme in tryptophan catabolic pathway. Herein, we investigated the immunosuppressive properties of the engineered MSCs (hTERT-MSCs-IDO1) on rat peripheral blood mononuclear cells (rPBMCs).

Methods: Rat PBMCs were isolated from freshly collected rat blood samples. Cell isolation was carried out on Lymphodex (Inno-Train). Lymphocyte inhibition assays were performed following co-culture experiments between untreated-hTERT-MSCs, interferon gamma treated cells (250 U/ml), hTERT-MSCs-GFP, and hTERT-MSCs-IDO1 (MSCs to PBMCs ratio of 1:3). hTERT-MSCs-GFP and hTERT-MSCs-IDO1 represent hTERT-MSCs transduced with lentiviral vectors containing control backbone and IDO1 gene, respectively. Following 3 and 5 days of co-culture experiments, cell viabilities of suspension cells were calculated using MTT assay.

Results: Functional analysis revealed that the hTERT-MSCs-IDO1 decreased the proliferation of xenogeneic rat PBMCs versus hTERT-MSCs-GFP (93.82% and 70.62% following 3 and 5 days of co-culture experiments, respectively). The highest level of inhibition was observed for IDO1 engineered cells as compared to other investigated groups. These differences were statistically significant on day 5 of co-culture.

Conclusion: Although, these results need more complementary studies, they confirm the immune-modulatory effects of hTERT-MSCs-IDO1 against rat PBMCs, mostly enriched for lymphocytes during isolation steps.

Keywords: hTERT-MSCs, Indoleamine 2, 3-dioxygenase (IDO1), Lymphocyte inhibition assay, Rat peripheral blood mononuclear cells.