

Comparative Study between Mesenchymal Stem Cells and Regulatory T-Cells in Macrophage Polarization for Organ Transplant Tolerance: In Vitro Study

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Abstract : Cell-based strategies may open therapeutic approaches that promote tolerance through manipulation of macrophages to increase long-term transplant survival rates and minimize side effects of the current immune suppressive regimens. The aim of the present study was, therefore, to test and compare the therapeutic potential of MSC and Tregs on macrophage polarization to develop an alternate cell-based treatment option in kidney transplantation. In the current protocol, macrophages from kidney transplant recipients with graft dysfunction were co-cultured with MSCs and Treg cells with and without cell-cell contact on transwell plates, further to quantitatively assess macrophage polarization in response to MSC and Treg treatment over time, M1 and M2 cell surface markers were used. Additionally, multiple soluble analytes were analyzed in cell supernatant by using bead-based immunoassays. Furthermore, to confirm our findings, gene expression analysis was done. MSCs induced the formation of M2 macrophages more than Tregs when macrophages M0 were cultured in transwell without cell contact. From this, we deduced the mechanism that soluble factors present in the MSCs condition media are involved in skewing of macrophages towards type 2 macrophages; similarly, in co-culture with cell-cell contact, MSCs resulted in more M2 type macrophages than Tregs. And an important finding of this study is the combination of both MSC-Treg showed significantly effective and consistent results in both with and without cell contact setups. Hence, it is suggestive to prefer MSCs over Tregs for secretome-based therapy and a combination of both for either therapy for effective transplantation outcomes. Our findings underline a key role of Tregs and MSCs in promoting macrophage polarization towards anti-inflammatory type. The study has great importance in prolongation of allograft and patient survival without any rejection by cell-based therapy, which induce self-tolerance and controlling infection.

Keywords : graft rejection, graft tolerance, macrophage polarization, mesenchymal stem cells, regulatory T cells, transplant immunology

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