Background: Macrophages are an immunological cell present in tumor microenvironment. Macrophages with the M2 phenotype promote tumor development through the immunosuppression of antitumor immunity. Previous studies indicate that bone marrow-derived mesenchymal stem/stromal cells (BM-MSCs) have the property of increasing M2 polarization in macrophages.1 We previously demonstrated the presence of MSCs in cervical cancer (CeCa-MSCs), promoting an inhibition of CD8 T lymphocyte cytotoxicity over tumor cells,2 suggesting an immune protective capacity in tumors, but to date, their effect over modulation in macrophage polarization remains unknown. In this study, we compared the capacities of MSCs from normal cervix (NCx) and CeCa to promote M2 macrophage polarization in a coculture system.

Methods: We evaluated in vitro the effect of MSCs in a cytokine-induced CD14+ monocytes toward M1- or M2-polarized macrophages system.

Results: Our results demonstrated that CeCa-MSCs, in contrast to NCx-MSCs, significantly decreased M1 macrophage cell surface marker expression (HLA-DR, CD80, CD86) and increased M2 macrophage expression (CD14, CD163, CD206, Arg1). Interestingly, compared with NCx-MSCs, in M2 macrophages generated from CeCa-MSC cocultures, we observed an increase in the percentage of phagocytic cells, in the intracellular production of IL-10 and IDO. Also we observed that macrophages generated have the ability to decrease proliferation of T cells and increase the capacity for the generation of CD4+CD25+FoxP3+ Tregs. This capacity to promote M2 macrophage polarization was correlated with the intracellular expression of macrophage colony-stimulating factor (M-CSF) and upregulation of IL-10 in CeCa-MSCs in cocultured with macrophages. Furthermore, the presence of M2 macrophages was correlated with the increased production of IL-10 and IL-1RA anti-inflammatory molecules.

Conclusions: Our in vitro results indicate that CeCa-MSCs, in contrast to NCx-MSCs, display an increased M2-macrophage polarization potential and suggest a role of CeCa-MSCs in antitumor immunity.

REFERENCES:

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