The Effect of Tumor Antigens and Heat Shock Proteins Complexes in the Presence of Mesenchymal Stem Cells 1 Derived Microvesicles on the Cytotoxicity of T Cells Stimulated With Dendritic Cells In vitro

Abstract:

Background & Objective: Immunotherapy is a therapeutic strategy that manipulates immune responses against tumor cells. The previous studies have shown that heat shock proteins-peptide complexes (HSP-PC) have critical role in MHC-I restricted TCD8+ responses. Evidence from several studies, demonstrate that TLR4-primed mesenchymal stem cells (MSCs), or MSC1, mostly elaborate pro-inflammatory mediators. In this regard, compared to MSCs, MSC-derived microvesicles (MVs) are more stable, induce stronger signaling and their functions do not exhaust over time. So, in the present study peripheral blood monocyte derived dendritic cells (MoDC) were used to load tumor antigens and stimulate T cell mediated responses in the present of MSC1-derived MVs with glial cancer *In vitro* and in rat model.

Methods: Tumor cell line, B92 was heated up to 43°C for 90 minutes prior to preparation of tumor cell lysate. After Isolation, proliferation and treatment of mesenchymal stem cells, MVs were purified by differential ultracentrifugation. Autologous T cells isolated from the nonadherent cells that harvested during the procedure to generate the MoDC, were incubated with tumor specific DCs in the presence of MSC1-derived MVs. For specific cytotoxic activity of delicate T cells by Flow cytometry analysis, they were cocultured with tumor cells in 96 well plates at final volume of 200 µl of CM at an effector: target ratio of 100:1.

Results: The T cell-mediated cytotoxicity assay by Flow cytometry analysis demonstrated

that tumor antigens plus MSC1-derived MVs don’t have significant affect on cytotoxic activity of tumor antigen and MSC1-derived MVs-primed T cells $P>0.05$.

Conclusion: These findings may offer new insight into the potential of MSC-derived MVs on cytotoxicity of T cells and by doing more researches in future hope that MSC1-derived MVs in the presence of tumor antigens have notable affect on cytotoxicity of T cells against brain tumor cells in vitro.

Keywords: Ag-HSP complex, MSC1, Exosome, Dendritic cells, T cell