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ANTI-TUMOUR EFFICACY OF MESENCHYMAL STEM CELL EXPRESSING TRAIL AGAINST LUNG CANCER STEM CELL

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SUMMARY

Introduction: Several studies have reported the ability of engineered mesenchymal stem cell (MSCs) expressing TNF-related apoptosis inducing ligand or TRAIL (MSC-TRAIL) to effectively mobilise and destroy tumour cells. However, the efficacy of MSC-TRAIL against a specific cancer stem cell (CSCs) subpopulation of CD133+ derived from lung cancer has not been reported. **Objective:** Thus, this study aims to investigate the *in vitro* efficacy of MSC-TRAIL against CSCs of a lung cancer. **Materials and methods:** Lentivirus was used to deliver TRAIL into MSCs and the cells were validated for TRAIL secretion using ELISA. The multipotent characteristics of MSC-TRAIL were evaluated based on trilineages differentiation and the expression of MSCs surface markers (CD44, CD90, CD105 and CD73) respectively. The CD133+ CSCs subpopulation was isolated from lung cancer cell line (H460) using high-performance cell sorter (BD FACSAria III) and characterised using sphere and clonogenic assays. The isolated CSCs were cultured with MSC-TRAIL or its conditioned medium and subjected for proliferation assay. **Results:** The efficacy of viral transduction yielded 81.7% of MSC-TRAIL. The TRAIL protein secretion was significantly higher ($p<0.01$) in the transduced MSCs as compared to the untransduced cells. MSC-TRAIL maintained its multipotent characteristics based on the positive histological staining of all three lineages and MSCs surface markers expression. Higher number of colonies, spheres and spheroid size ($p<0.001$) were noticed in the CSCs subpopulation proving the stem cell characteristics of these cells. Both the MSC-TRAIL and conditioned medium inhibited the proliferation of CD133+ cells demonstrating the effectiveness of MSC-TRAIL in targeting the population. **Conclusion:** The study is the first to demonstrate the efficacy of MSC-TRAIL against CD133+ CSCs of lung cancer, which enables a specific targeting of CSCs, thus paving the way towards a more effective treatment for lung cancer patients.

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