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Rat adipose-derived stem cells (RADSC) as a vehicle to deliver TNF-related apoptosis inducing ligand (TRAIL) into cancer microenvironment †

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Abstract: Adipose-derived stem cells (RADSC) play a multifaceted role in cancer metabolism and constitute a potential target for oncologic therapies. Local delivery of TNF-related apoptosis-inducing ligand (TRAIL) can limit tumour growth by selective binding to the death receptor (DR4/DR5) in cancer cells. In most healthy cells this pathway is blocked by decoy antagonists such as osteoprotegerin (OPG). This in-vitro study aimed to evaluate an oncologic treatment based on the delivery of TRAIL-transduced rADSC to the vicinity of breast adenocarcinoma cells (RBA). A plasmid containing transgene was produced based on puromycin-resistance-gene containing plasmid and amplified TRAIL gene from the Sprague-Dawley rat kidney. Lentiviral particles were produced in HEK293T cells. Cytotoxicity of TRAIL against RBA was measured using MTS Assay. Quantitative PCR analyses were conducted to confirm transgene overexpression and measure TRAIL-dependent receptors expression in both cell lines. Data analysis was done using the student's t-test. Cells were successfully transduced, and TRAIL expression was higher in transduced cells compared to controls. The expression of TRAIL-dependent receptors was higher in RADSC compared to RBA cells, however exogenous TRAIL is cytotoxic against RBA cells, not RADSC. All in all, the results show that TRAIL-RADSC may constitute a tool for delivery of anticancer cytokine to tumour microenvironment. The overexpression of TRAIL by RADSC also stimulates their growth leading to further increased cancer microenvironment penetration. Such active surveillance based on stable local production of anticancer cytokine can limit cancer recurrence when transplanted into the vicinity of cancer tissue.

Keywords: Mesenchymal Stem Cell; Breast Cancer; TRAIL; Gene Therapy

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