

SURFACE MODIFICATION OF MESENCHYMAL STEM CELLS WITH SELF-ASSEMBLED VESICLES FOR SYSTEMIC CELL TARGETING

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Cell therapy using mesenchymal stem cells (MSCs) has the potential to treat a wide range of diseases and tissue defects. However, one of the greatest challenges of cell therapy is to systemically deliver a large quantity of viable cells to a specific tissue with high engraftment efficiency. MSCs exhibit poor homing properties following systemic infusion which is likely due to the lack of relevant adhesion and chemokine receptors on their surface following culture expansion. To address this issue, we have developed a technique to non-invasively engineer the surface of MSCs with adhesion ligands using self-assembled vesicles. This technique offers a simple method to intercalate biotinylated lipid molecules into the lipid bilayer of the cell membrane without long term modification, which occurs during covalent or enzymatic modification.

To modify the cell surface, vesicles prepared from a biotinylated lipid were fused with the cell membrane followed by conjugation of streptavidin and biotinylated Sialyl Lewis^x (SLeX). The SLeX moiety represents the active site of the P-selectin glycoprotein ligand (PSGL-1), an important leukocyte ligand that participates in cell rolling adhesion. Previously, we have shown that SLeX modification of MSCs improves homing to the bone marrow or sites of inflammation. The adhesive interactions of SLeX modified MSCs were investigated under dynamic shear stress conditions on a P-selectin coated substrate in a parallel plate flow chamber assay. At a shear stress of 0.5 dynes/cm², SLeX modified MSCs exhibited rolling velocities that were 75% lower than those of the unmodified MSCs, indicating that the self-assembled-vesicles could successfully modify the MSCs and increase interaction with the P-selectin substrate. Moreover, MSCs' native phenotype including viability, proliferation, adhesion and multilineage differentiation potential was not significantly affected by incorporation of the biotinylated vesicles. This simple cell surface modification strategy with self-assembled vesicles presents a potentially useful approach to engineer the cell membrane.