

Mesenchymal stem cells and osteophilic polymer as promising agents in bone regeneration

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Introduction: Mesenchymal stem cells (MSCs) are an attractive stem cell source for transplantation. MSCs can easily differentiate into osteoblasts and increase in osteoblast number will have positive effect on the bone regeneration in such conditions as osteoporosis or Paget disease. To provide the targeted delivery of MSCs to bone we have synthesized a novel osteophilic polymer. The primary active sites of the polymer are bisphosphonate functional groups that target hydroxyapatite molecules (HA) on the bone surface. NHS groups on the other end of the molecule allow polymer to bind to the cell surface components. Coating of cell surfaces with the polymer would allow the cells to bind specifically to HA component of bone and localize the cellular repair functions to areas of injured bone.

Methods: In this study we have characterized polymer/cell and functionalized cells/bone chips interactions *in vitro*. Polymer functionalized cells were incubated with bone fragments for varying times and the stability of cell-bone binding was determined microscopically. Cytotoxic effect was evaluated using Luminescent proliferation assay (Cell Titer Glow, Promega). Differentiation to osteogenic lineage was performed with osteogenic media (StemPro osteogenesis kit, Life Technologies) and visualized with the help of alkaline phosphatase staining kit (Sigma Aldrich). The distribution of the polymer coated cells throughout the body *in vivo* was performed by *in vivo* imaging spectrum (IVIS, Caliper). The polymer coated cells were suspended in PBS buffer and injected intravenously through the tail vein. The imaging was performed at several time points until the polymer signal disappeared.

Results: The polymer coated cells were shown to be stably attached to bone fragments for at least 2 hours. The polymer is not cytotoxic and does not affect further differentiation of MSCs into osteoblasts. Injection of the polymer coated cells intravenously through the tail vein of mice has confirmed bone targeting potential of the polymer.

Conclusion: Overall, the osteophilic polymer and mesenchymal stem cell approach seem as promising agents in bone regeneration.