OSTEOPHILIC POLYMER AND MESENCHYMAL STEM CELLS IN BONE REGENERATION

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Key Words: osteoporosis, mesenchymal stem cells, ATRP synthesis, targeted cell delivery

Introduction: Mesenchymal stem cells (MSCs) are an attractive stem cell source for transplantation. MSCs can easily differentiate into osteoblasts and have positive effect on the bone regeneration in osteoporotic bone fracture. Age-related alterations shift bone metabolism to induced osteoclastic activity and reduction of osteoblasts that consequently result in progressive bone loss. In this case transplantation of osteoblast precursor cells, mesenchymal stem cells, may be an option.

Methods: For 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 MSCs with the polymer allowed the cells to bind specifically to HA component of bone and localize the cellular repair functions to areas of injured bone. Osteoporotic condition in rats was experimentally induced by bilateral ovariectomy and confirmed via measuring bone density and histological assessment. Ulna fracture model was performed in 4 groups (5 animals each) and each group received different solution (Polymer in PBS, MSCs in PBS, MSCs+Polymer in PBS). Group 1 served as a control. Injections were administrated locally at the site of the fracture every week during 1 month.

Results: Previous in vitro studies showed that polymer can be stably attached to cell surface for at least 4 hours and to bone fragments in vitro for at least 3 hours, confirming the bone targeting potential of the polymer. The polymer was not shown to be cytotoxic by cell viability assay (Luminescent Cell Viability Assay) and did not affect further differentiation of MSCs into osteocytes. Micro-CT morphometry analysis revealed significantly improved bone mass indicators up to 34%. Histological assessment showed formation of the young bone tissue from immature cells at fracture zone.

Conclusion: Osteophilic polymer was found to be an effective approach to navigate MSCs to the bone tissue and induce fracture regeneration in osteoporotic condition.