Stem Cell Therapy for Vertebral Bone Tissue Engineering

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Introduction

Vertebral compression fractures are the most common fragility fractures accounting for approximately 700,000 injuries per year. Since open surgery involves morbidity and implant failure in the osteoporotic patient population, new minimally invasive solution are being developed. These methods include injection of synthetic nonbiological material that does not resorb and remains a permanent foreign-body fixture. Therefore there is a clear clinical need for a biological solution for vertebral bone repair. We have previously shown that BMP-modified adipose-derived stem cells (ASCs) are capable of inducing spinal fusion in vivo.(1) In this study we hypothesized that direct injection of ASCs, transiently expressing BMP6, to a vertebral bone void defect would induce accelerated bone regeneration.

Materials and Methods

Bone void defects were created in coccygeus vertebra of Nude rats. The spine was exposed and a surgical drill was used to create a 1mm in diameter and 2 mm in depth void. Porcine ASCs were isolated and labeled with lentiviral vector that encodes for two reporter genes, Luciferase (Luc) and GFP. (2) Labeled ASCs were transfected with a BMP6 plasmid using the nucleofection. (1) 24-hours later the cells were suspended in fibrin gel and injected into the bone void. The control group was injected with fibrin gel only. The regeneration process was monitored in vivo using μCT, while cell survival was monitored using bioluminescent imaging (BLI) every two weeks. The operated vertebrae were harvested after 12 weeks, and analyzed using histology and immunohistochemistry against porcine vimentin.

Results

In vivo BLI detected the lucifearse-expressing cells at the implantation site for 12 weeks (Fig. 1). Since the Luc reporter gene in the injected cells is ubiquitin promoter-driven, gene silencing does not occur over time. Therefore the gradual decline of the signal probably indicates cell apoptosis that usually occur during MSC differentiation. μCT scans on day 1 demonstrated a large defect created in the vertebra (Fig. 2). Starting from 4 weeks post operation, considerable defect repair was seen in the group treated with ASC-BMP6, while complete repair was achieved three months post cell injection. Quantitative analysis of new bone formation indicated 7-folds higher bone volume in the defect site of stem cell-treated rats compared to the fibrin gel only group.

Discussion and Conclusions

In this study we have shown the potential of injected, BMP-modified, ASCs to repair vertebral bone defects in a rat model. These results could pave the way to a novel approach for the biological treatment of traumatic and osteoporosis-related vertebral bone injuries.

References

2. Z. Li et al., Stem Cells 26, 864 (Apr, 2008).

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