Mesenchymal Stem Cell Injection in Degenerated Intervertebral Discs: Cell Leakage May Induce Osteophytes Formation
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Introduction
Stem cell therapy for intervertebral disc regeneration has acquired increasing interest. Recent studies have shown that stem cell therapy might be a feasible and effective approach for the treatment of intervertebral disc degeneration (IDD). However, many unanswered questions remain in the translation to clinical therapies, such as the most efficacious stem cell type, the most reliable transplantation method including the carrier choice, the fate of stem cells after misdirected delivery, among others. Recently it has been reported that mesenchymal stem cells (MSC) are immunoprivileged and immunosuppressive suggesting they may be transplanted allogenically. This study analyzed the fate of allogenic MSC after injection into a rabbit stab model of IDD.

Materials and Methods
L2-3, L3-4 and L4-5 discs of 4 NWR rabbits were stabbed with 16G needle at 3mm dept to create IDD. Allogenic rabbit bone marrow MSCs were expanded in-vitro and MSC for injection at L2-3 were transduced with retroviral vector containing the marker gene eGFP with a 50% transduction efficiency. After 3 weeks, 1x10^5 MSCs were injected into the discs. The L2-3 received the transduced cells, and the other discs received non-transduced MSCs. Rabbits were followed by X-ray and MRI at 6 and 12 weeks after injection. At 12 weeks, animals were sacrificed and spines analyzed by gross anatomy histology and fluorescent microscopy.

Results
MRIs showed no sings of regeneration at any timepoints. X-ray and gross anatomy inspection demonstrated large anterolateral osteophytes (fig. 1A). Histological analysis showed that osteophytes were composed of mineralized tissue surrounded by chondrocytes (fig. 1B-C). In addition, analysis by confocal microscopy demonstrated the presence of the injected GFP labeled MSCs in the osteophytes (fig. 1C-D). Inflammatory cells were not observed in any injected discs.

Discussion and Conclusions
MSC injection in this rabbit stab model of degeneration did not demonstrate improvement in IDD as anticipated. These results raise concern that MSCs can migrate out of the nucleus, and undesirable bone formation can occur. While cause cannot be inferred from this study, the presence of MSCs in the osteophytes suggests a potential problem with this approach. Future work is needed to optimize the delivery method to make this therapeutic option a clinically viable tool.

Disclosures
Authors declare no conflict of interests.