

Regeneration of nucleus pulposus after discectomy by autologous mesenchymal stem cells: a rabbit model

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INTRODUCTION: There is evidence to suggest that mesenchymal stem cells (MSC) introduced into the degenerated intervertebral disc have the ability to survive and halt the degeneration process^{1, 2}. In clinical practice, one of the areas where this maybe useful, is using these cells combined with a scaffold for nucleus replacement after surgical excision of the disc. This study explores the ability of MSCs to survive and maintain disc height in a rabbit discectomy model.

METHODS: Autologous MSCs were isolated from 12 New Zealand white rabbits and expanded *ex vivo*. They were bromodeoxyuridine (BrdU)-labeled, seeded onto gelatin scaffolds and re-implanted into the rabbit after either a posterior discectomy (n=8) or anterior discectomy (n=4). 4 lumbar disc levels were operated per rabbit: 1 control level with scaffold; 1 sham level (discectomy alone); and 2 levels implanted with BrdU-labeled MSCs. Immuno-histochemical and radiographic analyses were performed up to 12 weeks.

RESULTS: Immunohistochemical examination showed only 1 (12%) posteriorly operated rabbit but 3 (75%) anteriorly operated rabbits retained the MSCs. The BrdU-labeled cells could be detected within the nucleus pulposus, the annulus fibrosus and the cartilaginous end-plates up to 12 weeks post-operatively (Figure 1). There was evidence of new bone and osteophyte formation. Disc height measurements reviewed that both the scaffold group and the MSCs-implanted group were able to better maintain disc height than the sham operated group.

DISCUSSION & CONCLUSIONS: The IVD is a particularly challenging environment, as it is avascular and subjected to high repetitive mechanical loading. Moreover, a discectomy model, where the nucleus is evacuated, is a more demanding model for the stem cells to work than previous disc degeneration models. Nevertheless, this study demonstrates that MSCs in combination with a scaffold has the potential to act as a nucleus replacement in patients undergoing surgical treatment. However cells could not be easily retained in

the posterior discectomy group probably because of the annular defect after posterior discectomy. Whereas in the anterior group, the annular flap may help to retain cells. For those that can retain cells we have demonstrated for the first time that these cells can remain inside the disc for up to 12 weeks. However, in none of the groups could disc height be maintained, and the scaffold alone group did just as well as the MSCs-implanted group. New bone formation and osteophyte formation could be an effect of the degenerative process or because of the transplanted MSCs transdifferentiating into osteoblasts. This study has showed that stem cell therapy has the potential to act as a nucleus replacement. Future work will need to assess the synthetic activity, the matrix composition and the fate of the retained MSCs. Work will also be needed to identify the best scaffold and cell source for this purpose.

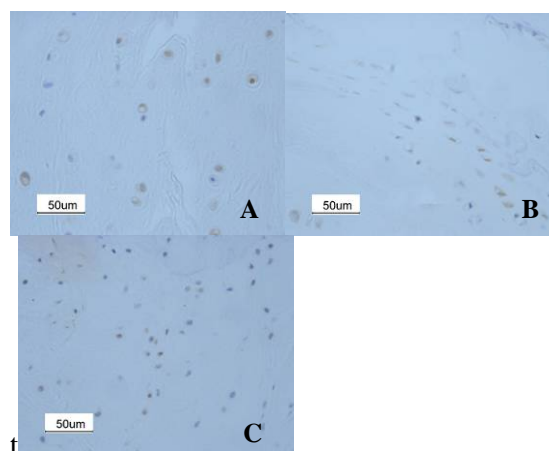


Fig. 1: The persistence of MSCs (brown cells) in all 3 disc compartments: the nucleus pulposus (A), the endplate (B) and the annulus fibrosus (C).

REFERENCES: ¹ D. Sakai, J. Mochida, Y. Yamamoto et al (2003) *Biomaterials* **24**(20): 3531-41. ² KMC Cheung, G. Ho, D Chan (2004) 39th Annual Meeting of the Scoliosis Research Society.

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