Potential of Human NP-like Cells Derived From Umbilical Cord to Treat Degenerative Disc Disease: Novel Mechanism for Disk Regeneration

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Introduction

Degenerative disc disease (DDD) is a common spinal disorder that manifests with lower back pain (Fig. 1). The degeneration of intervertebral disc (IVD) is characterized by the loss of extracellular matrix and dehydration of the nucleus pulposus (NP) of IVDs (Fig. 2). Currently, there is no biological treatment to cure this debilitating ailment.

Methods

In this study, we investigated the efficacy of NP-like cells (NPCs)

derived from the umbilical cord (UC) MSCs in restoring degenerated IVDs using a rabbit DDD model (Fig. 3). UC -MSCs were induced to differentiate into NPCs by using differentiation medium (DM) for two weeks, labeled with PKH26 and then injected into the degenerated IVDs (Fig. 4-5).

Figure 1.

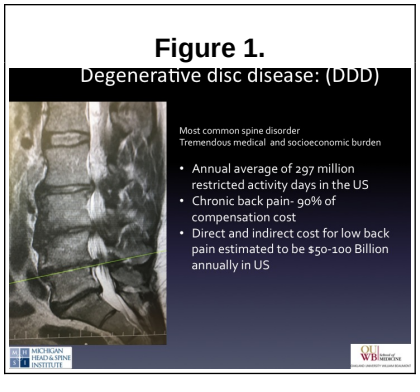


Figure 2.

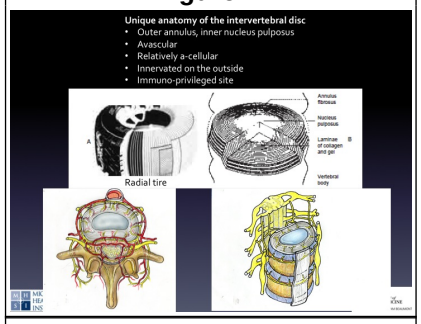
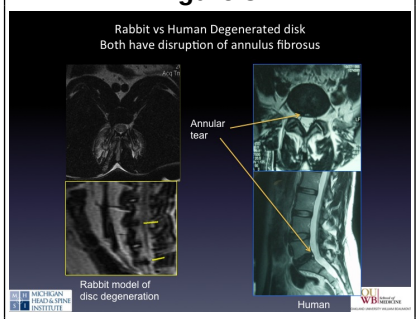
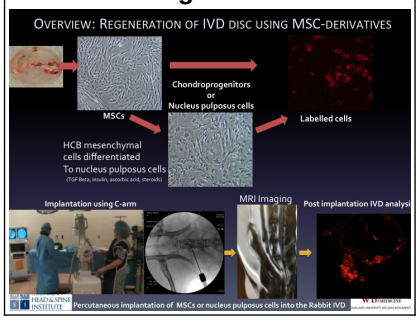


Figure 3.



MRI image of rabbit model of disc degeneration similar to human DDD

Figure 4.



Results

Eight weeks post-transplantation analysis showed that structure and cellularity of the NP improved only in the IVDs that received NPCs. Transplanted IVDs also had higher sGAG and water content compared to the sham and degenerated IVDs (Figs. 6-8). The transplanted cells survived, integrated, and dispersed in the damaged areas of the NP and were functionally active as they expressed human genes, SOX9, ACAN, COL2, FOXF1, KRT19, PAX6, CA12 and COMP as well as human proteins, SOX9, ACAN, COL2 and FOXF1 implicated in NP biosynthesis (Fig. 9).

Figure 5.

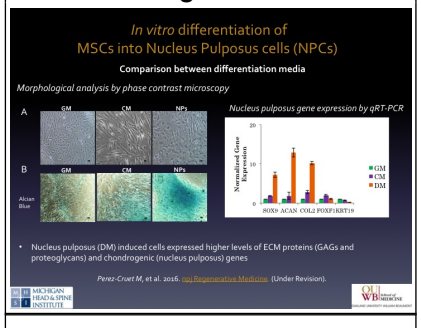


Figure 6.

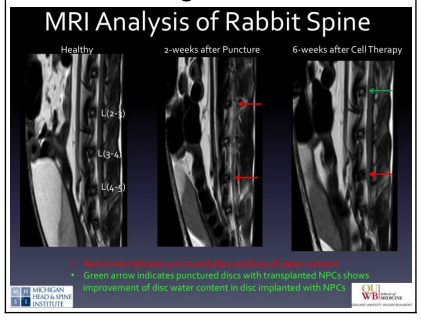
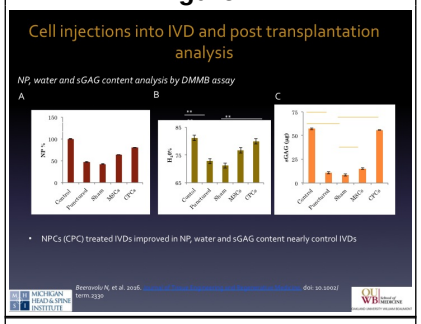


Figure 7.



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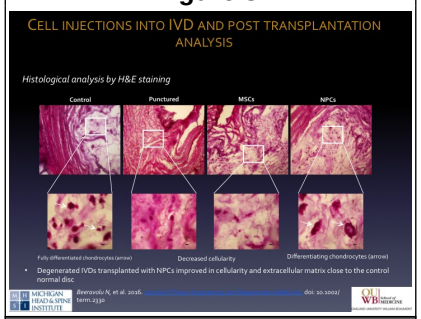

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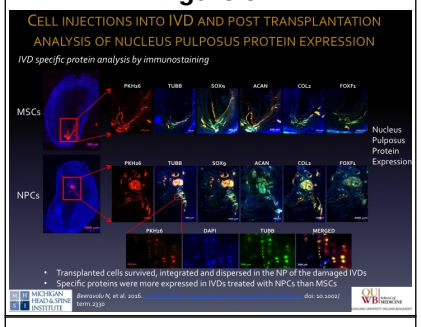
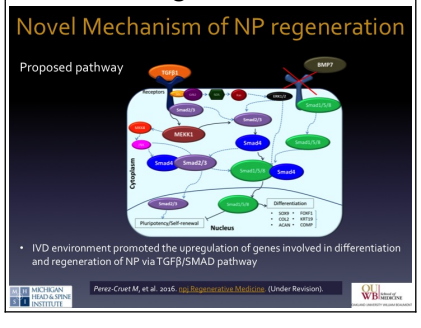


Figure 10.



Conclusions

These results suggest that NPCs were capable of homing to regenerate NP. The molecular mechanism for NP regeneration was proposed to be regulated via the TGFß1 pathway (Fig. 10). This study for the first time demonstrates the feasibility and efficacy of human NPCs derived from UC-MSCs to regenerate NP in a rabbit model. These findings should spur interest for clinical studies to treat DDD using NPCs.

References

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