

## From nucleus pulposus mesenchymal stem cells towards neural differentiation: an interesting prospect

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Regenerative medicine arouses great interest for the treatment of many neurological diseases. Since nucleus pulposus of the intervertebral discs is a postembryonic vestige of the notochord, it has been hypothesized that mesenchymal stem cells (MSCs) isolated from nucleus pulposus (NP-MSCs) can more easily differentiate into neurons. In this study, MSCs from nucleus pulposus were successfully isolated and characterized. Then, neural differentiation was induced by using a medium consisted of DMEM/F12 supplemented with B27 and the growth factors FGF and EGF for 10 days. Immunocytochemistry, molecular studies, SEM and TEM microscopy analyses were performed.

NP-MSCs exhibited the typical features of MSCs, revealing spindle-shape morphology, specific immunophenotype attributable to MSCs and the ability to differentiate in osteogenic and chondrogenic lineages. After neurodifferentiation induction, compared to NP-MSCs in only DMEM/F12, proliferation rate decreased and cells changed morphology acquiring an increased number of the so-called neural-like extensions. Neural progenitor marker NESTIN and mature neuronal marker ENO-LASE-2 were up-regulated, while GFAP was not detected. Moreover, cells after differentiation were small rounded and fusiform, with tendency to organize in clumps; they had elongated extrusions containing oriented cytoskeletal elements, classifiable as microtubules and intermediate filaments, as visualized by SEM and TEM microscopy. Dense vesicles similar to lipid droplet were also observed. NP-MSCs in differentiation medium were able to form neurospheres. In conclusion, even if more analysis have to be done and the way to treat neurodegenerative disease with regenerative medicine is still long, NP-MSCs represent a promising resource.

### References

- [1] Blanco et al. (2010) Isolation and characterization of mesenchymal stromal cells from human degenerated nucleus pulposus: comparison with bone marrow mesenchymal stromal cells from the same subjects. *Spine (Phila Pa 1976)* 35: 2259-65.
- [2] Uccelli et al. (2008) Mesenchymal stem cells in health and disease. *Nat Rev Immunol* 8: 726-36.

### Keywords

Mesenchymal stem cells from nucleus pulposus, neuronal differentiation, regenerative medicine