Human adipose mesenchymal stromal cells transplantation promotes intervertebral disc regeneration in Biglycan-deficient murine model of chronic and progressive disc degeneration

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INTRODUCTION: Intervertebral disc (IVD) degeneration is a major cause of back pain and represents an endemic problem for which treatment is costly and relatively ineffective. The purpose of the present study is to assess disc regeneration by adipose-derived stromal cells (ADSCs)¹ transplanted in Biglycan (BGN) deficient mice (Bgn⁻/⁻). BGN is an important proteoglycan of the extracellular matrix and its decrease has been correlated with intervertebral disc aging and degeneration. Bgn⁻/⁻ mice lack this protein and undergo spontaneous IVD degeneration during aging², thus representing a valuable in vivo model to study therapies that may delay IVD degeneration.

METHODS: To evaluate ADSCs efficacy, mice were injected with 8x10⁴ cells intradiscally (L1-L2) at 16 months old, an age in which mice showed severe IVD degeneration, confirmed by both 7T Magnetic Resonance Imaging (MRI)³ and histology. Placebo and ADSCs treated Bgn⁻/⁻ mice were assessed by 7T MRI analysis until 12 weeks post-transplantation. Mice were then sacrificed and investigated by histology and by immunohistochemistry for the presence of human cells, using anti-human nuclei (HuNu), and for the expression of BGN and aggrecan in the IVD treated area.

RESULTS: After treatment, in vivo 7T MRI showed a visible increase in signal intensity over time within the disc of mice that received ADSCs, while the placebos did not show such any variation. Moreover, in mice with ADSC-injected discs, ultrastructural analyses demonstrated the presence of human (anti-HuNu positive) cells even at 12 weeks after transplant, and these cells were found positive for the expression of the BGN proteoglycan. Furthermore this treatment determined an increase of aggrecan tissue levels. These results demonstrate that the injection of ADSCs into Bgn⁻/⁻ mouse model of spontaneous IVD degeneration promotes the new expression of human BGN and increases aggrecan levels, as demonstrated by MRI, histological and immunofluorescence findings.

DISCUSSION & CONCLUSIONS: In conclusion, we used a Bgn⁻/⁻ model to explore the effect of ADSCs in a progressive and spontaneous degenerative disc disease. Bgn⁻/⁻ mouse represents a unique model to study in vivo the time progression of IVD degeneration as a chronic and linear degenerative pattern, similar to the human IVD pathophysiology. Our data show, for the first time, that ADSCs transplantation is beneficial in arresting IVD degeneration in a mouse model, and suggest that this approach might be an effective treatment to delay degenerative disc disease.

REFERENCES: