Commentary

Gel and cells: A promising reparative strategy for degenerated intervertebral discs

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A R T I C L E   I N F O

Article History:
Received 30 March 2020
Accepted 30 March 2020
Available online xxx

One of the most common causes of physical disability is lower back pain, which affects overall well-being and work performance, with recent reports indicating a lifetime prevalence as high as 85% in industrialized countries [1]. The recent Global Burden of Disease study states that lower back pain is the most common musculoskeletal disorder and imposes the highest disability burden of all specific conditions in developed countries [2]. There are currently no disease-modifying therapies for lower back pain and, although there are several known risk factors, such as obesity, psychological factors, age and sex, and genetic variants, the underlying cellular and molecular cause(s) of back pain remain unclear [3].

While the exact etiology of lower back pain is unknown, a frequently associated pathology is the degeneration of the intervertebral disc (IVD), a specialized joint of the axial skeleton that serves to absorb and disperse compressive forces, to confer tensile and torsional strength, and to provide flexibility to the spine [4]. The mature IVD is a multi-component structure consisting of three distinct, yet interdependent specialized tissues: a gelatinous central nucleus pulposus (NP), encaised by the outer fibrous annulus fibrosus (AF), that together are sandwiched between the cartilage endplates that anchor the IVD to the adjacent, rostral and caudal vertebral bodies. IVD herniation is a common pathology of sciatica and is often treated by discectomy. While there have been previous reports on the application of BMSCs in various hydrogel biomaterial scaffolds for IVD repair [e.g., 10], a particularly intriguing finding reported here is the apparent, mutually enhancing interaction between BMSCs and NPCs, resulting in both BMSC differentiation into NPCs and activation of NPCs. Notochordal cells, which are developmental precursors of NPCs have previously been shown to stimulate BMSC differentiation towards a young NPC phenotype [9], thought to be mediated by secreted factors. However, it is not known that BMSCs have a reciprocal stimulatory effect on NPCs. The

DOI of original article: http://dx.doi.org/10.1016/j.ebiom.2020.102698.
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https://doi.org/10.1016/j.ebiom.2020.102756
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encapsulation of BMSCs by Ukeba et al. [6] likely enhanced the retention of BMSC-secreted factors, resulting in enhancement of NPC bioactivity observed in the 3D in vitro cultures, as well as activation of resident NPCs in the site of IVD degeneration in vivo. The absence of osteophyte formation also indicated that the rapid curing of the UPAL hydrogel prevented leakage of BMSCs. In this manner, the “Gel-Cells” approach may function as a means to efficiently capture the trophic activity of the BMSCs, although it is unknown whether the immunomodulatory activity of the BMSCs also played a role in the observed effects.

There are, however, some remaining hurdles for successful and practicable translation of the technology described by Ukeba et al. [6]. These include: (1) effective repair of the AF, the outer fibrous structure of the IVD, which is often compromised in degenerative disc diseases; (2) achieving material properties in the regenerated tissue that are comparable to those of the native NP, a critical requirement for its mechanical function; and (3) functional integration of the regenerated NP with the other components of the IVD, i.e., the AF and the cartilage endplates, for structural integrity and mechanical stability. Finally, given the continuous mechanically “pressing” need of the loaded environment of the IVD, it is essential that production of the new ECM in the “regenerated” IVD must be optimally matched, in time and scale, to biodegradation of the non-native alginate hydrogel scaffold, to achieve biocompatible and structural stability.

Disclosure

None

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