Intervertebral disc tissue engineering

Tissue engineering techniques, by replacing the damaged intervertebral disc (IVD) with scaffolds and appropriate cells, have emerged as a promising therapeutic approach to treat degenerative disc disease [1].

While a number of engineered discs have been developed, the average size of these constructs remains a fraction of the size of human intervertebral discs.

Gullbrand et al. fabricated medium (3 mm height x 10 mm diameter) and large (6 mm height x 20 mm diameter) sized disc-like angle ply structures (DAPS), encompassing size scales from the rabbit lumbar spine to the human cervical spine. Maturation of these engineered discs was evaluated over 15 weeks in culture by quantifying cell viability and metabolic activity, construct biochemical content, MRI T2 values, and mechanical properties. To assess the performance of the DAPS in the in vivo space, pre-cultured DAPS were implanted subcutaneously in athymic rats for 5 weeks.

The findings show that both sized DAPS matured functionally and compositionally during in vitro culture, as evidenced by increases in mechanical properties and biochemical content over time, yet large DAPS under-performed compared to medium DAPS. Subcutaneous implantation resulted in reductions in NP cell viability and GAG content at both size scales, with little effect on AF biochemistry or metabolic activity. These findings demonstrate that engineered discs at large size scales will mature during in vitro culture, however, future work will need to address the challenges of reduced cell viability and heterogeneous matrix distribution throughout the construct. Statement of Significance This work establishes, for the first time, tissue-engineered intervertebral discs for total disc replacement at large, clinically relevant length scales. Clinical translation of tissue-engineered discs will offer an alternative to mechanical disc arthroplasty and fusion procedures, and may contribute to a paradigm shift in the clinical care for patients with disc pathology and associated axial spine and neurogenic extremity pain [2].

Cell therapy for regeneration of intervertebral discs are regarded to hold promise for degenerative disc disease treatment, a condition that is strongly linked to lower back pain. A de novo self-assembling peptide hydrogel (SAPH), chosen for its biocompatibility, tailorable properties and nanofibrous architecture, was investigated as a cell carrier and scaffold for nucleus pulposus (NP) tissue engineering. Oscillatory rheology determined that the system would likely be deliverable via minimally invasive procedure and mechanical properties could be optimised to match the stiffness of the native human NP. After three-dimensional culture of NP cells (NPCs) in the SAPH, upregulation of NP-specific genes (KRT8, KRT18, FOXF1) confirmed that the system could restore the NP phenotype following de-differentiation during monolayer culture. Cell viability was high throughout culture whilst, similarly to NPCs in vivo, the viable cell population remained stable. Finally, the SAPH stimulated time-dependent increases in aggrecan and type II collagen deposition, two important NP extracellular matrix components. Results supported the hypothesis that the SAPH could be used as a cell delivery system and scaffold for the treatment of degenerative disc disease.

Lower back pain (LBP) prevalence is widespread due to an aging population and the limited efficacy of current treatments. As LBP is strongly associated with intervertebral disc (IVD) degeneration, it is thought that cell-based therapies could alleviate LBP by repairing IVD tissue. Various natural and synthetic biomaterials have been investigated as potential IVD tissue engineering scaffolds. Self-assembling peptide hydrogels (SAPHs) combine advantages of both natural and synthetic

biomaterials; for example they are biocompatible and have easily modifiable properties. The present study demonstrated that a de novo SAPH had comparable strength to the native tissue, was injectable, restored the IVD cell phenotype and stimulated deposition of appropriate matrix components. Results illustrated the promise of SAPHs as scaffolds for IVD tissue engineering [3].

1)
Chan LK, Leung VY, Tam V, Lu WW, Sze KY, Cheung KM. Decellularized bovine intervertebral disc as a natural scaffold for xenogenic cell studies. Acta Biomater. 2013 Feb;9(2):5262-72. doi: 10.1016/j.actbio.2012.09.005. Epub 2012 Sep 20. PubMed PMID: 23000521.
2)
Gullbrand SE, Kim DH, Bonnevie E, Ashinsky BG, Smith LJ, Elliott DM, Mauck RL, Smith HE. Towards the Scale up of Tissue Engineered Intervertebral Discs for Clinical Application. Acta Biomater. 2018 Feb 7. pii: S1742-7061(18)30070-9. doi: 10.1016/j.actbio.2018.01.050. [Epub ahead of print] PubMed PMID: 29427744.
3)
Wan S, Borland S, Richardson SM, Merry CL, Saiani A, Gough JE. Self-assembling peptide hydrogel for intervertebral disc tissue engineering. Acta Biomater. 2016 Dec;46:29-40. doi: 10.1016/j.actbio.2016.09.033. PubMed PMID: 27677593.