Cartilage regeneration

Adult articular cartilage has limited capacity of regeneration. Transforming growth factor β1 (TGF-β1) is known to regulate the formation of connective tissues and the Stupp group has designed self-assembled peptide nanofibers containing a phage-derived peptide sequence (HSNGLPL) with binding affinity to TGF-β1 (Shah et al. 2010). When implanted in a full thickness chondral defect in a rabbit model, these gels were shown to promote the regeneration of articular cartilage with or even without the addition of exogenous TGF-β1, as detected by formation of hyaline-like tissue within the defect space. The KLD-12 peptide hydrogel was used for encapsulating chondrocytes (Kisiday et al. 2002) and showed to support cell survival and to retain the chondrocytic phenotype with increased production of cartilage ECM components (glycosaminoglycans, type II collagen). Bone marrow stromal cells (BMSCs) were encapsulated within KLD-12 and RAD16-I peptide hydrogels (Kopesky et al. 2010). Chondrogenesis was shown to be superior when compared with agarose hydrogels, as shown by cartilage-specific ECM production. The effect of KLD-12 peptide hydrogel, with or without chondrogenic factors and allogenic BMSCs, on osteochondral repair was tested *in vivo* in a critically-sized rabbit cartilage defect model (Miller et al. 2010) and KLD-12 hydrogel alone could fill full-thickness osteochondral defects and improve cartilage repair.

Collagen-mimetic peptides ($(GPO)_5$) were conjugated to the C-terminal of KLD-12 peptide and the chondrogenic differentiation of BMSCs investigated *in vitro* (Kim et al. 2015). These gels promoted the expression of chondrogenic marker genes (collagen type II, aggrecan). In a different study, KLD-12 was coupled to a neuropeptide (RPKPQQFFGLM) and the gel injected in osteoarthritis (OA) rat knee model. After 6 weeks, the gel accelerated cartilage regeneration through recruitment of MSCs (Kim et al. 2016), demonstrating the potential of this conjugated hydrogel to delay the progression of OA and restore articular joint function without cell transplantation.

The chondrogenic differentiation of human adipose-derived stem cells (ADSCs) was investigated *in vitro* by 3D culture in RAD16-I gels combined with heparin (Fernández-Muiños et al. 2015). This bicomponent gel enhanced the chondrogenic commitment of ADSCs, as detected by the expression of cartilage specific markers.

Vascular regeneration

There is a need of cell-based therapies for ischemic tissue repair in cardiovascular diseases, as result of limited regeneration of cardiomyocytes. To overcome this limitation, a biocompatible matrix is normally required to support cell functions during the transplantation, once the direct cell transplantation (embryonic stem or endothelial progenitor cells) results in low cellular viability and minimal retention (Webber et al. 2010b). A gel made of PA nanofibers containing the RGDS sequence was used to encapsulate bone marrow-derived stem and progenitor cells *in vivo* (Webber et al. 2010b). Enhanced viability, proliferation and adhesion of encapsulated cells suggested the potential of these gels to be applied in cell therapies for ischemic diseases. In a subsequent study, incubation of bone marrow-derived pro-angiogenic cells (BMPACs) with these PA nanofibers *in vitro* enhanced cell adhesion and proliferation, while