formation between the attached neurons. Neural stem cells (NSCs), encapsulated into RADA16-I gels functionalized with different functional motifs (SKPPGTSS, PFSSTKT and RGDS), and cultured in serum-free medium were able to differentiate into progenitor neural cells, neurons, astrocytes and oligodendrocytes (Koutsopoulos and Zhang 2013). The brain repair ability of these gels was also demonstrated using a severed optic tract in a hamster model. Injection of peptide solution at the lesion site created a permissive environment for regenerated axons to reconnect to target tissues with sufficient density to promote functional recovery, as demonstrated by the return of lost vision (Ellis-Behnke et al. 2006). Reconstruction of acutely injured brain with these peptide gels was also observed (Guo et al. 2009). RADA16-I peptide gel was also used for transplantation of neural progenitor cells and Schwann cells into the transected dorsal column of spinal cord of rats (Guo et al. 2007). The gel was shown to promote survival, migration and differentiation of both cells, as well as migration of host cells, and growth of blood vessels and axons into the gels.

Other functional motifs, such as the bone marrow homing peptide 1 (BMHP1) motif (PFSSTKT) obtained by phage display, were also used to functionalize RADA16 and KLD12 peptides (Caprini et al. 2013; Gelain et al. 2006; Gelain et al. 2012), or to derive new self-assembling peptides (Cigognini et al. 2014; Gelain et al. 2011), for culturing and controlling NSC behavior for nervous tissue regeneration. Promising results were obtained in terms of *in vitro* NSC differentiation and *in vivo* nervous tissue regrowth.

Bone regeneration

The application of PAs for bone regeneration has been reviewed elsewhere (Matson et al. 2011) and some of the functional motifs incorporated in the PA design include peptide sequences containing the phosphoserine (S(P)) residue to induce hydroxyapatite mineralization and the RGD for cell adhesion (Hartgerink et al. 2001). A nanofiber gel combining these signalling epitopes was tested in a rat femoral critical size defect and significant bone formation was observed (Mata et al. 2010). To induce osteoblast differentiation and stimulate bone formation, PAs were functionalized at the N-terminal with a phage-derived peptide (TSPHVPY) that binds to bone morphogenetic protein 2 (BMP-2) (Lee et al. 2015a). *In vivo* studies, using the BMP-2-binding nanofibres in a translational model of bone regeneration (rat posterolateral lumbar intertransverse spinal fusion model), showed that this system allowed a 10-fold reduction in the BMP-2 dose to achieve 100% fusion rate. The observed efficacy was explained by the ability of the BMP-2-binding peptide nanofibres to both capture exogenously delivered or endogenously expressed BMP-2.

RADA16 peptide-based gels have also been demonstrated to be valuable in enhancing bone regeneration (Semino 2008; Misawa et al. 2006; Horii et al. 2007). When functionalized with RGDS and DGEA sequences, human mesenchymal stem cells (MSCs) cultured on these gels showed osteogenic differentiation with and without the addition of osteogenic media (Anderson et al. 2011). RADA peptides containing BMP receptor-binding peptides (Hosseinkhani et al. 2007; Lee et al. 2009) were also explored due to its osteoinductive potential to be applied in bone repair therapies.