that negatively charged peptide amphiphiles hydrogels were non-toxic when formed using divalent metal cations and interestingly served as nutrient source for cells such as MC3T3-E1 (murine, bone fibroblast) (Beniash et al. 2005). Peptide amphiphiles can also be modified to contain bioactive residues. For example self-assembling amphiphiles containing the neuroactive amino acid motif IKVAV, derived from laminin, enhanced axon regeneration, reduced glial scar formation and led improved hindlimb movement in mouse models after spinal cord injury (Tysseling-Mattiace et al. 2008). Heparin-binding peptide amphiphiles, containing a Cardin-Weintraub heparin-binding domain, were shown to specifically bind to heparin sulphate-like glycosminoglycans leading to self-assembly and hydrogel formation (Ghanaati et al. 2009). This hydrogel promoted angiogenesis and healing of chronic wounds. As the peptide hydrogel degraded the growth of vascularized connective tissue was observed over 30 days.

The importance of charge within the primary molecular structure was confirmed by the Hartgerink group who formed a peptide-based ABA block system. The A blocks are composed of charged amino acid residues with B composed of alternating hydrophobic and hydrophilic residues. Addition of multivalent ions of opposing charge, such as magnesium cation (Mg^{2+}) and phosphate anion $(PO_4)^{-3}$, to the A block are utilized to trigger hydrogelation (Dong et al. 2007). For example lysine containing multi-domain peptide 1 (MDP1) (KK-SLSLSLSLSLSL-KK) successfully formed a hydrogel in the presence of negatively charged PO_4^{-3} anions (Aulisa et al. 2009). Serine acted as a neutral, hydrophilic amino acid with B and increased hydrogen bonding between nanofibers and therefore improved gel strength. MDPs was demonstrated to have application as a tissue scaffold with inclusion of an enzyme cleavable KGRGDS bioactive motif (as part of terminal A block) improving cell proliferation in dental mesenchymal stem cells (Galler et al. 2010).

Oxidation/Reduction-Responsive Hydrogels

An area of emerging interest is the use of reducing conditions to stimulate self-assembly and hydrogelation, harnessing relative conformational changes in cysteines disulphide bonds. Bowerman and Nilsson demonstrated the cyclized disulphide bonding of the peptide CH3COC-$(FKFE)_2$CG-NH_2 could prevent self-assembly to a β-sheet, nanofibrous architecture in an oxidized state (Bowerman and Nilsson 2010). Reduction of the disulphide bond allows the peptide to switch to a thermodynamically preferred, low energy, β-sheet conformation forming a viscoelastic hydrogel. As the authors suggested such peptides could be of value for localized delivery of chemotherapeutic drugs to tumours which often possess an extracellular reducing environment.

Thermo-Responsive Hydrogels

The MAX group of peptides were also demonstrated to possess temperature responsive hydrogel formation. Alteration of the pH responsive MAX1 motif by substitution of one (position 16) or two (and position 7) valines of the peptide primary sequence with the less hydrophobic amino acid threonine, creates MAX2 (H_2N-VKVKVKVKV^{D}PPTKVKTKVKV-$CONH_2$) and MAX3 (H_2N-VKVKVKTKV^{D}PPTKVKTKVKV-$CONH_2$) peptides (Pochan et al. 2003). These