attenuating apoptosis (Tongers et al. 2014). In a murine model of hind limb ischemia, an intramuscular injection of BMPACs within the RGDS containing PA gel, resulted in greater retention of cells, enhanced capillary density, increased limb perfusion and reduced necrosis/amputation, when compared to treatment with cells alone. PA gels with binding ability to heparin were observed to have binding ability for paracrine factors from hypoxic conditioned stem cell media (Webber et al. 2010a). When injected in coronary artery ligation, the preservation of hemodynamic function in a mouse ischemia (reperfusion model of acute myocardial infarction) was observed and revascularization in chronic rat ischemic hind limb models was stimulated.

RADA16 gels have also shown to support the survival of encapsulated endothelial and myocardial cells (Narmoneva et al. 2004) and the potential to create a 3D micro-environment when injected in myocardium by recruiting both endogenous endothelial and smooth muscle cells with stimulation of vascularization (Davis et al. 2005). When injected into the heart tissue after myocardial infarction, RADA16-I nanofiber gel containing vascular endothelial growth factor was shown to create a microenvironment for arteriogenesis and cardiac repair (Lin et al. 2012).

Hydrogel Functionalization

Many types of natural and synthetic hydrogels possess inherently low bioactivity, which is advantageous for avoiding immunogenic responses and improving biocompatibility. However, this lack of bioactivity limits the ability to control or direct cell behaviour for tissue engineering and regenerative medicine applications. Biofunctionalization is therefore an important top-down strategy for creating instructive hydrogels capable of eliciting specific cellular responses.

To date, a range of different materials have been modified with small molecules, peptides, and polysaccharides, as well as larger recombinant proteins. Examples of hydrogel materials amenable to bio-functionalization include synthetic polymers such as poly(ethylene glycol) (PEG) (Hern and Hubbell 1998; Shin et al. 2002; DeForest et al. 2009; Phelps et al. 2012), poly(hydroxyethylene methacrylate) (Bi et al. 2004; Jacob et al. 2005), and polyvinyl alcohol (Schmedlen et al. 2002). PEG-based hydrogels have been extensively studied due to their excellent anti-fouling properties and ease of modification (Hern and Hubbell 1998; Mann et al. 2001; Lee et al. 2008). A number of natural hydrogels, such as alginate (Rowley et al. 1999), chitosan (Ho et al. 2005), and hyaluronic acid (Shu et al. 2004; Gramlich et al. 2013) can also functionalised using similar strategies. Short synthetic peptides are one of the most common molecules used to improve bioactivity of hydrogels as they are stable and easily synthesized with sequence specificity. Peptides containing the fibronectin-mimetic arginine-glycine-aspartic (RGD) motif have been frequently used to create cell adhesive hydrogels and improve cell viability (Hern and Hubbell 1998; Shin et al. 2002; Mann et al. 2001; Rowley et al. 1999). Other peptides used to modify cell function within hydrogel materials include collagen mimetic sequences (Lee et al. 2008; Reyes and García 2003; Connelly et al. 2011), laminin-mimetic sequences (Bellamkonda et al. 1995; Yu and Shoichet 2005; Chung et al. 2008), and matrix metalo-proteinase (MMP) degradable sequences (Phelps et al. 2012; Mann et al. 2001; Gilbert et al. 2010). Finally, modification of hydrogels with small molecules can be used to modulate gel chemistry