between CB[6] and DAH or SPM molecules in the precursor solutions. Hydrogel formation occurs at mild conditions, allowing the direct encapsulation of cells and sensitive molecules, like growth factors. These gels showed *in vivo* stability up to 11 days after subcutaneous injection in nude mice (Park et al. 2012) and encapsulation of human MSCs (hMSCs) and differentiation agents (transforming growth factor-β3 and/or dexamethasone) within these gels showed effiective chondrogenic differentiation of hMSCs (Jung et al. 2014).

These supramolecular hydrogels show potential as a minimally invasive injectable hydrogels for therapeutic delivery of cells or growth factors and may have great utility in many regenerative medicine applications, such as artificial environments for the controlled differentiation of stem cells, soft tissue reconstruction, nucleus pulpous replacement or mechanical stabilization of myocardial infarct.

(Bio)Engineering HA Hydrogels to Control Cell Behaviour

HA hydrogels can be engineered in several ways to control the behaviour of encapsulated cells. Tuning their mechanical properties, through controlled degradation and/or degree of crosslinking, can regulate cell mechanosensing and topographical patterns can be used to direct cell migration. However, regardless of the crosslinking mechanism, bioactive molecules must be incorporated into the hydrogel matrix to help direct cell behaviour. These biomolecules can be full-length extracellular matrix proteins, like collagen, fibronectin (FN) and laminin, or small peptide sequences derived from these proteins (Table 2). In addition, a variety of bioconjugation techniques (Ahadian et al. 2015) can be used to couple one or more biomolecules to obtain controllable bioconjugates (Fig. 1D) for specific interactions with cells (gel formation for cell encapsulation, binding sites for cell adhesion, matrix degradation for cell migration). Bioconjugated HA hydrogels with multiple chemical, biological and physical functionalities have been developed (Table 2) to mimic different aspects of the ECM (Lam et al. 2014; Guvendiren and Burdick 2013).

Applications of HA Hydrogels in Regenerative Medicine

HA hydrogels have broad utility within regenerative medicine. They have been integrated with 3D bioprinting (Skardal and Atala 2015; Hong et al. 2013) and used for: engineering the stem cell niche; delivery of growth factors and cells; wound healing and cartilage tissue engineering (Burdick and Prestwich 2011; Cai et al. 2005; Kim et al. 2011; Prestwich 2008; 2011).

Previously described HA-based hydrogels have been optimized to address clinical needs and provide reliable 3D matrices with controlled viscoelasticity for cell culture. Some of these hydrogel technologies have been translated into commercial products (Table 3). These commercially available hydrogels have permitted the development of numerous studies where they were used as 3D scaffolds for capillary-like structure formation from endothelial colony-forming cells to generate vascularized tissue constructs (Yee et al. 2011), co-culture of MSCs and macrophages in 3D (Hanson et al. 2011), 3D culture and maintenance of hepatocyte function *in vitro* (Skardal et al. 2012), culture of human astrocytes in defined 3D microenvironment to recapitulate