following a similar initiation mechanism except that a type-II photoinitiator (e.g., eosin-Y) is used to created thiyl radicals from thiol-containing crosslinkers (Shih et al. 2013; Shih and Lin 2013; Fraser et al. 2014). The use of visible light eliminates the biosafety concerns of UV light, which some argue that it might cause cellular damages or genetic mutation. Light and radical mediated step-growth polymerizations are beneficial in that the gelation kinetics and bioconjugation can be achieved and controlled spatiotemporally. This feature is extremely useful when studying cell fate process under the influence of dynamic microenvironmental cues.

Another increasingly explored step-growth polymerization is the 'Click' chemistry, which is used to describe highly efficient and quantitative reactions between mutually reactive functional groups (Hoyle and Bowman 2010). Hubbell et al. established click-based hydrogels using functional PEG macromers (e.g., PEG-acrylate or PEG-vinylsulfone) and bis-cysteine containing MMP-sensitive peptide sequence (Lutolf and Hubbell 2003; Lutolf et al. 2003; Lutolf et al. 2003a). Methacrylate, acrylate, and maleimide-terminated macromers can also be used to crosslink with bis-cysteine peptides for forming cell-laden biomimetic hydrogels. Other notable click chemistries developed in recent years include native chemical ligation (Hu et al. 2009; Su et al. 2010; Jung et al. 2013; Strehin et al. 2013), oxime click chemistry (Grover et al. 2012; Grover et al. 2013; Lin et al. 2013), azide-alkyne addition (Polizzotti et al. 2008; DeForest et al. 2009), Diels-Alder reaction (Koehler et al. 2013, Jiang et al. 2014) and tetrazine-norbornene chemistry (Alge et al. 2013; Zhang et al. 2014). Similar to the Michael-type conjugation reaction, the reactions of these orthogonal click chemistries are independent of light irradiation nor do they generate propagating radicals during gel crosslinking. Furthermore, the gelation process is amenable to create 'injectable hydrogel', which is highly valuable for translational and clinically relevant applications.

Engineered polypeptides

Genetic engineering is a powerful tool for creating 'designer' peptides with modular properties. The design of these engineered peptides are often inspired by the structures of natural macromolecules, such as elastin and resilin (Su et al. 2014; Lau and Kiick 2015). Elastin is one of the major structural proteins found in many native tissues, including tendons, ligaments, and blood vessels. The elastic nature of elastin stems from the extensive crosslinks of the protein, as well as the canonical peptide sequence VPGXG repeat where X represents any natural amino acid other than proline (Annabi et al. 2013; Lampe et al. 2013; Wang et al. 2014; Lau and Kiick 2015; Zhang et al. 2015). Various elastin-like polypeptides (ELPs) have been designed and produced recombinantly for forming biosynthetic scaffolds suitable for 3D cell culture (MacEwan and Chilkoti 2010; Altunbas and Pochan 2012). The sequence of ELPs can be designed such that the resulting polypeptides can be readily crosslinked, either physically or chemically, and with preferential and predictable properties (e.g., extensibility, elasticity, and tensile strength). In addition, cell adhesive ligands (e.g., RGD peptide) can be easily incorporated either within the ELP peptide sequence or modified post-gelation through thiol-maleimide Michael-type addition.