

Table 1. Functionalized HA for hydrogel formation via different crosslinking mechanisms.

HA-derivative(s)	Crosslinker(s)	Crosslinking mechanism/Gel formation	References
Native HA (Fig. 1A)	Diepoxybutane (DEB) Divinyl sulfone (DVS)	Reaction of HA hydroxyl groups with diepoxides under basic conditions. Hydroxyl groups of HA.	(Neffe et al. 2011) (Borzacchiello et al. 2015)
Aldehyde- or oxidized-HA (Oxi-HA, obtained by periodate oxidation)	Adipic acid dihydrazide (ADH)	Schiff-base addition reaction (reaction between aldehydes in oxi-HA with amines of ADH to form imine bond).	(Shoham et al. 2013; Su et al. 2010)
Hydrazide-modified HA (ADH-HA, Fig. 1B-vi) conjugated with <i>N</i> -acryloxysuccinimide (AC-NHS) (AC-ADH-HA) AC-HA (Fig. 1C-xi) MA-HA (Fig. 1B-v)	PEG tetra-thiols (PEG-SH ₄) MMP-degradable peptide crosslinker GREG/PQG//GQERCG GCRDVPMSQMRGGDRCG Dithiothreitol (DTT)	Michael-type addition (reaction of acrylates with thiols of PEG-SH ₄ or cysteine (C) from the peptide linkers). Maleimide groups react with thiols (6.5 < pH < 7.5) forming a stable thioether linkage that is not reversible (i.e., the bond cannot be cleaved with reducing agents).	(Kim et al. 2007; Hong et al. 2013) (Lam and Segura 2013; Lei et al. 2011) (Feng et al. 2014)
(Meth)acrylated HA (ME-HA, AC-HA, Fig. 1C-x) Vinyl esters HA (VE-HA, Fig. 1C-xii)	DTT	Reaction of acrylate groups with thiols at the ends of DTT (Michael-type addition polymerisation). UV/Vis-photopolymerization with single (Irgacure 2959, TEOA/eosin Y/NVP) or two-photon initiator (P2CK).	(Qin et al. 2014; Lei et al. 2011) (Park et al. 2003) (Guvendiren and Burdick 2012)
Thiolated HA (SH-HA, Fig. 1B-i)	Poly(ethylene glycol) divinyl sulfone (PEGDVS), PEG diacrylate (PEGDA)	Michael-type addition (reaction of vinyl groups with free thiols).	(Addington et al. 2015; Pike et al. 2006)
Tyramine-HA (Tyr-HA, Fig. 1B-iv)	Horseradish peroxidase (HRP)/H ₂ O ₂	Enzyme-mediated oxidative coupling of Tyr with formation of di-Tyr.	(Loebel et al. 2015; Xu et al. 2015)