Force-mediated dynamic chemistry in hydrogels to control cell adhesion

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Conventional hydrogels used in biomedical applications lack the dynamic and responsive nature of the natural extracellular matrix, which plays a critical role in regulating cellular behaviours in response to internal or external stimuli such as force. To address this issue, a promising approach is to incorporate mechanophores, molecules that undergo chemical changes in response to mechanical stress, into hydrogels. Despite being frequently employed in polymer systems, mechanophores have rarely been investigated in aqueous-based hydrogel systems due to their hydrophobic nature. In this study, we report a simple synthetic method to introduce anthracene-maleimide (AM) mechanophores into polyethylene glycol (PEG) hydrogels. The AM adducts were conjugated at the periphery of hydrophilic PEG molecules to render their hydrophobicity and decorated with methacrylate groups to allow co-polymerisation with PEG-dimethacrylate (PEG-DM) to form hydrogels. Under external force, the AM adducts undergo retro Diels–Alder reaction to release maleimide handles, which can then conjugate with cysteine-containing cell-binding peptides (GRGDSC) *via* the spontaneous thiol-ene reaction. In vitro experiment demonstrated selective cell growth at the points of compression, confirming the force-responsive nature of our hydrogel. Our study highlights a promising approach to develop novel hydrogels that can actively respond to mechanical cues and regulate cell behaviours, offering exciting opportunities for biomedical applications.

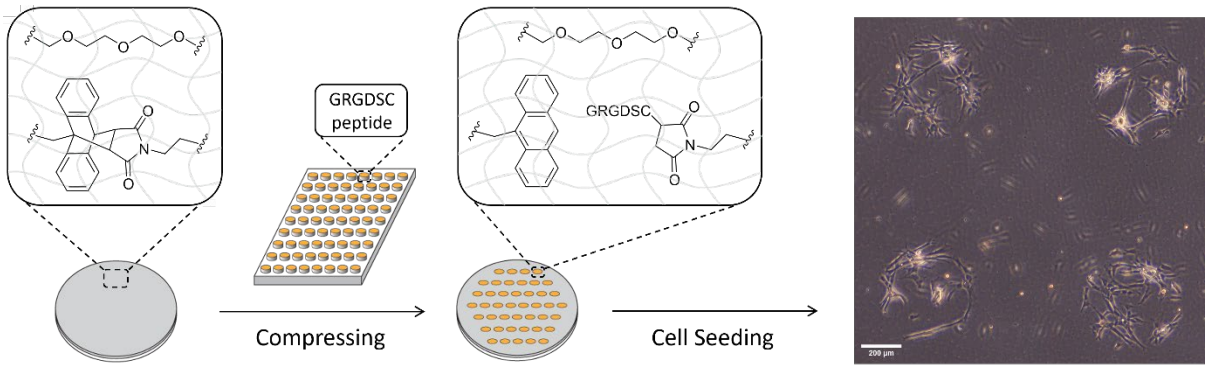

Figure 1: Schematic overview of anthracene-maleimide functionalised PEG hydrogels and selected cell growth at the points of compression.