Dynamic Biomolecule Binding and Release from Mechanophore Laden Hydrogels

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Biomaterials play a crucial role in both treating and understanding various pathological conditions. In tissue engineering, an integral focus is restoring tissue function using mimetic biomaterials[1]. However, native tissue is a highly complex matrix that provides biophysical and biochemical cues to cells, driving dynamic cell-matrix interactions [2]. Among these interactions, biomolecule sequestration and release are essential in shaping cellular behaviour and function [3] . Although, replicating this intricate interplay and deciphering its influence on dynamic cellular processes remain significant challenges. Many biomaterials have been designed to bridge this gap, with hydrogels being among the most promising. However, many of these materials are inherently static and lack the adaptability of native tissue.

A key strategy in developing dynamic hydrogel systems is incorporating stimuli-responsive motifs, such as mechanophores, that undergo chemical changes under mechanical or chemical stimuli [4,5]. In this work, we have synthesised a novel small molecule releasing mechanophore hydrogel crosslinker that is both mechanically and chemically responsive, with an amine reactive arm for dynamic biomolecule binding. By leveraging amine-reactive chemistry, we have conjugated bioactive peptides and small molecules to hydrogel networks, creating a hydrogel matrix capable of releasing bound molecules via a retro Diels-Alder reaction triggered by mechanical or chemical stimuli. Utilising this mechanism, we were able to achieve release of a bound Arg-Gly-Asp (RGD) adhesive peptide with simultaneous conjugation of another Pro-His-Ser-Arg-Asn (PHSRN) adhesive sequence. Results show that our system supports high viability of adipose-derived mesenchymal stem cells (ADSCs) and is capable of dynamically modulating the adhesive phenotypes of cultured cells in this way. We anticipate that our hydrogel matrices will be a powerful tool for controlling more complex cellular responses and advancing smart biomaterials for tissue restoration.

References

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