Responsive DNA-Crosslinked Hydrogels For ECM Mimicking

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The extracellular matrix (ECM) is a complex and heterogeneous network consisting of proteins, proteoglycans and other soluble molecules. It has a reciprocal relationship with cells: one shapes the other and viceversa. In particular, the mechanical properties of ECMs greatly influence cell adhesion, migration, proliferation and differentiation, and therefore tunable control over synthetic ECM is essential for successful cell culture.
Conventional methods for culturing cells or tissues on 2D substrates failed to mimic the *in vivo* behaviour and a 3D ECM mimicking structure has been pursued. In this context, hydrogels show great potential. Even more, since the ECM is a dynamic environment in continuous change, responsiveness is a feature required from these 3D structures. In the past two decades, DNA has attracted considerable attention as programmable cross-linker to control and fine-tune the self-assembly and properties of responsive hydrogels in a regime matching the natural ECM[1,2,3].

In this study we aim to produce responsive DNA-crosslinked PEG hydrogel. Thiol-modified PEG precursors with different molecular weight and shape are cross-linked by synthetic DNA oligos of varying length and valency in order to obtain a modular library of gel-forming building blocks. Microrheology studies are performed on the hydrogel samples for the evaluation of their viscoelastic properties by particle tracking of small polystyrene beads dispersed in the solution prior to gelification. Responsiveness of the hydrogels to different stimuli such as temperature, pH, restriction enzymes, redox reactions and even competitive DNA strands will be investigated. Biofunctionalization is ensured through incorporation of cell-binding DNA particles developed in our laboratory in order to form adhesion "hotspots" for cells in a dynamic environment.

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