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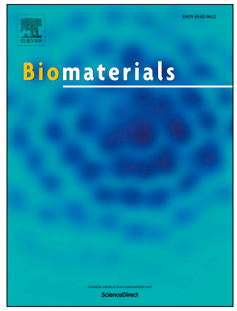

Assembling and decorating hyaluronan hydrogels with twin protein superglues to mimic cell-cell interactions

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Assembling and decorating hyaluronan hydrogels with twin protein superglues to mimic cell-cell interactions

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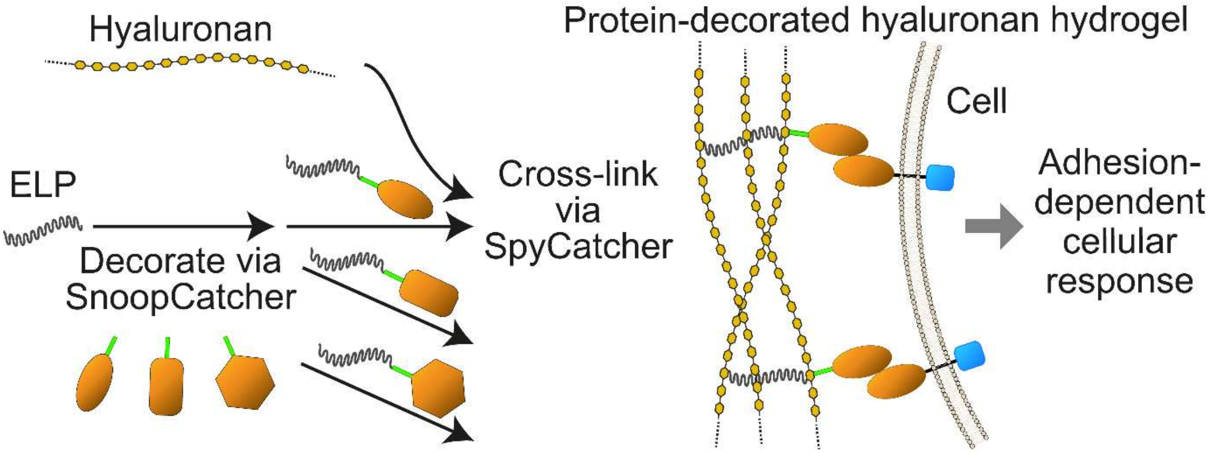
Abstract

Simple polymeric scaffolds have yielded dramatic effects on cell behavior. For more sophisticated phenotypes, precise and efficient chemistries are desired to incorporate proteins into these scaffolds. Here we derivatize hyaluronan with an elastin-like polypeptide containing telechelic SpyTags (HA-SpyTag). Our second network component, the TriCatcher protein, had two SpyCatchers and a terminal SnoopCatcher. Mixing HA-SpyTag with TriCatcher led to rapid hydrogel formation, via spontaneous amidation. SnoopCatcher allowed modular network decoration with SnoopTagJr-linked adhesion molecules, through orthogonal transamidation. This programmed scaffold enables the testing of how individual matrix-anchored protein interactions affect cell behavior. Epithelial cell adhesion molecule (EpCAM) regulates cell behavior and migration, with important effects in cancer. EpCAM-anchoring to the hydrogel induced disassembly of non-malignant mammary spheres in 3D culture. Integrating signaling proteins into biomaterials via efficient biocompatible chemistry should reveal key cues to control cell behavior.

Graphical Abstract



Keywords

Protein engineering; bioconjugation; polysaccharide; hyaluronic acid; glycobiology; bioengineering.

Introduction

Biomaterials have the potential to revolutionize drug delivery, tissue engineering and regenerative medicine.[1] Biomaterials have shown initial success in promoting the development of sophisticated multi-component tissues, including segments of skin and bone.[2, 3] To mimic native tissue, polymers must possess a precise combination of mechanical, structural and biochemical features.[4] Most work on biomaterials has focused on identifying suitable repetitive polymers able to drive cellular behavior.[1-3] Proteins are harder to couple specifically than peptides or repetitive polymers, but can provide valuable