

Regenerative Medicine Bioconjugated Hydrogel Scaffolds

Subjects: Medicinal Chemistry

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Definition

Materials used for regenerative medicine purposes pose a series of challenges in terms of biocompatibility, adaptability and functionality. A way to design functional and compatible materials that mimic soft tissue is to exploit synthetic hydrogels. To widen their activity scope, hydrogels can be coupled with molecular cues to promote tissue regeneration or trigger regeneration processes. Within this entry we assess the criteria to choose the design of a bioconjugated for regenerative medicine purposes, giving relevant examples from the current literature.

1. Introduction

The aim of regenerative medicine is to restore and rebuild damaged or dead tissue by providing molecular signals that promote tissue growth, whilst granting physical support to the cells to proliferate.^{[1][2]} Achieving this, however, comes with a series of challenges, both in terms of signal delivery and of scaffold properties. The influx of molecular signals to the tissue can not be delivered all at once, but is required to stay constant overtime, to promote a homogeneous and sustained growth.^[3] Thus, even though research has made outstanding progress with sustained release technologies, these tend to clash with the majority of the scaffolding technology proposed so far. In fact, most of formulation products can release a drug overtime whilst preventing its degradation, but are formulated in a way that they are not capable of mimicking soft tissue properly. This means that once the molecular cue is inserted in a wrong support within the body, the body will start rejecting it, causing inflammation and allergic reactions.^[4]

2. Hydrogels

Hydrogels are a class of materials that possess similar mechanical properties to soft tissue and can deliver cues over time. Hydrogels are 3D crosslinked polymeric networks fully swollen in their volume by water, which can be tailored to mimic the extracellular matrix.^[5] They are characterized by a soft and elastic structure, with high porosity which involves not only adaptability to the surrounding environment, but also bioavailability of small molecules. Since hydrogels seemed to be perfect candidates to be used in regenerative medicine, the latest efforts in the field were directed to design hydrogels that would satisfy a long list of requirements in terms of biocompatibility, adaptability and chemical functionality. In general, a hydrogel scaffold should fulfill these 3 requirements:

1. Provide support to the new tissue whilst making space for it by degrading naturally if necessary.
2. Mimic the mechanical properties of the tissue, in terms of softness, strength and elasticity.
3. Provide conditions and molecular signals for cell growth, differentiation and proliferation.

Hydrogels composed of synthetic polymers can be chemically designed to degrade at a controlled pace, by just inserting cleavable segments.^[6] The same way, tailoring the nature of the monomers, crosslink density and chemistry and chain architecture, the resulting gel can possess mechanical properties that are made similar to the environment in which the hydrogel should be used.^[7] One of the main functional advantages that comes with synthetic polymers is that monomers with different functionalities can be combined resulting in gels that are responsive to several stimuli at the same time, being able to change their swelling, mechanical properties and physical properties according to the environmental conditions. This allows to use these materials for in situ gel formation, or in situ/on demand release.^{[8][9]} Hydrogels and their micro to nanosized counterpart, microgels, can release on demand small drugs^[10], proteins^[11] and ions^[12] whilst maintaining functionality and biocompatibility. A hydrogel that has perfect mechanical properties but is not able to deliver a molecular cue will not promote cellular growth and correct tissue regeneration. Proteins, growth factors, small peptides and nucleic acids are all molecular signals that cells receive and to which they respond by differentiating, growing and proliferating. All these cues are however very difficult to be directly delivered to the target, and require a formulation that sets them free at the target whilst protecting them and preventing them from degradation. Thus, combining these

molecules with hydrogels provides a system in which the synthetic scaffold sustains the tissue while it is growing.

Carefully choosing the right combination of scaffold and biomolecular cue allows to promote tissue regeneration whilst minimizing invasive surgery and painful side effects.

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Keywords

hydrogel, regenerative medicine, biomolecules

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