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Promoting tissue regeneration with supramolecules

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Abstract

Supramolecules are the polymeric molecules which are generated by macromolecular non-covalent bonding. Since they can mimic the natural cell microenvironment which plays an important role in tissue regeneration with a plethora of aspects, supramolecules are highly popular in regenerative medicine area. They are non-toxic, biodegradable, biocompatible and they can be modified for the purpose of disease treatment and control. They can be used for encapsulation of the important growth factors, particular stem cell types and drugs; they are able to release those molecules by stimulation or changes in their surface or bond structures. They are injectable for localized applications and in some cases, they degrade to become nutrients for the surrounding cells after they complete their mission.

Introduction

Repairing or replacing lost limbs and serious tissue damages are one of the hot topics in the medicine for a long time. Particular tissues and organs cannot regenerate properly. Some events such as birth defections, traumatic injuries, aging, illnesses or cancers cause tissue damages and limb losses, which eventually alter human functions and life quality. In order to create solutions in the field, regenerative medicine has been extensively dedicating effort and resources on this topic for a long time.

Biomaterials are the most popular elements of the regenerative medicine. Their biocompatible, biodegradable, nontoxic and functionalization by modifications in their chemical structures are the main foundations of their popularity [1].

Supramolecules are one of the most popular biomaterials in the regenerative medicine. They hold advantages over other biopolymer types; they can be modified, functionalized, they are self-healing, non-toxic, stimuli responsive and non-immunogenic [1,2]. Supramolacules are the polymers which consist of macromolecules with noncovalent bonds such as hydrophobic interactions, hydrogen bonds and metal-organic interactions [1,2,4]. Their functions depend on their structures similar to those of the proteins and they can also be changed by modifications during manufacturing or by nature. The changes in their structures play an important role in their stimuli responsive properties [4].

Supramolecules mimic fibril structure of the extracellular matrix (ECM) which consists of proteins like elastin, laminin, proteoglycans and collagens [3]. ECM is the natural microenvironment of cells; they support and act as scaffolds for cell and tissue [5]; they also promote strong interactions between important bioactive proteins, protein subunits and polysaccharides which plays important role in cell signaling [3]. These signals provide cell migrations, adhesions, proliferations and differentiations which promotes tissue regeneration [2,5].

Results

Treating brain injuries and defects are really hard and almost impossible in some cases because of the characteristic of brain structure and neuronal cell features. Presence of blood-brain barrier; and neuronal cells inability to proliferate limit the treatment methods and tools. Recent study about the treatment of the brain injury is promising by using special shaped self-assembling peptide hydrogels which mimic ECM and allow release of growth factors. In this study, scientists designed a jigsaw-shaped protein hydrogels which contains specials motifs for generating different surface structures which provides multiple functions for this supramolecule. This supramolecule is injectable when it is encapsulated, in that way it is useful for a localized treatment method. This fiber forming peptide has hydrophobic surface which allows strong binding, self-assembling and efficient release of the growth factors. The interactions between guest and host molecules are processed thermodynamically. The strong affinity between host and guest molecules increases slowly as controlled release of the guest molecules is achieved. On the other hand, host-guest molecule pairs can arrest guest molecules for inhibiting their release. As a result, this study showed that the injection of this supramolecule promoted growth factor release which leads to the angiogenesis and neuro-protection which is a must for neuronal recovery [5].

In another study, scientists enhanced motion of supramolecules for the treatment of the spinal cord injury. They synthesized ''dancing'' supramolecules with two peptide sequence as scaffolds for enhancing growth factor release. This supramolecules released two distinct signals: one of them activated FGF-2 receptor, the other one activated β1-integrin receptor; both of them allowed neuronal cell survival. As a result, in paralyzed mice, overly-motive supramolecules promoted blood vessel formation, nerve regeneration, myelination, motor neuron survival, axon regrowth and glial scarring reduction when injected in the injured part of the spinal cord. After the supramolecule completed its mission, it degraded and released nutrient molecules for the surrounding cells [6].

Bone-cartilage tissue recovery is also critical for the mobility and life quality. The mostly used strategy is delivering bioactive factors and stem cells locally. These elements play important role in bone-cartilage repair. In this study, scientist prepared supramolecular hydrogel and they delivered this material with SDF-1 chemokine which promotes proliferation of bone marrow stem cells and BMP-2 which stimulates differentiation of bone marrow stem cells for promoting periodontal bone regeneration. Also, this supramolecular hydrogel mimicked ECM that enabled a convenient macroenvironment for the stem cell adhesion and function [7].

Wound healing includes multiple factors like epidermal growth factors (AGF) and FGF-2 and it is a complex process. These factors are activated and released for stimulating the wound healing. In wound healing, growth factors are critical but they are prone to proteolytic degradation because of the inflammation process in the wounded area. Scientists designed photo-sensitive supramolecules for UV controlled EGF release. In mouse models, supramolecular hydrogel encapsulated EGF application showed the fast wound recovery and 10% in the wound size reduction. Also, these materials showed antimicrobial activity when they were enriched with chitosan and silver ion on the wound area [7].

Conclusion

As damaged tissues are hard to recover, biopolymers like supramolecules are the main focus of the regenerative medicine. They have versatile properties such as non-immunogenic, non-toxic, stimuli-responsive and degrading into the nutrients therefore they hold advantages over other biopolymer types. Supramolecules can gain functions by modifications in their chemical structures, as a result of that, in theory, their potential in regenerative medicine has no boundary. There are a wide variety of studies in the literature about supramolecules and their modified versions for skin treatment to central nervous system regeneration. Besides, some of those studies report successful outcomes in the animal models; still, there is a very long way ahead. Working with supramolecules for the regenerative medicine requires multidisciplinary understanding and ability. With the help of disciplines such as Medicine, Biology, Biotechnology, Bioengineering, Chemical engineering, Material sciences and Physics engineering, the road can be shortened.

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