Superporous Extracellular Matrix Mimics for On-demand Release of Growth Factors Based on Nucleic Acid Aptamers and Superporous Hydrogels

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Statement of Purpose: Biomaterials that can mimic the extracellular matrix to release growth factors on demand are important in the treatment of numerous complicated human diseases. Great efforts have been made to develop environment-responsive biomaterials that can alter their structural integrity and/or pore size to control the release of growth factors when exposed to a stimulus. However, it remains challenging to develop a biomimetic material that has high-efficiency retention and on-demand release of growth factors. In this work, a novel extracellular matrix mimic was investigated by using superporous hydrogels and nucleic acid aptamers. Superporous hydrogels are highly permeable, which allows cells to penetrate and enables the hydrogels to respond rapidly to the stimulation. However, the high permeability would compromise the retention efficiency of growth factors. This problem was solved by integrating nucleic acid aptamers into the superporous hydrogels without compromising the merit of high permeability. Nucleic acid aptamers are single-stranded oligonucleotides screened from nucleic acid libraries that bind specific targets with high affinity. In addition to high binding specificity and strength against their targets, aptamers are also chemically robust and can be used to functionalize numerous biomaterials without losing their binding functionalities. More importantly, unlike other affinity ligands, the binding functionality of nucleic acid aptamers can be precisely regulated through hybridization with complementary oligonucleotides. We evaluated the ability of functionalized superporous hydrogels to retain a large concentration of growth factors and the ability of complementary oligonucleotides to release the growth factors for on-demand release.

Methods: Superporous hydrogels were formed by the free radical polymerization of poly(ethylene glycol) with or without nucleic acid aptamers. The model aptamer used is specific for platelet-derived growth factor BB (PDGF-BB). The superporous hydrogels were dehydrated and subsequently soaked in the solution of the growth factor for loading. After the loaded superporous hydrogels were incubated in the release medium, the medium was collected and the amount of PDGF-BB in the medium was quantified using an enzyme-linked immunosorbent assay (ELISA). To trigger the release of PDGF-BB, complementary oligonucleotides of various concentrations were added to the release medium. In addition to the release test, the superporous hydrogels were characterized with numerous tools such as rheology.

Results: The release kinetics of PDGF-BB from the aptamer-functionalized superporous hydrogel was affected by the binding affinity of the aptamer. An aptamer with a lower affinity for the target resulted in a faster release rate. Additionally, the release rate of PDGF-BB could also be controlled by adjusting the concentration of the aptamer in the hydrogel. A larger concentration of aptamers resulted in a slower release rate. Lastly, PDGF-BB could be released on-demand by treating the hydrogel with complementary oligonucleotides. The amount of PDGF-BB release correlated to the concentration of the complementary oligonucleotides and the triggering time.

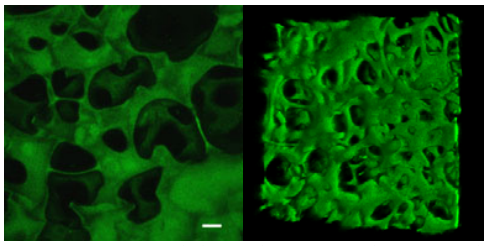

Figure 1. Two- and three-dimensional view of the superporous hydrogel obtained by confocal microscopy, scale bar = 100 um.

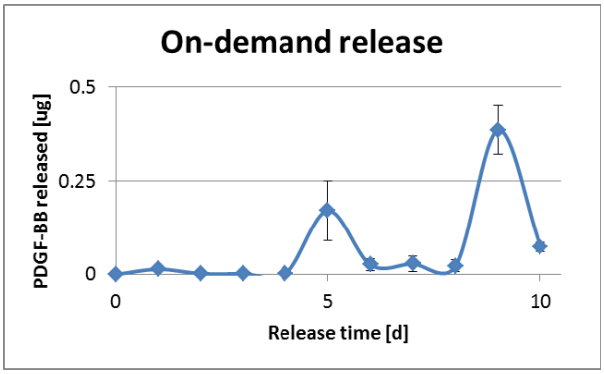

Figure 2. The release of PDGF-BB can be triggered using complementary oligonucleotides. The superporous hydrogels were treated on days 5 and 10 for one hour each.

Conclusions: Aptamers can be chemically integrated into superporous hydrogels. Importantly, the incorporation of the aptamers into the hydrogels can be used for the controlled release of growth factors. The release rate of the target growth factor can be adjusted by changing the binding affinity and the aptamer concentration. Moreover, complementary sequences can be used to regulate the release rate of the loaded growth factors. Thus, aptamer-functionalized superporous hydrogels hold great potential to mimic the functionality of the extracellular matrix and may have clinical implication in tissue regenerative applications. Ongoing studies will illustrate the in vivo bioactivity of the aptamer-functionalized superporous hydrogels in stimulating tissue growth.