An arginine-based polycation/heparin matrix for the controlled delivery of growth factors

Blaine Zern, Anh Nguyen, and Yadong Wang
Department of Biomedical Engineering, School of Chemistry & Biochemistry, and Petit Institute for Bioengineering & Biosciences, Georgia Institute of Technology, Atlanta, GA 30332, USA

Statement of Purpose: Coronary heart disease, the accumulation of fatty deposits in the arterial wall that results in tissue ischemia, is one of the leading causes of mortality in the United States. Therapeutic angiogenesis is the development of new blood vessel formation from pre-existing vasculature under the direction of exogenous mediators and is an attractive approach to treat this disease[1]. There are a multitude of factors that have been shown to induce angiogenesis and fibroblast growth factor-2 (FGF-2) is one that has been studied extensively. In order for FGF-2 to be introduced safely & efficiently, it has to be delivered in a local and controlled manner. In this approach, a positively charged, biodegradable polymer has been synthesized and used to self-assemble with a negatively charged polysaccharide, heparin, to form non-covalent networks. These networks have then been used to deliver therapeutic growth factor with a controlled, localized release.

Methods: The arginine-based polymer was synthesized via polycondensation reaction of equimolar amounts of diglycidol succinate and arginine ethyl ester. The resultant polymer (PSR, Figure 1A) was characterized via FTIR, NMR, and DSC. To ensure PSR was not cytotoxic to cells, MTT, Caspase-3 levels, and Live/Dead was performed using baboon smooth muscle cells. PSR’s ability to interact with heparin was characterized by SEM and dynamic light scattering experiments. The electrostatic network’s aptitude to load and release growth factor was investigated using I-125 FGF-2.

A. B.

![Figure 1: SEM image of PSR/heparin matrix](image)

![Figure 2: Release profile of HMW & LMW PSR FGF-2 from network](image)

Conclusions: We have designed and synthesized a biocompatible polymer with integrated arginine functional groups. This polymer has proven to be positively charged thus enabling PSR to interact with heparin electrostatically. This strategy to deliver growth factor has demonstrated a sustained release of FGF-2 over a four week period. Furthermore, PSR/heparin networks have demonstrated the capacity to adapt release rates of growth factor from the network according to molecular weight of the polycation. Also, the versatile design of PSR allows for a tunable polymer that can be modified for optimal transfection efficiency. Future investigation includes bioactivity of released FGF-2 & altering polycation and polyanion weight ratios to examine how this affects the release profile of the matrix.

References: