Controlled and sustained release of adeno-associated viral vectors from electrospun scaffolds

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ABSTRACT SUMMARY

The combination of viral gene delivery and scaffolds that control viral release in a controlled manner greatly enables tissue engineering applications. In this study, adeno-associated virus (AAV), which has been known safety and high gene delivery efficiency in human gene therapy as therapeutic vectors, was encapsulated by electrospinning. To control the release of viral vectors from the scaffolds, several strategies were employed; i) blended mixtures of elastin-like polypeptides (ELPs) and poly(ε-caprolactone) (PCL), ii) Core and sheath layers composed of two different biomaterials. Fibroblasts were adhered and transduced on the scaffolds. Combinatorial interactions between ELP and PCL chains with varying ratios significantly altered wettability, elastic modulus and strain of the ELP/PCL composites.

The capacity of ELP/PCL composites to modulate the controlled release of AAV -mediated gene delivery for subsequent high-efficiency cellular transduction will provide tremendous opportunities for a variety of tissue engineering applications.

INTRODUCTION

Virus-mediated gene delivery aroused to be efficient way for therapeutic gene therapy and tissue engineering [1]. Adeno-associated viral vectors (AAV) are known as safe, non-pathogenic and efficient vectors for human gene therapy. AAV is a highly efficient vehicle for the delivery of therapeutic genes to both dividing and non-dividing cells [2-4].

EXPERIMENTAL METHODS

The release profile of AAV from the scaffolds was controlled by altering i) chemical compositions [5], and ii) physical inner structures.

Specifically, i) AAV vectors were encapsulated by electrospinning blended elastin-like polypeptides (ELPs), which are water soluble and thermal responsive, and poly(ε-caprolactone) (PCL). The biomaterials were mixed with various weight ratios to control viral release.

ii) Two viral vectors, each encoding different growth factor, were encapsulated in core and shell of electrospun fibers and released in the controlled manners, respectively. Core and sheath of the nanofibers were composed of photocrosslinkable materials and the degree of crosslink of each material was controlled to regulate the viral release profiles.

RESULTS AND DISCUSSION

i) AAV vectors were released from the scaffolds composed of blended mixtures of ELP and PCL in a controlled manner, as a function of ambient temperatures and weight ratios. And fibroblasts adherent on nanofibrous scaffolds were efficiently transduced. Combinatorial interactions between ELP and PCL chains by physical blending significantly altered the physical and mechanical properties (i.e. wettability, elastic modulus, strain, etc.) of the composite fibrous matrices. Optimizing the weight ratios between of ELP and PCL, the viral release and cellular transduction profile were altered and the scaffold composed of ELP/PCL = 3/7 showed its capability of sustained viral release and cellular transduction.
ii) Double layered structure was successfully fabricated in the nanofibers. Each layer (i.e. core and shell) contained AAVs encoding different growth factors and whose release rate was also controlled by the layered structure and the degree of crosslink of the materials composing the layer. Furthermore, synergistic effect of AAVs from the core and shell to the physiological changes of cell adherent on the scaffold was shown in a term of neurite extension.

CONCLUSION
The presented strategies to orchestrate the controlled release of AAV and AAV-mediated gene delivery with high transduction efficiency will provide enormous opportunities for various tissue engineering applications. These systems can be combined with the topographical changes of the scaffold surfaces to enhance the neuronal differentiation or neurite extension.

REFERENCES