

Nano-hybrid Gel Scaffold for Biopharmaceuticals Delivery and Soft Tissue Engineering

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Statement of Purpose

Biodegradable hydrogels have served as highly functional scaffolds for tissue reconstruction in addition with cells and growth factors (GFs). It has been proven in animal models that vascular endothelial growth factor (VEGF) plays a key role as a major regulator of vasculogenesis and angiogenesis in tissue engineering. Delivering the VEGF-entrapped polysaccharide nanoparticles in a hydrogel scaffold can serve as an alternative approach and may hold greater therapeutic value in terms of engineered tissue survival due to its unique delivery system. In this study, we report the synthesis of a multifunctional nano-fibrous hydrogel integrated with the VEGF-entrapped polysaccharide nanoparticles that are capable of inducing adipose-derived stem cells (ASCs) proliferation and differentiation for adipogenesis *in vitro*.

Methods

The nano-fibrous hydrogel was produced via biological conjugation of biotin terminated star-shaped poly(ethylene glycol) (PEG-Biotin) and streptavidin functionalized hyaluronic acid (HA-Streptavidin). The polysaccharide nanoparticles were non-covalently assembled via electrostatic interactions between low molecular weight heparin (LMWH) and *N,N,N*-trimethylchitosan chloride (TMC). VEGF was entrapped in the LMWH/TMC nanoparticles by affinity interactions with LMWH. The potential application of this nano-hybrid scaffold as an injectable vehicle in *in vitro* adipogenesis was examined by encapsulation of human ASCs.

Results

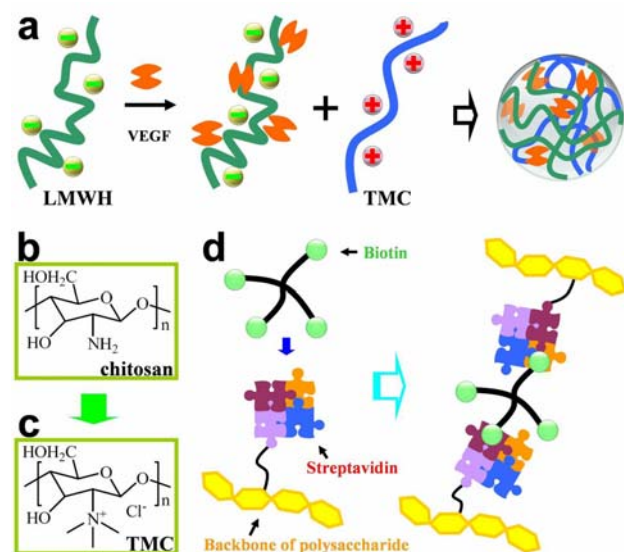


Fig. 1. (a) Schematic of assembly of VEGF loaded nanoparticles. Nanoparticles assembled via electrostatic

interaction of LMWH and TMC. VEGF was entrapped in LMWH/TMC nanoparticles via affinity interaction mediated by LMWH. (b,c) Chemical structures of chitosan and TMC. (d) Schematic of hydrogel network based on the biological Biotin-Avidin conjugation.

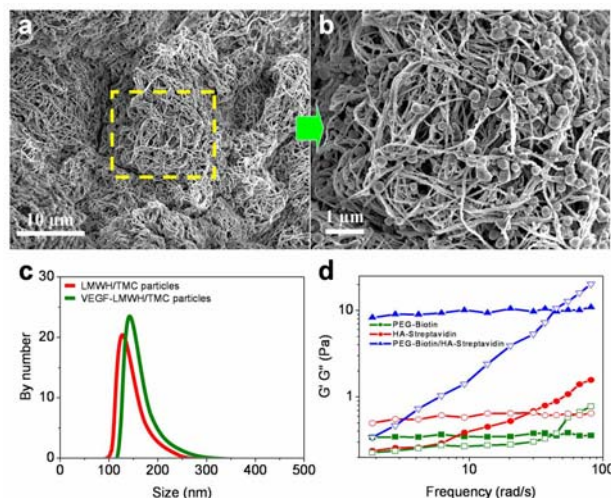


Fig. 2. (a,b) SEM images characterized the morphologies of nano-hybrid scaffolds. (c) Size distribution of LMWH/TMC nanoparticle. (d) Microrheological characterization of viscoelastic properties of PEG-Biotin/HA-Streptavidin hydrogel. The volume ratio of PEG-Biotin and HA-Streptavidin was fixed with 1:1.

Conclusions

In this study, we have developed a biological methodology to conjugate an injectable scaffold basing HA and PEG with novel nano-hybrid architectures that specifically allows for targeted ASCs encapsulation. VEGF was efficiently entrapped and delivered through polysaccharide nanoparticles which was assembled by a cationization of chitosan derivative and low molecular weight heparin via the electrostatic interaction. The VEGF loaded polysaccharide nanoparticles were integrated into nano-fibrous HA-PEG hydrogel network via Biotin-Avidin bioconjugation. The results suggest the potential utility of this unique design of nano-hybrid scaffold in directing proliferation and differentiation of ASCs in ECM-mimetic scaffolds *in vitro*. We anticipate that this multifunctional nano-hybrid scaffold can render the formulation of a therapeutically effective platform for soft tissue engineering application.

References

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- [2] H. Tan, X. Gao, J. Sun, C. Xiao, X. Hu. *Chem. Commun.* 2013, 49: 11554-11556.