STAR-SHAPED POLYPEPTIDES AS EFFICIENT NANOCARRIERS FOR GENE DELIVERY IN BONE REGENERATION

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ABSTRACT

The field of tissue engineering is increasingly recognizing that gene therapy can be employed for modulating in vivo cellular response thereby guiding tissue regeneration. However, the field lacks a versatile and biocompatible gene delivery platform capable of efficiently delivering transgenes to mesenchymal stem cells (MSCs). In this paper we describe the systematic exploration of architectural variations of star-shaped poly(L-lysine) polypeptide (star-PLL), 1 derived from the ring-opening polymerization of N-carboxyanhydride (NCA) with varying number and length of poly(L-lysine) arms as potential nonviral gene delivery vectors for MSCs. 2 We demonstrate that star-PLL vectors are capable of self-assembling with pDNA to form stable, cationic nanomedicines. Moreover, the feasibility of starPLL polyplexes is demonstrated in vivo for the healing of large, critically sized, segmental bone defects, which remains an unmet clinical need in modern orthopedic medicine. The approach utilizes starPLL/pDNA loaded biomaterial scaffolds as 3D templates to guide the regenerative process.

Fig. 1: Star poly(L-lysine)/pDNA polyplexes (left); polyplexes incorporated into collagen scaffold (centre); rodent model healing of critical bone defect using gene activated scaffold (right).

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References: