Peptide Amphiphile NanoSlurry as an Improved BMP-2 Carrier for Spinal Arthrodesis

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INTRODUCTION: Advances in biologics and other bone graft substitutes have improved spine fusion rates; however, there still exists a need for a product that elicits high fusion rates with minimal adverse effects. Recombinant human bone morphogenetic protein-2 (rhBMP-2) applied onto an absorbable collagen sponge (ACS) promotes fusion rates of >90% in humans. However, the supraphysiologic dose required when rhBMP-2 is utilized with this carrier can lead to serious complications. In previous work, we evaluated nanofiber scaffolds composed of peptide amphiphiles (PA), which localize both exogenous and endogenous BMP-2, thereby reducing the requisite dose of exogenous growth factor for successful fusion. However, a need still exists to optimize both handling properties and efficacy.

METHODS: Proof of principle work was performed on female Sprague-Dawley rats that underwent L4-L5 fusion. Efficacy was then tested in the more stringent New Zealand white rabbit L5-L6 fusion model. For the rat studies, animals received either a peptide amphiphile nanogel—collagen slurry (NanoSlurry), control collagen slurry, or ACS alone pre-loaded with 100 ng rhBMP-2 (per animal; 50 ng/scaffold), which is a dose that does not promote fusion when applied on ACS. For the more stringent rabbit PLF model, animals received either the NanoSlurry or ACS pre-loaded with either 30 or 60 µg rhBMP-2 per rabbit. All animal procedures were approved by the Northwestern University IACUC. Bone regeneration and spine fusion were assessed in both rats and rabbits using radiographs, fusion scoring, and microCT imaging. Fusion scores were determined by blinded manual palpation using an established scoring system: 0 = no bridging bone, 1 = unilateral bridging, and 2 = bilateral bridging. Spines with an average score of 1 or higher were considered successfully fused.

RESULTS SECTION: NanoSlurry pre-loaded with 100 ng rhBMP-2 elicited a significantly higher mean fusion score relative to equivalently pre-loaded ACS (p<0.001) or control slurry (p<0.001) in the rat PLF model. Successful fusion was seen in 100% of rats treated with NanoSlurry + 100 ng rhBMP-2. This was significantly higher than fusion rates of equivalently preloaded ACS (0%) and control collagen slurry (8%). Similarly, fusion rates in rabbits treated with the NanoSlurry were significantly higher than equivalently pre-loaded ACS (100% vs 50%) respectively for the 60 µg groups (p<0.05); 100% vs 0% for the 30 µg groups (p<0.05).

DISCUSSION: Previous work has established 10 µg rhBMP-2 (per animal) applied on ACS results in successful fusion at a rate of 100% in the rat PLF model. Our data suggest that in this model, the NanoSlurry can effectively reduce the requirement for rhBMP-2 by a factor of 100 relative to ACS, which is the current FDA-approved carrier for the growth factor. This success also translated to the more stringent rabbit PLF model, suggesting that this technology may be robust enough for success in the clinical setting.

SIGNIFICANCE: The purpose of this study was to develop a peptide amphiphile nanogel system with optimized structural and handling properties, with the intent of reducing the amount of rhBMP-2 necessary to achieve bone regeneration and successful spine fusion. A slurry composed of peptide amphiphile nanofibers and collagen particles was formed into a malleable paste that could be used to fill bone defects and potentially reduce the exogenous growth-factor necessary to achieve spine arthrodesis.

IMAGES AND TABLES:

Figure 1.

![Image](attachment:image1.png)

Fig 1. Fusion scores and rates evaluating the NanoSlurry in the rat (A-B) and rabbit (C-D) posterolateral spine fusion (PLF) models. *p < 0.05, **p < 0.001.