Injectable hydrogels to locally regenerate tissue

Inventors:

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Brief Description

Injectable Hydrogel with Immobilized BMP-2 Mimetic Peptide for Local Bone Regeneration

Problem

Osteoporosis is a disease characterized by a decrease in bone mineral density, thereby increasing the risk of sustaining a fragility fracture. Most medical therapies are systemic and do not restore bone in areas of need, leading to undesirable side effects. Treating bone fractures often involves expensive and stressful surgery using plate and screw technology resulting in inflammation and long recovery times. Accordingly, there is **a long-felt need for improved methods to locally combat osteoporosis and prevent future bone fractures.** In 2018, the total annual expense of providing care associated with osteoporosis fractures was $57 billion and is expected to rise to $95 billion in 2040.

Solution

Injectable hydrogels can locally deliver therapeutics with spatial precision, and our team has developed an injectable hydrogel containing a peptide mimic of bone morphogenetic protein-2 (BMP-2). This technology can work alongside, or independently of stem cell implantation, to locally regenerate bone tissue when needed as a potential treatment for local osteoporosis.

Technology

Injectable hydrogels are created using hyaluronic acid modified with norbornene (HANor) or tetrazine (HATet) which upon mixing click into covalently cross-linked Nor-Tet hydrogels. The inventors have shown this injectable hydrogel may be used to treat osteoporosis. As a therapeutic the Inventors used a peptide mimetic of growth factor **BMP-2** specific to the **DWIVA peptide** sequence. HANor macromers were modified with methacrylates to immobilize the osteogenic thiolated BMP-2 mimetic DWIVA peptides through coupling of the thiols in BMP-2 to the methacrylates on the HANor macromer, with coupling confirmed by 1H NMR spectroscopy. The DWIVA peptides presented in this immobilized form increased alkaline phosphatase (ALP) expression in mesenchymal stem cell cultured atop 2D and encapsulated within 3D Nor-Tet hydrogels. Injection of bioactive Nor-Tet hydrogels into hollow intramedullary canals of Lewis rat femurs showed a local increase in trabecular bone density as determined by micro-CT imaging (Fig.1).

Advantages

- Local application reduces systemic side-effect risks
- Prophylactic treatment possible with companion bone densitometry tests

Stage of Development

in vivo proof of concept

Partnerships

Co-Development, Licensing

Intellectual Property

US Provisional Patent Application

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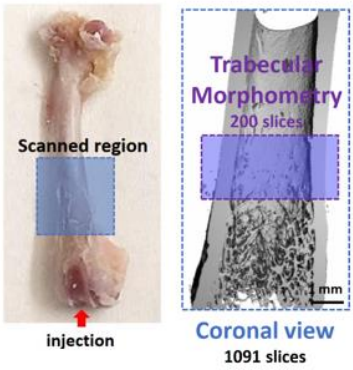
Figure 1:

A.



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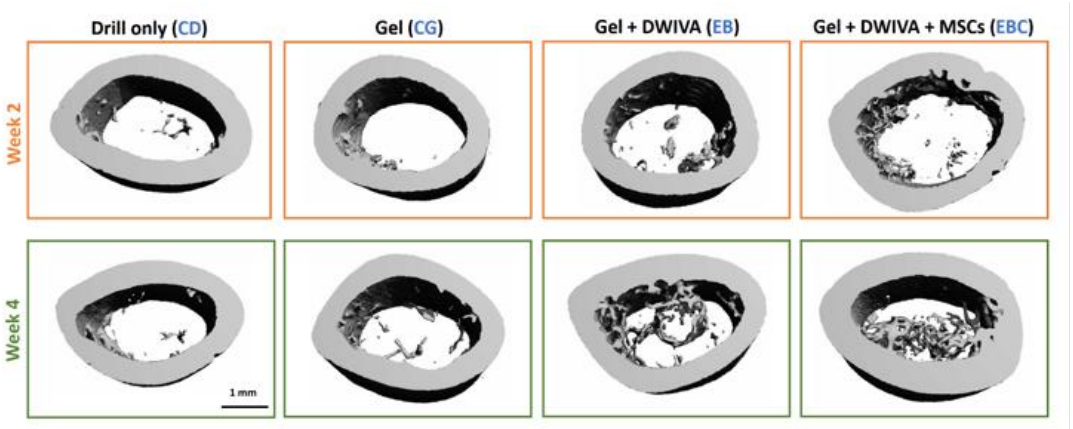

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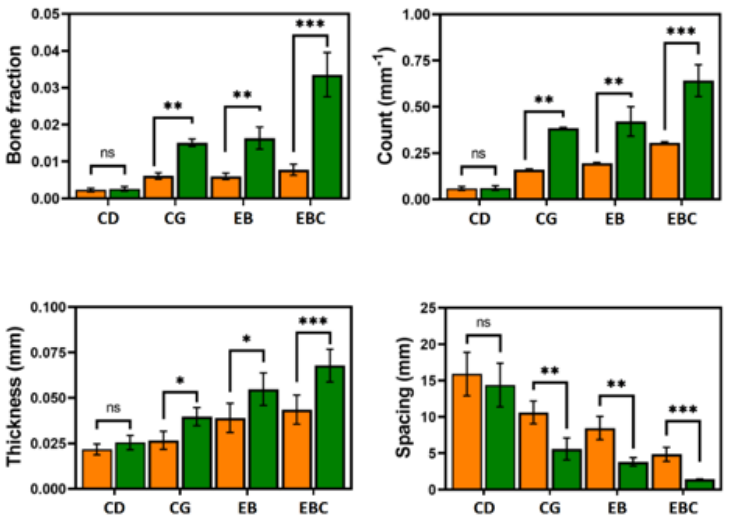

Fig. 1A-1C demonstrate that DWIVA-functionalized hydrogels induce trabecular bone growth in vivo. Fig. 1A: the sites of injection and CT imagining. Fig. 1B: comparison of drilled femurs not treated with hydrogel ("CD"), treated with hydrogels not functionalized with DWIVA peptide and without mesenchymal stem cells ("CG"), treated with hydrogels functionalized with DWIVA peptide but without mesenchymal stem cell ("EB"), or treated with hydrogels functionalized with DWIVA peptide and includes mesenchymal stem cells ("EBC") at two weeks and four weeks. Fig. 1C: quantification results for Fig. 1B. Bar graphs are shown as mean ± SD, (n ≥ 3 samples per condition) with nonsignificant differences denoted as ns, and significant differences determined with ANOVA followed by Tukey's post hoc test where *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$. Scale bars: (A,B) 1 mm.