Mechanobiology-Informed Regenerative Medicine: Dose-Dependent Release of Placental Growth Factor from a Functionalized Collagen-Based Scaffold Promotes Angiogenesis and Critically Sized Bone Defect Healing

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Introduction

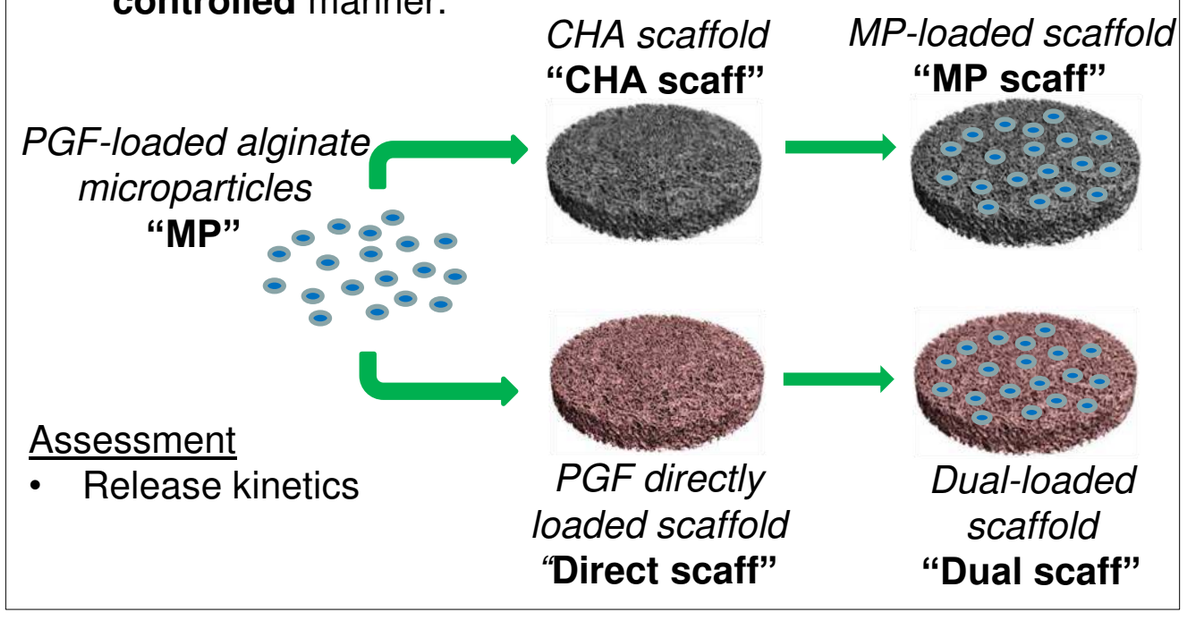
- Concerns surrounding the use of rhBMPs for bone repair [1].
  - Need for scaffold-based **controlled delivery** systems and **novel, alternative therapeutics**.
- Functionalized **collagen/hydroxyapatite (CHA)** scaffolds.
  - Drug-loaded alginate microparticles (MPs) [2].
  - Direct loading of drugs into scaffolds [3].
- **Mechanobiology-informed regenerative medicine.**
  - Placental growth factor (PGF).
  - A mechanically augmented gene [4].
  - Dose-dependent effect on angiogenesis/osteogenesis.
    - 50 ng/mL ↑ angiogenesis, 10 ng/mL ↑ osteogenesis.

Hypothesis

It is possible to leverage the **dose-dependent effect of PGF** to deliver both **pro-angiogenic and pro-osteogenic** cues and thereby promote **regeneration** of critically sized defects.

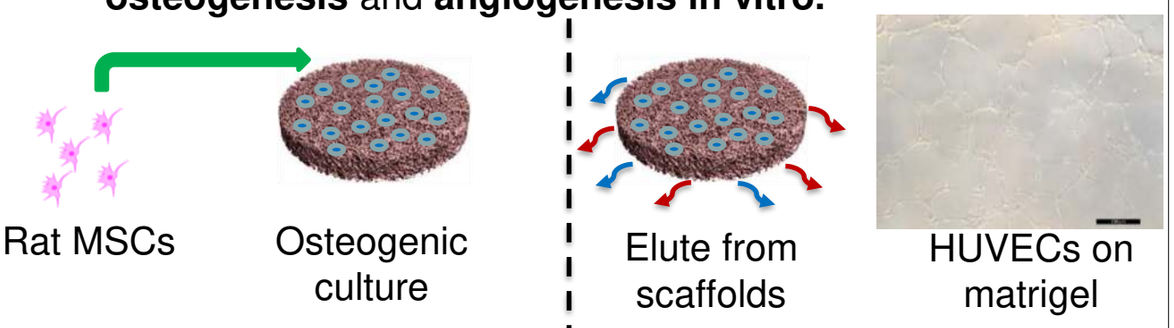
Objectives

1. Functionalize a CHA scaffold to deliver PGF in a **dose-controlled** manner.



Assessment
- Release kinetics

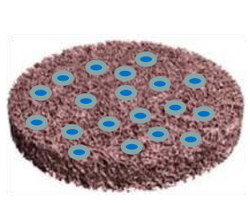
2. Assess the capacity of functionalized scaffolds to promote **osteogenesis** and **angiogenesis in vitro.**



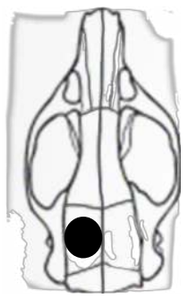
Osteogenic assessment
- Alkaline phosphatase activity
- Calcium production

Angiogenic assessment
- Number of vascular junctions formed by engineered vessels

3. Evaluate the capacity of functionalized scaffolds to promote **regeneration of critically sized defects.**



Optimized scaffold

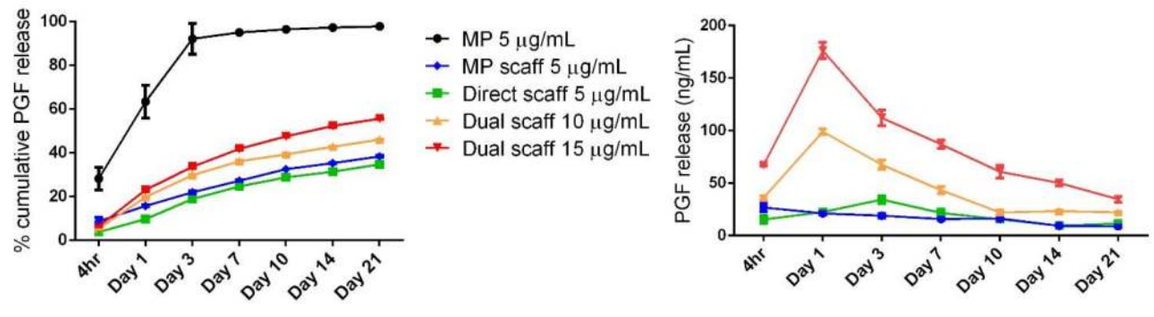


7 mm rat calvarial defect

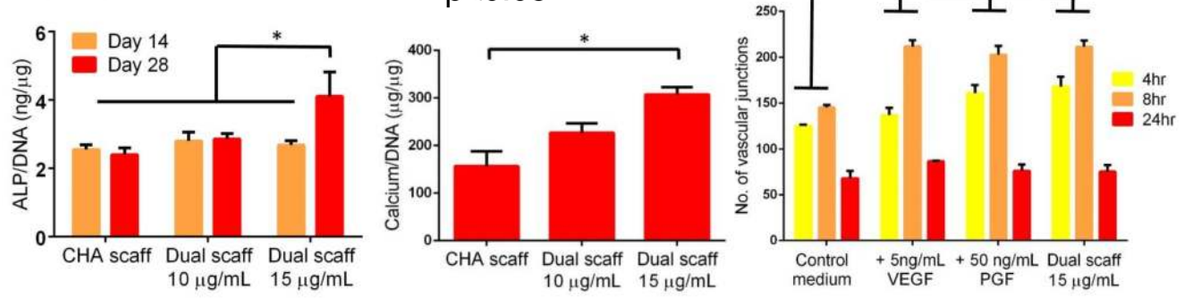
Assessment (28 days)
- New bone formation
- Neovascularization

Results

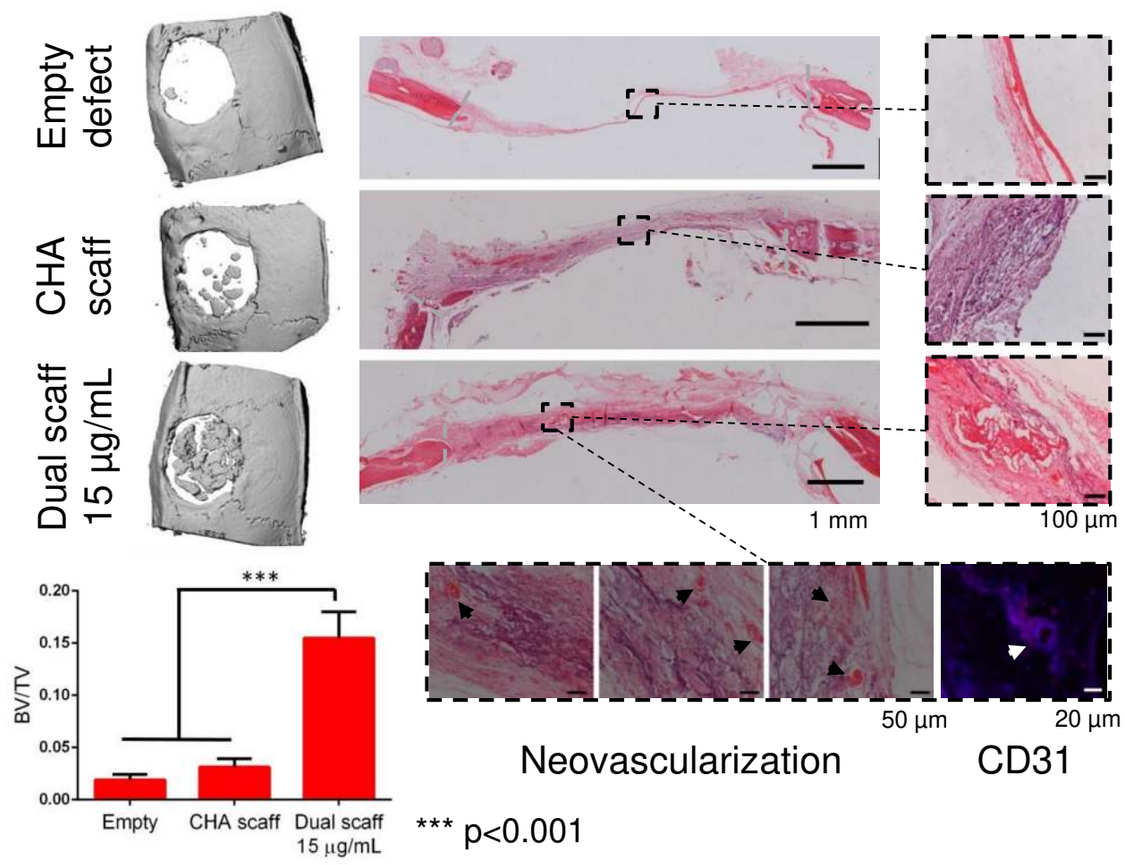
PGF-functionalized scaffolds with optimized release kinetics were fabricated.



PGF-functionalized scaffolds promote osteogenesis and angiogenesis in vitro * p<0.05



PGF-functionalized scaffolds promote regeneration of critically-sized defects



*** p<0.001

Discussion

- We have developed a novel, PGF-functionalized scaffold capable of promoting angiogenesis and osteogenesis in vitro and bone regeneration in vivo.
- This highlights the potential of PGF to deliver both pro-angiogenic and pro-osteogenic cues without the addition of another growth factor or protein.
- **Mechanobiology-informed regenerative medicine**
  1. Identify a therapeutic candidate through mechanobiology
  2. Design an appropriate scaffold delivery system
  3. Demonstrate the efficacy of the scaffold in vivo

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References

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