HARLEYLAB

Mineralized Collagen Scaffold Pore Structure Enhances Immunomodulatory Potential of Mesenchymal Stem Cells

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ILLINOIS

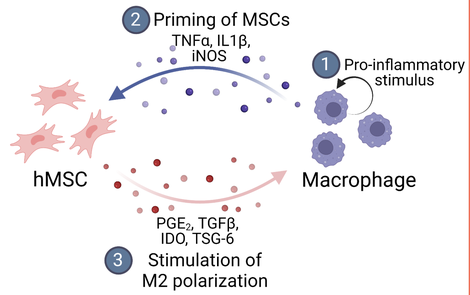
Creating biomaterials for craniomaxillofacial repair

Craniomaxillofacial (CMF) bone defects

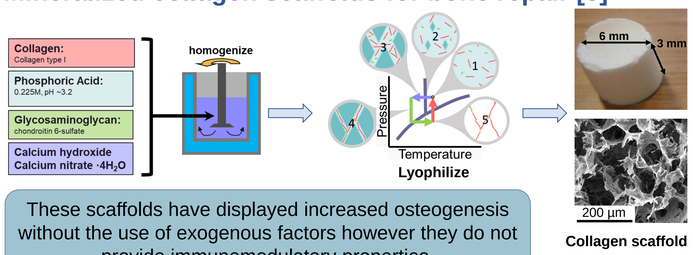
CMF bone defects can arise from congenital, post-oncologic, and traumatic injuries that cannot heal naturally due to their overwhelming size, and thus require surgical intervention. Recent studies examining battlefield injuries experienced by U.S. Soldiers in Iraq and Afghanistan found 26% of all survivable battlefield injuries localized to the maxillofacial area. There is an extraordinary unmet need for regenerative strategies for CMF bone defects. **Our goal is to design a biomaterial that can promote hMSC osteogenesis while temporally modulating the inflammatory environment.**

Crosstalk between MSCs and macrophages in the bone microenvironment

Paracrine interactions are the strongest between MSCs and macrophages. These affect both MSC and MΦ behavior in the wound microenvironment.



Mineralized collagen scaffolds for bone repair [3]



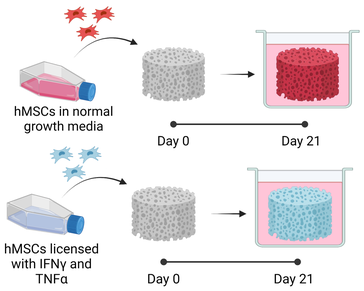
These scaffolds have displayed increased osteogenesis without the use of exogenous factors however they do not provide immunomodulatory properties.

Overall Hypothesis: Primed hMSCs will display heightened immunomodulatory potential and decreased osteogenic potential in a scaffold dependent manner.

Aim 1: Examine the effects of priming hMSCs on their osteogenic potential.

Aim 2: Examine the effects of priming hMSCs on their immunomodulatory potential.

Experimental Layout



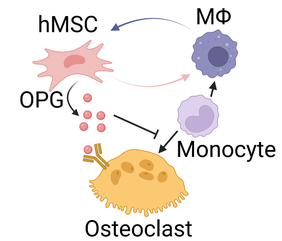
Will assess osteogenic and immunomodulatory potential of basal (N) and primed (T) hMSCs as a function of scaffold type:
Isotropic pores (Iso)
Anisotropic pores (Ani)
Heparin (Hep)

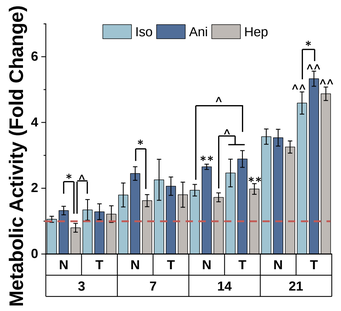
[1] Niknejad et al., 2008 [2] Liu et, al, Frontiers in Cell and Developmental Biology, 2021 [3] Harley B. et al., (2010)

hMSC osteogenic response as a function of scaffold type and inflammatory state

Influence of scaffold type and hMSC Inflammatory stimulation on metabolic activity and osteogenesis

N: Normal/Basal hMSCs
T: Treated/Primed hMSCs with inflammatory factors





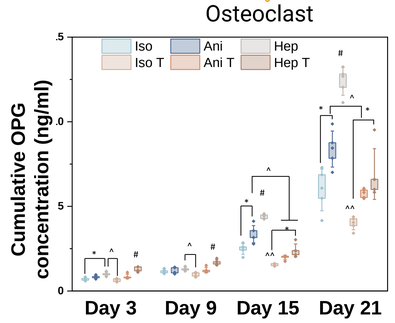


Figure 1: (left) hMSC metabolic activity measured via AlamarBlue over 21 days. (N) indicates basal conditions, (T) indicates inflammatory stimulated conditions. **(right)** Cumulative release of osteoprotegerin (OPG) over 21 days. Symbols indicate significance at a level of $p < 0.05$. *: significance between indicated groups of same treatment, ^: significance between indicated groups of different treatment, **: significance between all groups of same treatment, ^^: significance between indicated group and all other groups of other treatment, #: significance between indicated groups and all other groups

- hMSCs exhibit increased metabolic activity on anisotropic scaffolds regardless of inflammatory status
- hMSCs secrete the greatest amount of OPG under basal conditions in response to Heparin scaffolds

Influence of inflammatory stimulation on mineral formation

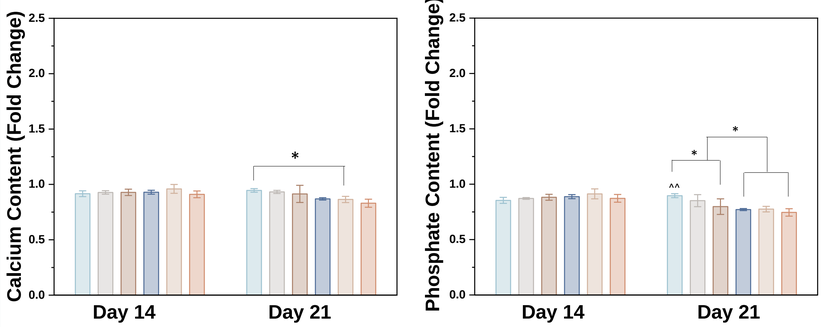


Figure 2: Calcium and phosphate content measured via ICP. Symbols indicate significance at a level of $p < 0.05$. * Significance between indicated groups, ^^ significance between indicated group and all other groups of other treatment

- All scaffold groups displayed similar mineral formation at early stages of culture
- In late stages the Isotropic scaffold under basal condition displayed significantly more phosphate content compared to all inflammatory stimulated groups

V. Kolliopoulos, M. Polanek, Influences of scaffold structure and composition on hMSC immunomodulatory potential. (*in preparation*)

hMSC gene expression influenced by priming in a scaffold dependent manner

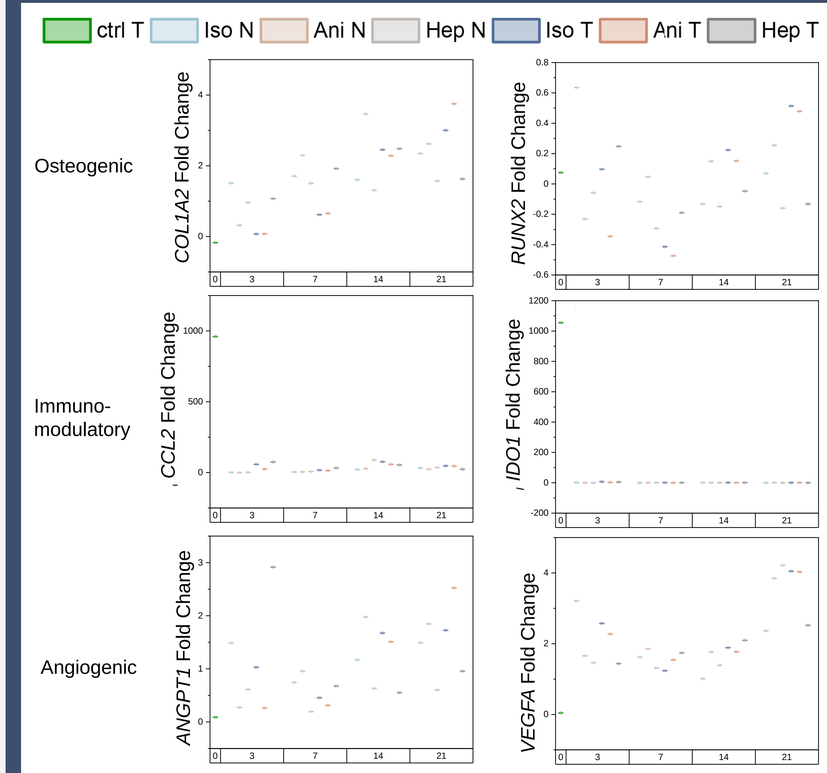


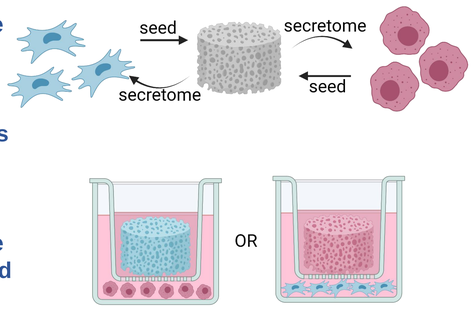
Figure 3: Select osteogenic, immunomodulatory, and angiogenic gene expression measured via NanoString (n=1) of basal and primed hMSCs seeded on isotropic, anisotropic, or heparin containing scaffolds.

- Anisotropic scaffolds display an increase in osteogenic gene expression in late stages for both basal and primed hMSCs
- Seeding primed hMSCs on mineralized collagen scaffolds decreases expression of immunomodulatory genes
- Anisotropic scaffolds increase angiogenic gene expression in both basal and primed hMSCs

V. Kolliopoulos, M. Polanek, Influences of scaffold structure and composition on hMSC immunomodulatory potential. (*in preparation*)

Future Work

Our goal is to design a biomaterial that can promote hMSC osteogenesis while temporally modulating the inflammatory environment. Therefore, future experiments will elucidate the crosstalk interactions of hMSCs and immune cells like macrophages and how these interactions can be modulated via biomaterial influences.



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