Engineered porous hydrogels to promote bone healing

S Pravato[1], H Guan[2], B M Carrara[1], M Jacobs[1], M Monticelli[1], L Moser[1], T Zambelli[2], M Ehrbar[1]

[1]Department of Obstetrics, University and University Hospital of Zurich, Zurich Switzerland.
[2]Laboratory of Biosensors and Bioelectronics, Institute for Biomedical Engineering, ETH Zurich, Zurich, Switzerland.

Background

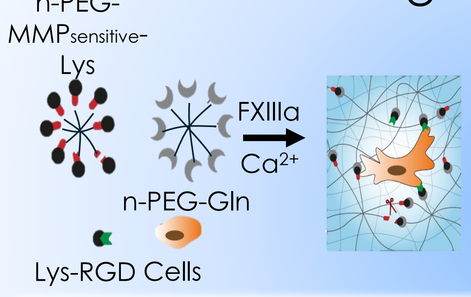
When large bone defects are present, current approaches utilize sponges, scaffold or hydrogels to ensure cell recruitment, survival, and spreading. However, these methods lack construct stability over time and exhibit homogeneous properties. The aim of this project is to develop a heterogeneous microporous hydrogel, which will enhance bone healing by facilitating the delivery of cells, growth factors, and recruitment of cells from the host tissue.

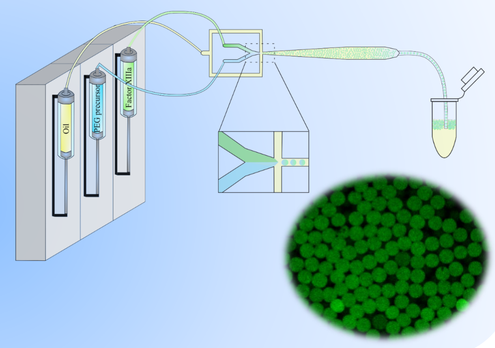
Problem:



Large bone defects not spontaneously healing

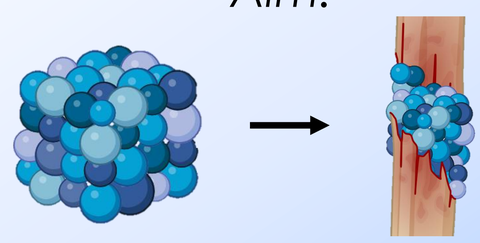
Microgels production:





PEG is enzymatically crosslinked with FXIIIa. Microgels are mainly produced with microfluidic method.

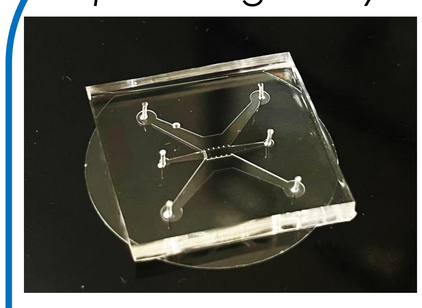
Aim:

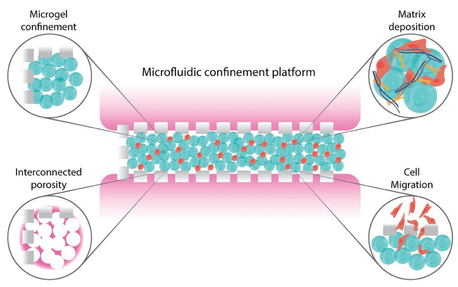


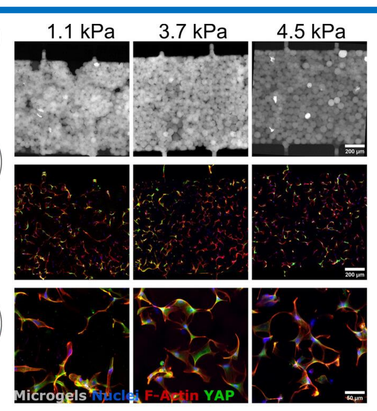
Heterogeneous MAP hydrogel → Bone tissue graft

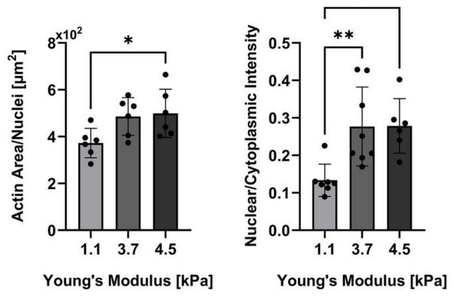
In vitro studies

Spreading assay



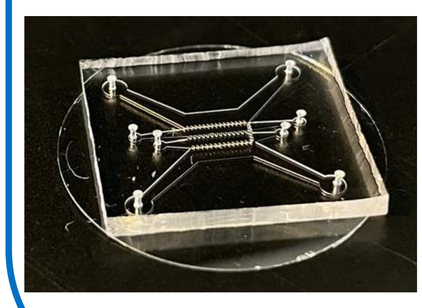


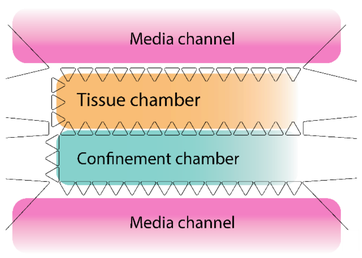


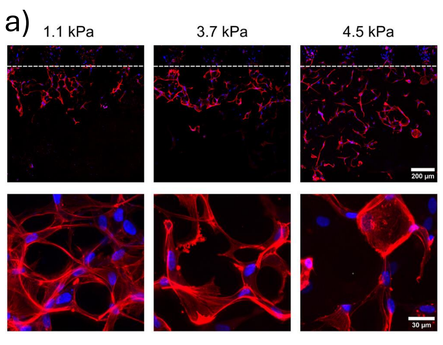


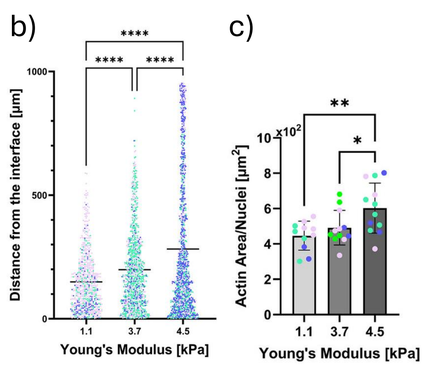
a) YAP expression in hBM-MSCs cultured with microgels of varying stiffness. b) Actin spreading area in response to microgel stiffness. c) Nuclear-to-cytoplasmic YAP intensity ratio.

Migration assay







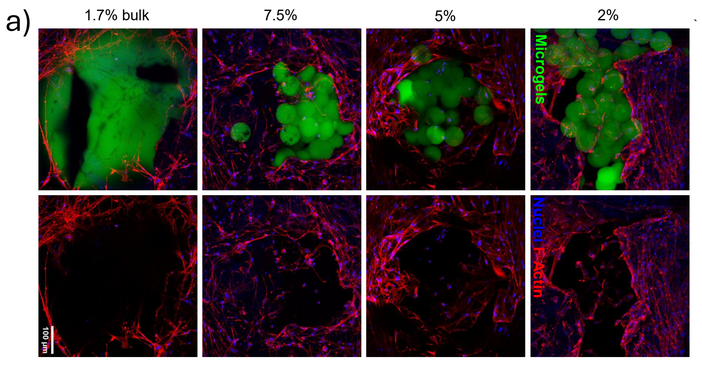


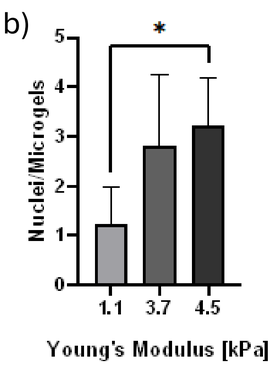
a) Migration of hBM-MSCs through microgels of varying stiffness. b) Distance of migration from the interface c) Actin spreading area in response to microgel stiffness.

Krattiger, Emiroglu, Pravato, et al. – 2024, Adv. Functional Materials

Pravato, et al. – 2025, Adv. Functional Materials

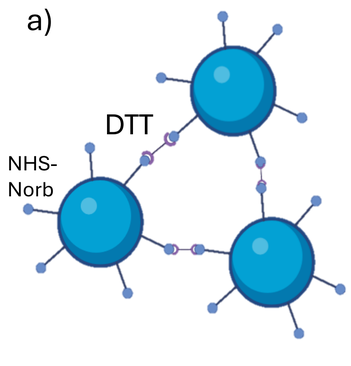
Ex-vivo studies

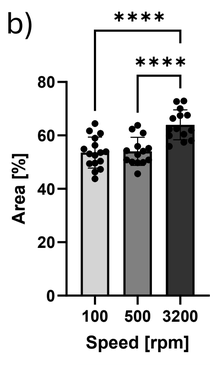


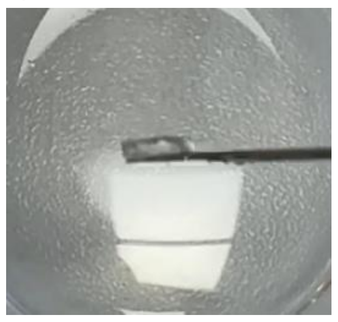


a) Cellular invasion from the edges of a bone hole into TG-PEG microgel assemblies with low, intermediate, and high stiffness, as well as soft bulk TG-PEG hydrogels. b) Quantitative analysis of the number of migrated cells per microgel.

MAP hydrogel formation







Secondary crosslinking for MAP hydrogel formation. a) Schematic of microgels conjugation using NHS–norbornene sites, DTT and LAP under UV light. b) Increasing centrifugation speeds resulting in more compact scaffolds c) Formation of MAP hydrogels.

Outlook:

In this project, a microporous hydrogel will be formed by microgels with heterogeneous properties. By enclosing cells within microgels and adjusting the composition and ratio of the microgels, we will create a diverse bone structure. These structures will be evaluated and enhanced regarding the in vitro migration and differentiation of cells, as well as their ability to promote bone healing in vivo.