3D microenvironments: biological response and characterization of cell-cell and cell-material interactions

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Researchers have known for decades that biochemical factors influence eukaryotic cell behavior. However, in the past decade evidence has been mounting that the physical environment, like the topography, porosity, pore geometry, and substrate stiffness, also significantly influences cell fate. Therefore, the ability to precisely engineer both chemical and physical properties of the cellular micro and nano environment will enable important advances in research in many scientific areas relevant to healthcare and medicine.

The scientific objective here is thus to engineer complex biomaterials systems for unprecedented control of the cellular environment. Specifically, the team will engineer novel 3D multiscale micro and nano environments in order to make scientific advances in understanding the roles of cell-cell and cell-material interactions at the micro and nano scales and enhance cell differentiation and tissue formation, primarily in the context of bone repair and regeneration.

The specific activities of this project include:

- Designing, optimizing, and fabricating novel 3D nano and micro environments in 3D printed hydroxyapatite and titanium scaffolds to study cell behavior.
- Coating these rigid substrates with polymeric coatings to enable additional control over the 3D micro and nano cellular environment. The coatings allow the local stiffness and biochemistry (i.e. with biomolecules) to be tuned. With the rigid substrate one will dictate the geometry of the microenvironment but the surface coating will guide cell sensing.
- Exploiting capillary forces to sequester cells within the uncoated and coated pores of the designed architectured materials as it has been recently evidenced for porous hydroxyapatite materials (Fig. 3).
- Using high resolution electron microscopies and fluorescent microscopy to assess nano scale cell-cell and cell-material interactions
- Assessing the biological response of the cells to the microenvironment using gene and protein expression, as well as imaging.

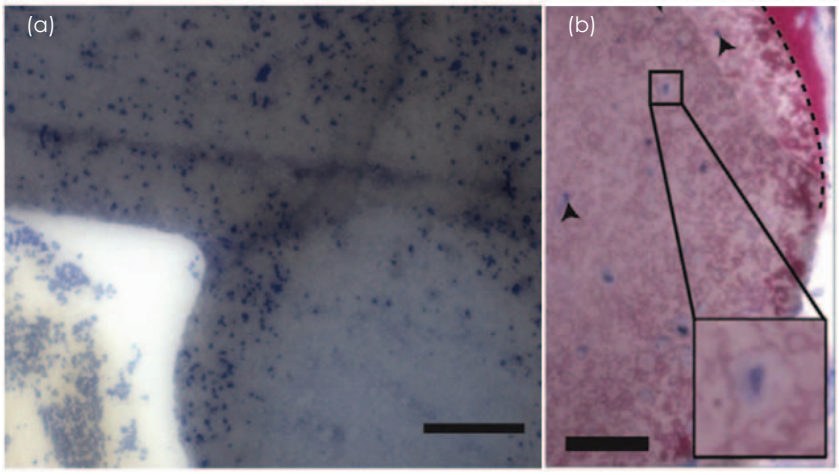

Fig. 4: Optical histology shows cells in porous HAP sample implanted in a pig mandible for (a) 30 minutes to show cell infiltration (blue nuclei) and (b) three weeks to show bone formation (red/pink). The dotted line demarcates the substrate edge edge.

Scale bar is 100 for (a) and and 50 microns for (b).

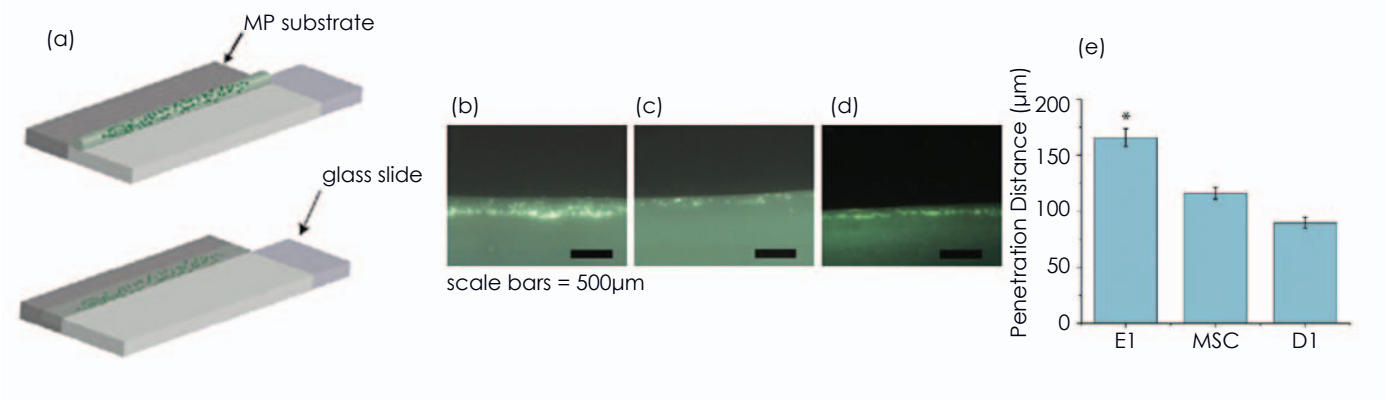

Fig. 3 : Capillary forces induce cell penetration and sequestration. (a) Experimental procedure. The substrate contacts the cell suspension on the slide edge and cells are drawn in. (b, c, d) are images of E1, MSC and D1 cell penetration, respectively. (e) Average penetration distance for the different cell types : E1s penetrate significantly further than MSCs and D1s.