Self-Crosslinking Complex Hydrogels with Supramolecular Interactions for Immunomodulation

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Hydrogels are widely used for cell encapsulation and delivery applications [1]. One such application is encapsulation of innate immunity cells such as macrophages for achieving phenotype control. However, most hydrogel formulations require crosslinking agents to form a strong 3D network which can significantly affect the biological properties of the formed network. In this project, self-crosslinking hydrogels based on optimised mixtures of natural polymer derivatives will be developed in order to create a 3D microenvrionment for macrophages that exhibits an anti-inflammatory phenotype. The final hydrogel composition will be further optimized to render it printable with commercially available bioprinters [2]. The optimal hydrogel compositions to guide Macrophage differentiation will be selected according to the following parameters:

a) Hydrogel stiffness and mesh size: the mechanical properties of the hydrogels will be varied to match the optimal stiffness values for anti-inflammatory macrophage (M2) differentiation. Additionally, different mesh sizes will be tested for the diffusion of nutrients in dependence of the hydrogel swelling properties under perfusion conditions.

b) Hydrogel denaturation/degradation profiles: the degradation of the gels will be quantified in the absence and the presence of the macrophages (via fluorescently labelled gel components to monitor their removal) in order to determine the stability of the gels during macrophage differentiation. In the case of low stability, an outer layer of highly crosslinked/thin shell hydrogels will be designed which will keep the integrity of the gels without endangering the nutrient and gas transfer.

c) Macrophage phenotype markers: The macrophage phenotype will be monitored at gene expression (measured with RT-PCR), protein expression (Western Blotting, ELISA) and ECM deposition (biochemical assays) levels at different time points.

The student will be involved in a collaborative project in strong collaborations with chemists, physico-chemists and biologists. Students with a master degree in material science, cell biology, bioengineering are welcome to apply to this position. They should be open-mind and they should appreciate teamwork.

[1] Koenig, G, et al. "Cell-laden Hydrogel/Titanium Microhybrids: Site-specific cell delivery to metallic implants for improved integration." Acta Biomaterialia 33, 301 (2016).
[2] Bertassoni, Luiz E., et al. "Direct-write bioprinting of cell-laden methacrylated gelatin hydrogels." Biofabrication 6.2: 024105 (2014).

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