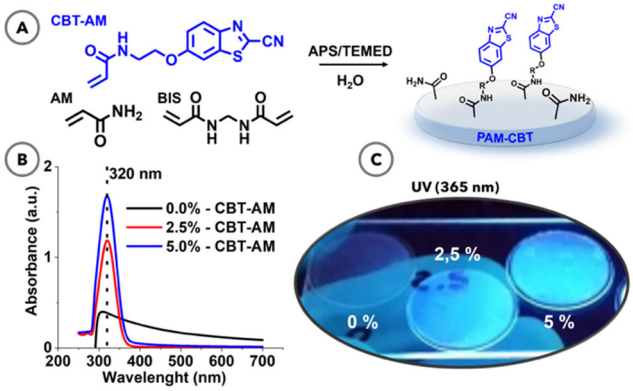
High-throughput fabrication of biofunctionalized polyacrylamide hydrogels as models for 2D cell culture

Understanding and controlling cell-materials interactions is key to modulate cell behavior in tissue engineered constructs. Polyacrylamide (PAM) hydrogels are used as 2D models for cell culture, allowing the study of cell response to specific biochemical and biophysical cues. Because of their characteristic protein repellence, PAM gels need to be biofunctionalized with cell-adhesive ligands in a controlled and tunable fashion, thus controlled and robust biofunctionalization strategies are necessary. Existing approaches to biofunctionalized PAM gels are suboptimal [1]. Therefore, developing **chemical strategies towards controlled PAM bioconjugation** is of great interest [2]. Another challenge in the field is the fabrication of biofunctionalized PAM gels that **support high throughput 2D cell biology** studies.

In this project, novel strategies that facilitate the biofunctionalization of PAM hydrogels with cell-adhesive ligands will be developed and adapted to the fabrication of high throughput platforms for cell biology investigation. Novel monomers featuring functional groups to specifically bind bioligands and that are compatible with PAM preparation will be investigated. PAM hydrogels with controlled mechanical and chemical properties will be obtained. Pendant moieties in the gel can later be used to covalently bind biomolecules (such as cell-adhesive RGD peptide) in a single step, under physiological conditions, and at tunable concentrations. Next, the effect of these bound ligands on cell behavior will be studied. This strategy will be useful to fabricate 2D-cell culture models with tunable biophysical and biochemical properties. In a final stage of the project, the fabrication of these hydrogels will be adapted towards high throughput platforms for 2D cell culture. Optionally, in combination with organ-on-chip technologies, their application as models for study of host immune response will be tested.

This project involves the synthesis of candidates in the chemical laboratory, the proof of concept of copolymerization to fabricate PAM substrates, and the biomaterial characterization (physical-chemical, mechanical, and biological). Successful PAM materials will be tested as 2D cell culture substrates for investigation of a variety of cell biology applications in a high throughput manner.



Keywords: free-radical polymerization, hydrogel fabrication, 2D cell culture substrates, bioconjugation of ligands, mechanical properties, biochemical properties, high throughput cell biology.

Figure 1. A) Reaction scheme showing preparation of PAM-CBT hydrogels. B) UV-Vis spectroscopy characterization of PAM-CBT gels. C) Pictures of fluorescent PAM-CBT gels attached to coverslips, when irradiated at 365 nm.

References:

[1] A. Farrukh, J. Paez, M. Salierno, A del Campo*. *Angew. Chem. Int. Ed.* **2016**, 55, 2092.
[2] A. Wolfel, M. Jin, J. I. Paez*, *Front. Chem.* **2022** 10:1012443.