

## **DIGITAL MANUFACTURING OF POROUS FUNCTIONALLY GRADED HYDROGELS BEARING FUNCTION-ENCODING PEPTIDES**

Within the human body, the osteochondral (OC) region – i.e., the region located at the interface between hyaline cartilage and bone tissues – represents a remarkable example of how nature is capable of assembling extraordinary complex structural-functional living materials with a precise organization from the nano to the macro scale. As one can imagine, replicating in vitro, such complexity is a daunting task, and, as of today, this is still an open challenge for tissue engineering and regenerative medicine.

In this project, we aim to tackle this challenge and possibly develop a new route for biofabrication in one step of advanced materials that recapitulate both the transitions in composition and architecture typical of the osteochondral regions. We aim to accomplish this goal by developing **new bioactive inks** and **microfluidic printing heads** that will be combined with our **custom digital manufacturing platform**.

Such tools should enable the design and manufacture of 3D porous functionally graded materials (pFGMs) that mimic the structural and functional organization of the OC region. This interface exhibits a gradient in its chemical and biological composition, with varying porosity ranging from a trabecular to a solid structure and different cell types, posing a challenge to induce biomimetic differentiation of stem cells within a single culture system. In this context, a key aspect of our project will be the formulation of bioinks containing functional-encoded peptides – which will be synthesized during the project – to support better the differentiation of human mesenchymal stem cells towards cartilage/bone tissues and the remodeling of the matrix. We expect that the combination of 3D printing and microfluidics will allow for unprecedented and on-demand control over local material properties, including pore size, pore connectivity, material composition, and biological activity.

We strongly believe that the successful outcome of the proposed project may offer significant potential to unveil novel technology that will facilitate the optimal reconstruction of interfacial tissue.