

Master 2 Internship – 6 months
SyMMES – CIBEST team, Grenoble

Influence of biomaterial stiffness and architecture on hMSC osteogenic differentiation

Context

Bone is a dynamic tissue in which cells, extracellular matrix (ECM), growth factors and mechanical cues interact to maintain tissue homeostasis. During cancer progression, tumor-derived signals can remodel distant organs and contribute to the formation of a permissive pre-metastatic niche. The mechanisms underlying this process remain incompletely understood.

Renal cell carcinoma (RCC) frequently gives rise to osteolytic bone metastases [1]. However, how RCC cells interact with and condition the human bone microenvironment before and during metastatic colonization remains poorly understood.

Our team has developed a biomimetic bone niche platform combining controlled biochemical functionalization of biomaterials with microfluidic culture systems [2,3,4]. This model allows us to investigate how biochemical, mechanical and tumor-derived signals influence human mesenchymal stem cells (hMSCs) and their microenvironment. Previous results have shown that osteogenic differentiation of hMSCs is associated with glycocalyx changes, including modifications in chondroitin sulfate sulfation patterns.

Project

The main objective of this internship will be to investigate how biomaterial stiffness and architecture influence the osteogenic differentiation of hMSCs within our biomimetic bone niche platform as shown in Figure 1.

The student will culture hMSCs on biomaterials with different stiffnesses and architectures and compare their osteogenic differentiation under these conditions. Differentiation will be assessed by quantitative PCR (qPCR) analysis of osteogenic marker expression and immunofluorescence (IF) analysis. Together, these approaches will characterize the cellular response to the mechanical and structural properties of the culture environment.

Depending on experimental progress, the student may also characterize the glycocalyx of hMSCs in 3D BAM, with particular attention to chondroitin sulfate. This work would explore whether glycocalyx changes accompany differentiation in a three-dimensional environment. If the core differentiation studies progress well and time permits, interactions with RCC cells may be explored as a further extension of the project.

Techniques

The student will gain experience in hMSCs cell culture on biomaterials, osteogenic differentiation, qPCR, IF and quantitative image analysis. They will also learn how to fabricate and fictionalize 3D biomaterials.

Candidate profile

We are looking for a motivated and experimentally oriented Master 2 or final-year engineering student with a background in cell biology, biotechnology, bioengineering, biomaterials or a related discipline. Practical laboratory experience and an interest in cell-microenvironment interactions are expected.

The candidate should be curious, rigorous and quantitative data analysis. Previous experience in mammalian cell culture, qPCR or IF would be an advantage. The student will be supported in developing increasing experimental autonomy.

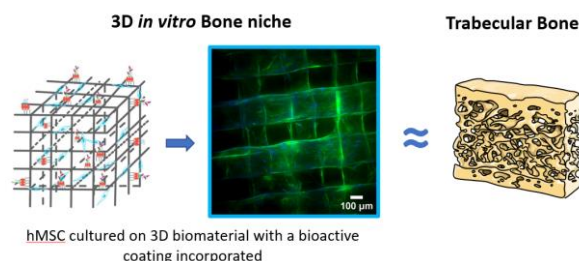
Duration: 6 months

Location: CIBEST team, SyMMES, IRIG, CEA-Grenoble

Supervision: Alima Chali (PhD student), Elisa Migliorini (CNRS resarcler)

Starting date: February 2027

Application: CV and a short motivation letter to alima.chali@cea.fr



[1] B. Cesana, C. Cochet, and O. Filhol, "New players in the landscape of renal cell carcinoma bone metastasis and therapeutic opportunities," *Int. J. Cancer*, vol. 156, pp. 475–487, 2025, doi: 10.1002/ijc.35181.

[2] J. Sefkow-Werner, P. Machillot, A. Sales, E. Castro-Ramirez, M. Degardin, D. Boturny, E. A. Cavalcanti-Adam, C. Albiges-Rizo, C. Picart, and E. Migliorini, "Heparan sulfate co-immobilized with cRGD ligands and BMP2 on biomimetic platforms promotes BMP2-mediated osteogenic differentiation," *Acta Biomaterialia*, vol. 114, pp. 90–103, 2020, doi: 10.1016/j.actbio.2020.07.015.

[3] E. Migliorini, P. Horn, T. Haraszti, D. Thakar, R. Sadir, F. Baleux, H. Lortat-Jacob, R. P. Richter, and C. Picart, "Enhanced biological activity of BMP-2 bound to surface-grafted heparan sulfate," *Advanced Biosystems*, vol. 1, no. 4, Art. no. 1600041, 2017, doi: 10.1002/adbi.201600041.

[4] I. Arnaldos-Pérez, P. Machillot, K. Geistlich, L. Marchadier, V. Maguer Satta, E. Migliorini, L. Guyon, S. Lefort, C. Albiges-Rizo, and C. Picart, "Biomaterials-enabled revelation of sustained p-Smad signaling and abnormal adhesion of leukemia-derived bone marrow stem cells," *Biomaterials*, vol. 333, Art. no. 124142, 2026, doi: 10.1016/j.biomaterials.2026.124142.