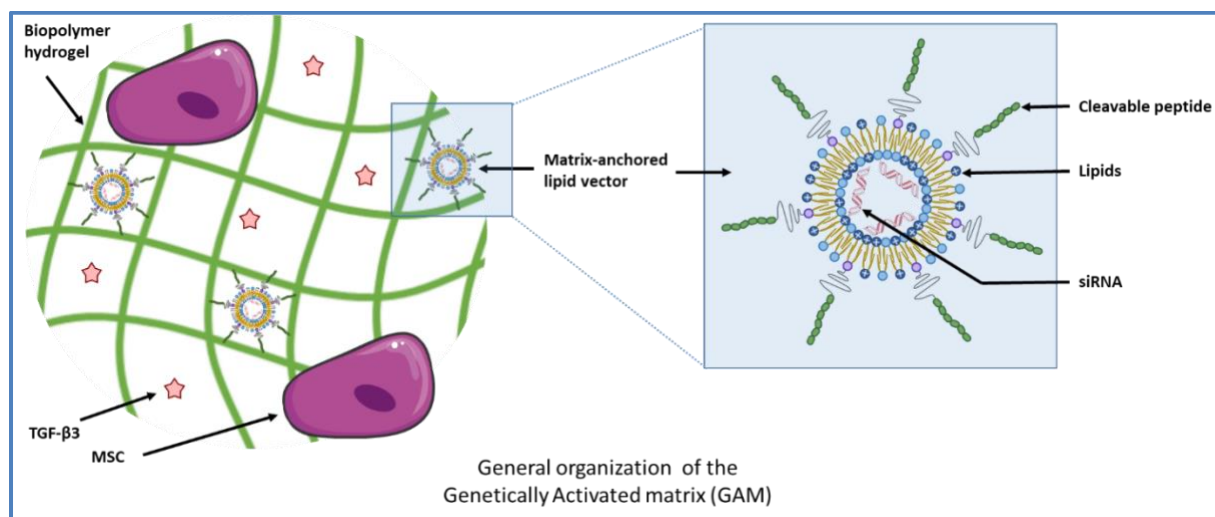


**Master internship proposal
(Opened to M1 and M2 students)**

« Gene activated matrix for cartilage repair »

Context:

The combination of Mesenchymal Stromal Cells (MSC) with active injectable carriers brings about innovative solutions to current issues in the field of tissue engineering. In particular, repair of adult articular cartilage lesions remains a clinical challenge because of the limited self-healing capacity of cartilage. We demonstrated previously that the open porosity of homemade collagen microspheres allows for the entrapment and progressive release of TGF- β 3, which efficiently triggered the chondrogenic differentiation of MSC in vitro and in vivo, and the production of neo-cartilage tissue. However, one major hurdle in MSC-based therapies for cartilage repair is their late hypertrophic differentiation and subsequent tissue calcification, characterized by the secretion of specific markers such as type X collagen, alkaline phosphatase, osteocalcin and metalloprotease 13 (MMP13). To tackle this challenge, we identified Runx2, which plays a central role in chondrocyte hypertrophy, as the main molecular target to be repressed. Indeed, Runx2 has been widely described to up-regulate the expression of hypertrophic markers. We previously demonstrated that the transient down-regulation of this factor can be achieved with a specific siRNA targeting Runx2. Here, we intend to deliver siRunx2 from collagen microspheres also used as an injectable support for BM-MSC and as a TGF- β 3 reservoir. However, efficient down-regulation of Runx2 with siRNA requires transfection vectors to bring the nucleic acid to its nuclear target within the cells. These vectors will be loaded into collagen microspheres and anchored to the matrix via cleavable peptides.



Bibliography:

- Mathieu, M. Vigier, S, Labour, MN, Jorgensen, C., Belamie, E.* and Noel, D.*, Induction Of Mesenchymal Stem Cell Differentiation And Cartilage Formation By Cross-Linker-Free Collagen Microspheres 2014 European Cells & Materials 28 : 82-97
- Salvador, J. Berthelot, J.; Bony, C., Robin, B., Lai Kee Him, J., Noël, D.*, Belamie*, E., Morille* M. Size-tunable lipid vectors for controlled local delivery of siRNA from gene activated matrix, accepted in Acta Biomater.

Scientific environment:

The experimental work will be done at ICGM (Institut Charles Gerhardt Montpellier, <https://www.icgm.fr>) on the Pôle Chimie Balard (1919 route de Mende 34293 Montpellier Cedex 5). It is part of an ANR project "Spacecart" supervised by Pr Emmanuel BELAMIE and Dr Marie MORILLE, and the selected candidate will work in close association with a postdoctoral fellow, Baptiste ROBIN. Other frequent interactions will involve two PhD students also engaged in the project, at IBMM (peptide synthesis and modifications, <https://ibmm.umontpellier.fr>) and IRMB (Institute for Regenerative Medicine and Biotherapy, <https://irmb-montpellier.fr>).

Missions:

The selected candidate will be in charge of associating the vector with the injectable hydrogel particles. The matrix will be functionalized (i) to increase its mechanical properties and (ii) allow the covalent anchoring of siRNA nanovectors. The functionalization of the nanovector surface will also be studied, to optimize the anchoring. The specific tasks will be adapted depending on the actual advancement of the project. Several characterization techniques will be used for this study: Dynamic Light Scattering, Nanoparticle Tracking Analysis, UV-Vis Spectroscopy, Fluorescence Spectroscopy, Confocal Microscopy, Electron Microscopy, etc...

Qualifications:

Applicants should be a Master student in pharmacy, biochemistry or chemistry applied to healthcare materials, with an interest for formulation and tissue engineering. No specific technical skill is required for application, a part of the allocated time will be dedicated to training on the techniques cited above (theory and practice). We expect the candidates to be highly motivated, to show curiosity and willingness to learn.

Duration: 6 months.

Start: January-July 2024

Location:

- Institut Charles Gerhardt de Montpellier (ICGM), Team Macromolecular Material and Chemistry (Bâtiment Balard – Campus CNRS route de Mende), France.

Application details and further information:

Pr Emmanuel Belamie emmanuel.belamie@umontpellier.fr

Dr Marie MORILLE marie.morille@umontpellier.fr and