

PhD position in mRNA nanomedicine

Start date: October 2025

Lipid Encapsulated mRNA for Bone Repair

Project summary: The project aims to develop functionalized lipid nanoparticles (LNPs) to deliver mRNA encoding the BMP2 protein, in order to induce bone repair. This strategy combines LNPs optimized to target ceramics used in bone tissue engineering, and autologous blood cells as tissue engineering products. This interdisciplinary project brings together two complementary teams: CBM for LNP formulation and B3OA for biological validation. Expected results include proof of concept for bone regeneration and innovative solutions for orthopedic and maxillofacial surgeons.

Objectives: The use of LNPs in regenerative medicine presents challenges, including non-specific biodistribution and variable transfection efficiency depending on the target cells. To improve targeting, different LNP formulations will be produced with specific ligands to target hydroxyapatite ceramics used in bone repair.

Methodology : At least 3 types of hydrophobic ligand-anchor conjugates (ligand architecture and density) will be tested. LNPs will be characterized before evaluation in cell lines and primary cells (MSCs) in presence of ceramics. The best functionalized LNPs will be evaluated in a mouse model to determine their expression kinetics and ability to induce bone formation.

The PhD student will be co-supervised by Delphine Logeart (B3OA) and Federico Perche (CBM) and will first receive training in mRNA synthesis and LNP formulation at the CBM in Orléans, then carry out tests on cell models and participate in in vivo experiments at the B3OA in Paris.

Host laboratory 1: B3OA (Paris, France, <https://www.b3oa.cnrs.fr/>) research team is made up of biologists, orthopedic surgeons, dentists, veterinarians, radiologists and engineers (~ 40 members). Its expertise lies in the development of strategies for the repair and imaging of skeletal tissues.

Host laboratory 2: CBM (Orléans, France, <http://cbm.cnrs-orleans.fr/en/le-laboratoire-accueil/>) accounts for ~ 90 permanent scientists from physics, chemistry and biology. Key instrumentation includes: NMR, mass spectrometers, peptide synthesizers, HPLCs, ITC, FIDA, flow cytometry, and confocal microscopy.

Expected candidate profile: experience in biochemistry, genetics, nanomedicine or molecular biology. Experience in biotherapies or regenerative medicine is an advantage.

Gross salary: 2200 € per month

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Representative publications of the host research group:

Structural and functional characterization of a histidylated liposome for mRNA delivery. Ngalle-Loth A, et al., *J Control Release* 2025 Jan 7:S0168-3659(25)00012-4. doi: 10.1016/j.jconrel.2025.01.010

3D-printed Osteoinductive Polymeric Scaffolds with Optimized Architecture to Repair a Sheep Metatarsal Critical-Size Bone Defect. Garot C, et al. *Adv Healthc Mater.* 2023 Sep 1:e2301692. doi: 10.1002/adhm.202301692.

The Lower in Vivo Osteogenicity of Adipose Tissue-Derived Stem Cells Correlates with a Higher Innate Immune Response. Maroquenne M, et al. *Stem Cell Rev Rep* 2023; 19: 2869–2885.

Neutral lipopolyplexes for in vivo delivery of conventional and replicative RNA vaccine. Perche F et al. *Mol Ther Nucleic Acids* 2019 Sep 6; 17:767-775.

Patent on mRNA sequence engineering WO2024231621 - Synthetic nucleic acid and therapeutic uses thereof. Medjmedj A, Ngalle-Loth A, Perche F