Project 1

Resolving the architecture of mRNA lipid nanoparticles through advanced NMR techniques

Synopsis/Abstract:

The PhD student will work on a multidisciplinary project involving the LAGEPP, Gepharm Team, and the Very High Field NMR Center of Lyon (CRMN).

The LAGEPP is a research lab affiliated with CNRS Université Claude Bernard Lyon 1, focused on chemical, pharmaceutical, and biochemical engineering, with a pharmaceutical engineering group that excels in drug delivery and formulation. Equipped with high-performance tools, LAGEPP is well-suited for pharmaceutical and nanomedicine development.

The CRMN, affiliated with CNRS, Université Claude Bernard Lyon 1, and ENS Lyon, is a leading research center specializing in nuclear magnetic resonance (NMR). CRMN teams are internationally recognized for advancing NMR methodologies and instrumentation, extending its applications, and exploring compound structures and dynamics at the atomic level across biology, chemistry, and physics.

Missions: The aim of the thesis project is to contribute to the development of innovative analytical approaches to ex-amine the internal atomic, molecular and nanoscale structure of mRNA-loaded lipid nanoparticles. The final goal is to identify the location of the mRNA cargo, probing its hydration and secondary structural elements as well as its interactions with LNP components.

Activities:

• The student will prepare tailored mRNA strand that will incorporate isotopically enriched ^{15}N and ^{13}C isotopes, and/or fluorescent nucleotides.

• The student will formulate the mRNA-based nanosystems by encapsulation or by complexation using the microfluidic techniques. The obtained particles will be characterize by standard methods such as electron microscopy to assess their size, polydispersity, and morphology

• The student will evaluate the mRNA stability in the formulation, to ensure that the developed methods are not affecting the functionality of the macromolecule.

• The student will implement high-resolution NMR experiments in the solid-state to characterize the mRNA-loaded LNPs

Skills and competences to be acquired: The student will learn the importance of the bibliographic research, that will be accompanied daily the practical work in the laboratory. Of key importance will be the work organization, and the ability to draft reports to track the laboratory activities. Furthermore, the student will acquire strong presentation skills in front of a heterogenous group.

Experience: Chemistry, Physical chemistry, Analytical chemistry

Supervisors names, Affiliations, eMail addresses for contact:
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Proposed collaboration within ArchiFun network (not mandatory at this stage):

Proposed list of secondments (not mandatory, but recommended if known already):

Main ArchiFun theme involved:

☐ Host-pathogen interactions;

☐ Mechanisms of bacterial resistance and cancer onsets;

☐ Neurodegenerative and autoimmune diseases;

☐ Translational research in prevalent diseases;

☐ Physiology and ecology;

☐ Neurosciences and cognition.