LABORATOIRE DES BIOMOLECULES - LBM
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MS-ID of dynamic polymer vectorization systems at Sorbonne Université, Paris - 2024

One-year post-doctoral position to address mass spectrometry analysis, identification/characterization and quantification of dynamic covalent polymer vectors that deliver siRNA cargoes into living cells.

Context:

The ANR consortium project is dedicated to the self-assembly of unprecedented pH-responsive – undergoing conformational changes upon cell uptake that promote endosomal escape siRNA release in the cytoplasm – amphiphilic dynamic covalent polymers for generating targeted nano-vectors of siRNA capable of adaptation on two different scales: i) following siRNA recognition and complexation, and ii) throughout the penetration through cell membranes. The proposed methodology combines a cell-based functional screening which exploits the templating effect whereby siRNA triggers the formation of its own vector, with a cutting-edge mass spectrometry technique to enable the identification/characterization and quantification of the selected nano-vectors that have been transported inside cells. The ambition of this project is to discover self-fabricated multi-component siRNA vectors that adapt throughout the different steps of the delivery process in order to maximize its efficacy.

Objectives of the project:

The overall consortium project involves the design of amphiphilic dynamic combinatorial polymers in order to overcome delivery barriers and implement accurate bio-analytical methods on cell-based assays to identify and quantify cell-selected self-fabricated siRNA vectors. We expect two major outcomes of this work: 1) the new multi-component amphiphilic dynamic combinatorial polymers should display a great siRNA activity; and 2) the newly-set mass spectrometry approach will enable to quantify and identify/characterize the dynamic combinatorial polymers best internalized by cells. This particular study of selection and adaptation of dynamic combinatorial polymers to cell membrane binding and cell internalization is unprecedented in the field of dynamic covalent/combinatorial chemistry geared toward delivery applications.

The post-doctoral candidate will be in charge of the MALDI-TOF MS analysis of the siRNA-templated dynamic vectorization polymeric systems developed in this ANR-granted consortium project.

Expected results:

- To specifically reveal by MALDI-TOF MS, the mass and thus deduce the length of the oligomers formed and their overall structure produced through siRNA templating.
- To specifically characterize by MALDI-TOF MS the dynamic combinatorial polymers that are internalized into cells.
- To quantify the efficiency of the cell penetration of the dynamic combinatorial polymers.

Keywords:

Mass spectrometry; MALDI-TOF; dynamic covalent polymers; lipids-polymers hybrids; self-assembly; analytical characterization, identification and quantification; cellular delivery systems; vectorization;

Location, duration and salary:

Experimental work will be done over a 12-month period at LBM on the campus Pierre and Marie Curie of Sorbonne Université, Paris, France. The salary will be evaluated according the number of years of experience after the PhD, starting from 2,700 € (gross salary).

Starting date: 1rst of January 2024

Candidate Profile:

Applicants should have a PhD in analytical chemistry and mass spectrometry with an experience on the analysis of biological systems and be willing to get involved in an interdisciplinary project. Autonomy, scientific rigor and ethics, communication capacity and team spirit will be crucial. An evidenced experience in MALDI-TOF MS quantification of biological objects, peptide fragmentation and bio-analytical chemistry will be greatly appreciated.

Project advisors:

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Application, including a CV, two reference letters, detailed contacts, should be sent by email to emmanuelle.sachon@sorbonne-universite.fr and sandrine.sagan@sorbonne-universite.fr.