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Postdoctoral position (M/F): Peptide Targeting of siRNAs to RISC to Enhance Their Biological Activity

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Offer title : Postdoctoral position (M/F): Peptide Targeting of siRNAs to RISC to Enhance Their Biological Activity (H/F)

Reference : UPR4301-LAELEG-039

Number of position : 1

Workplace : ORLEANS

Date of publication : 04 December 2024

Type of Contract : Researcher in FTC

Contract Period : 18 months

Expected date of employment : 1 March 2025

Proportion of work : Full Time

Remuneration : between 2 991 € and 4 166 € depending on experience

Desired level of education : Doctorate

Experience required : 1 to 4 years

Section(s) CN : 20 - Molecular and structural biology, biochemistry

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Missions

Five siRNAs are clinically approved, including 4 conjugated with saccharides. However, their therapeutic efficacy is limited by the very low proportion of siRNA that reaches the RNA Induced Silencing Complex (RISC) after internalization. The proposed work consists of intracellular targeting of siRNA to RISC. Increased loading of siRNAs into RISC will result in drastically increased biological activity at an equivalent dose. The proposed work involves evaluating new peptide-siRNA conjugates to target RISC. The evaluation of these conjugates includes the synthesis and purification of peptides, conjugation of peptides to siRNA and, characterization of the conjugates. Different linkers will be compared both in terms of interaction with recombinant proteins in vitro and silencing in cellular models

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Activities

Peptide purification

Conjugation of peptides to siRNA

Characterization of conjugates

Molecular interaction studies using Biolayer interferometry, FIDA, filter binding assay

Cell electroporation and silencing evaluation

Skills

The candidate must have skills in conjugation chemistry and analytical chemistry (LC-MS).

Experience in conjugation chemistry

Protein purification skills

Experience with nucleic acids would be a plus but is not a prerequisite

Ability to work autonomously and rigorously

Work Context

The CBM (UPR 4301) is a CNRS research unit of 140 people where several groups work in synergy at the interface between physics, biology and chemistry (<http://cbm.cnrs-orleans.fr>). The recruited person will carry out their activities within two teams. The "Macromolecular Assemblies and Complex Systems" team (<http://cbm.cnrs-orleans.fr/en/research/research-teams/fundamental-and-translational-aspects-of-health-and-well-being-team/molecular-assemblies-and-complex-systems/>) and the Synthetic Proteins and Bio-orthogonal Chemistry team (<http://cbm.cnrs-orleans.fr/en/research/research-teams/equipe-aspects-moleculaires-du-vivant/synthetic-protein-and-bioorthogonal-chemistry/>).

This recruitment is financed as part of the EMergence@CNRS Chimie 2025 project "Peptide targeting from siRNA to RISC".

Constraints and risks

The risks are primarily associated with the handling of chemical products and the cultivation of cell lines.

One of the experiments involves the manipulation of radioactive isotopes (³²P)

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