Research Group: IQS Laboratories of Biochemistry, Brain Metabolism and Nano Therapies
Project: COMPUTATIONAL DESIGN OF SHORT PEPTIDES TO DRIVE NANOPARTICLES TO THE BRAIN FOR THE TREATMENT OF NEUROLOGICAL DISORDERS, SUCH AS LAFORA DISEASE

Brief description:

Despite significant progress in our understanding of molecular and biological processes in the brain and associated diseases, many neurological conditions remain untreatable. One of the main challenges for the treatment of neurological disorders is that biological barriers that naturally protect the central nervous system (CNS) also limit drug access. In particular, the blood-brain barrier (BBB) severely restricts the entry of most systemically administered therapeutics, thereby narrowing effective treatment options.

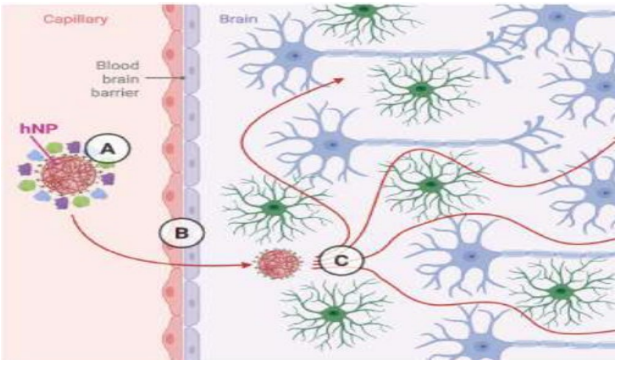

Figure 1. *Active transport of mRNA-loaded nanoparticles across de blood brain barrier aimed in this project.*

We are currently utilizing cutting-edge techniques, including nanotechnology and artificial intelligence, to develop next-generation nanomedicines able to effectively reach the brain and provide therapeutic benefit. Our technology is based in innovative mRNA-loaded nanoparticles (NPs) able to transfect cells and release the genetic material to express in-situ therapeutic proteins. Selective targeting to desired cell populations can be achieved by grafting these nanoparticles with peptides with high affinity for specific cell-receptors.

Objective:

In this project you will design a library of short peptides that bind to specific receptors involved in transcytosis across the BBB. You will employ structural bioinformatics tools in combination with cutting-edge generative artificial intelligence models, computer-based high-throughput protein engineering and molecular dynamics simulations. The peptides you design will be later synthesized and their affinity to the receptors measured experimentally. Successful candidates will be used as building blocks of our NPs in our strategy to drive mRNA nanocarriers to the brain.

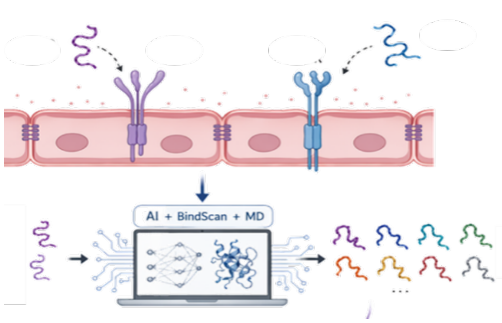

Figure 2. *Computational pipeline for the design of peptides targeting cell receptors.*

Technical skills:

You will learn how to apply a variety of computational techniques to address a biologically relevant problem, including:

- Protein Structure Analysis and Comparative Evolution (MULTISEQ, HMM)
- Generative AI Structure Prediction (AlphaFold, Boltz)
- Generative AI Protein Design (RFdifusion, Boltz)
- Computer-Assisted Protein Engineering (BINDSCAN)
- Molecular Dynamics Simulations (GROMACS)
- Data Processing and Visualization (VMD)

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