

Master Bioinformatique

Année 2024-2025

Stage M2– janvier à juin 2025

Laboratoire, adresse et tutelles

Equipe : Modeling bioMolecular Systems (MoMS)
Laboratoire : Molecular Microbiology and Structural Biochemistry (MMSB)
7 passage du Vercors, 69007 Lyon
CNRS & Univ. Lyon 1

Thématique générale du laboratoire ou du groupe de recherche (par mots clés)

Computational biology, Computer simulations
Biological membranes, Membrane proteins

Thème du stage proposé (en 10 lignes, si possible)

The adenylate cyclase (CyaA) toxin is a key virulence factor produced by *Bordetella pertussis*, the causative agent of whooping cough. CyaA can translocate its catalytic domain directly across the plasma membrane of the host cell without permanently breaking such membrane. Deprived of the toxic fragment, CyaA-based proteins can be used to transport different molecular cargos (e.g., antigens, drugs, etc.) into various types of eukaryotic cells. One useful protein fragment has been already isolated, named P454, but its translocation efficiency is limited: not all cargoes can be translocated efficiently by P454; in particular, proteins with high negative net charge or with large folded structural elements cannot be transported. Our goal is to (i) understand the mechanism of P454 translocation ; and (ii) optimize the sequence of P454 to enhance its translocation efficiency and enable transport of a broader range of antigens. To this end, we will use advanced molecular dynamics simulations of P454 and an artificial intelligence algorithm to guide the design of mutants. Our predictions will be tested in vitro and in vivo by our collaborators at Institut Pasteur (Paris).

Méthodologies et/ou techniques qui seront utilisées

Molecular dynamics simulations
Metadynamics, free energy calculations
Artificial intelligence, genetic algorithms

Compétences attendues en debut de stage

Basic knowledge of structural biology (protein structure)
Basic concepts on computer simulations of macromolecules
Programming : Python, bash
Familiarity with Linux operating system

Personne(s) à contacter

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References: [CyaA translocation across eukaryotic cell membranes](#). A Abettan, MH Nguyen, D Ladant, L Monticelli, A Chenal, *Frontiers in Molecular Biosciences* (2024) 11, 1359408.