Postdoctoral researcher position in cellular biology / biophysics

Institute of Chemistry and Biology of Membranes and Nanoobjects (CBMN, UMR 5248 CNRS)

The group "Methodological developments in AFM for biological applications" at the CBMN (Bordeaux) is currently seeking a postdoctoral researcher specialized in **structural, mechanical, dynamical and functional characterization of cells** interacting with bacterial peptide assemblies. This is a highly interdisciplinary project, funded by an ERC StG, at the frontier between **cellular and structural biology, and biophysics**, notably combining **atomic force microscopy (AFM) and advanced fluorescence and confocal microscopy**.

Project Background. *Staphylococcus aureus*, an opportunistic pathogen resistant to many antibiotics, relies on a broad arsenal of virulence factors to colonize the host and cause infection. Among them, phenol-soluble modulins (PSMs) are a family of amphiphilic peptides that play a key role in (i) biofilm structuring and maturation, (ii) host cell lysis through membrane disruption, and (iii) activation of the inflammatory response *via* specific membrane receptors. Beyond their biological functions, PSMs exhibit a strong propensity to self-assemble into amyloid fibrils with diverse architectures, potentially linked to their cytotoxic and/or pro-inflammatory activities. However, the molecular mechanisms underlying PSM functions remain largely poorly understood.

Project Objective. We aim to understand how the physicochemical properties and self-assembly dynamics of PSMs govern their interactions with cellular membranes — both at the lipid and receptor levels — and ultimately control host cell death and inflammatory response *via* the G protein-coupled receptor FPR2. To address this question, the project will adopt an *in cellulo* and multi-scale approach, ranging from live-cell studies to single-molecule analysis, in order to identify the structural, physicochemical, and dynamic determinants involved. The research will be structured around two complementary methodological axes:

1. **Link between peptide–membrane interactions and cytotoxicity**
   Combining viability assays, fluorescence microscopy (confocal, TIRF), and atomic force microscopy (AFM) under physiological conditions, we aim to monitor in real time the morphological and mechanical alterations induced by different PSM assemblies.

2. **Quantitative study of PSM–FPR2 interactions**
   Based on cellular engineering (transient receptor expression), and the reconstitution of complex membranes (proteoliposomes, supported lipid bilayers), we aim to analyse the recognition mechanism involved in immune activation. Single-molecule force spectroscopy experiments (AFM) will be coupled with the investigation of activated signaling pathways using bioluminescence resonance energy transfer (BRET) and fluorescence resonance energy transfer (FRET) approaches.

This project integrates expertise in membrane biophysics, cell biology, and advanced imaging, spanning from the cellular to the molecular scale. **It is intentionally flexible: depending on the candidate's expertise and interests, it may focus more specifically on peptide–lipid interactions, receptor recognition mechanisms**, or the development of advanced biophysical approaches, thereby offering substantial scientific freedom and strong potential for impact.

Project environment. The project will be supervised by Marion Mathelié-Guinlet at the Institute of Chemistry and Biology of Membranes and Nano-Objects (CBMN), University of Bordeaux, within the framework of her **ERC Starting Grant PUMBA**. This funding will support the project environment and the potential extension of the postdoctoral contract. In this context, the postdoc will have access to state-of-the-art facilities at the CBMN for structural and nanomechanical investigation of biological systems and correlative imaging. Besides, CBMN provides a perfect, dynamic and stimulating environment for this project, as we significantly collaborate with different teams, experts in cellular / molecular biology, physical-chemistry, and front-end methodological developments to address major challenges in the field of peptide-membrane interactions.

Candidate profile. We invite applications from innovative and motivated candidates with background in **experimental biophysics or cellular biology**, or closely related fields, who are intrigued by exploring and coupling cutting-edge methods to unravel the so far enigmatic structure-function relationship of bacterial functional amyloids. We are looking for someone **proactive, independent, with good organizational and communication skills**, and ability to work in a team environment. The candidate must have :

- Strong knowledge in cellular biology
- Experience with lipids and/or G protein-coupled receptors
- Expertise in confocal microscopy; TIRF expertise will be appreciated.
- Expertise in atomic force microscopy
- Knowledge of biophysical techniques applied to peptides/proteins
- Handling of chemical and biological materials

Interested? Applications should be sent, with the following documents, to Marion Mathelié-Guinlet (marion.mathelie-guinlet@u-bordeaux.fr):

- A full resume
- List of publications
- A short motivation letter (max. 1-2 p.)
- At least one letter of reference
- A copy of the PhD degree certificate (for PhD students at the end of their PhD, you may indicate when your PhD defense is scheduled).

Please do not hesitate to contact us if you need any information before applying.