Direction
des **ressources humaines**
Université de Strasbourg

Engineer in biological techniques

1. Position identification

Title of post : Engineer in biological techniques

Type of contract : Fixed-term contract

Category (A,B or C) : A

Contract/project period : 10 months **Expected date of employment :** March 1st, 2025

Proportion of work : 100%

Workplace : UMR 7021 CNRS, Laboratory of Bioimaging and Pathologies (LBP), Faculty of Pharmacy, Team Biophotonics of molecular and cellular interactions (BIMC).

Desired level of education : Master 2

Experience required : 1-3 years

Contact(s) for information on the position (identity, position, e-mail address, telephone) :

Toshihide KOBAYASHI, INSERM Emeritus Research Director

Yves MELY, Professor of Biophysics, Head of the team BIMC

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Date of publication : November 22nd, 2024

Closing date for the receipt of applications : December 20th, 2024

2. Research project or operation

Choose, adapt and implement biology techniques as part of the scientific project « *Regulation of cellular sphingomyelin dynamics* » of the team Biophotonics of molecular and cellular interactions (BIMC).

We are looking for a highly motivated skilled engineer in molecular cell biology interested in carrying out one year multidisciplinary research project « Regulation of cellular sphingomyelin dynamics » at the Laboratory of Bioimaging and Pathologies in Strasbourg, supported by ANR. The candidate will design and conduct experiments to uncover the dynamics of cellular sphingomyelin dynamics and the function of sphingomyelin in the cytoplasmic membrane.

Project description: Our body contains thousands of different lipid species. These lipids are not randomly distributed in a cell. Even in one membrane, the lipid composition of the outer and inner leaflets of the lipid bilayer is different. However, how this asymmetry is built, maintained and regulated remains poorly understood as is the physiological significance of lipid asymmetry. Sphingomyelin (SM) is a major mammalian sphingolipid, which localizes almost exclusively to the outer leaflet of the plasma membrane. There, SM forms

specific lipid domains together with cholesterol. These lipid domains are postulated to be involved in a number of pathophysiological events as diverse as membrane traffic to signal transduction. SM is also a reservoir of a bioactive lipid, ceramide. Outer leaflet SM is degraded by acid SMase (aSMase), which is a secreted enzyme. aSMase activity on the cell surface is involved in a number of events including apoptosis, viral infection and tumor metastasis. Interestingly enough, in addition to aSMase, cells contain cytosolic SMase, neutral SMase (nSMase). nSMase is also involved in a diverse set of signaling pathways, including apoptosis and exosome release. This raises an open question in the field of membrane biology. Since SM is predominantly at the outer leaflet, how can it be transferred to the inner leaflet?

Today, it is assumed that the asymmetric distribution of glycerophospholipids in the PM is controlled on site by flippases, floppases, and scramblases. Bulk SM is synthesized on the lumenal side of the Golgi apparatus by SM synthase 1. SM is then transported to the outer leaflet of the PM by vesicular traffic, whereas local SM is synthesized on the extracellular side of the PM by SM synthase 2. Thus, the asymmetric distribution of SM is established by the SM synthases. No protein that catalyzes the transbilayer movement of SM has been identified, however evidences show that SM is also present at the inner leaflet of the PM. Using a dedicated genome-wide screen, we identified protein candidates potentially regulating the asymmetric distribution of SM at the PM. We establish for one candidate PMP2 that it functions at dynamic deformation of the PM to induce transbilayer lipid movement. We have identified a second protein candidate GGA1, an intracellular membrane traffic protein and we hypothesize that GGA1 functions at the organelle level to induce transbilayer lipid movement of SM. This project will address the mechanism by which GGA1 and accessory protein(s) regulate the transbilayer movement of SM.

Until recently SM was supposed to be only at the extracellular side of the PM, very little is known about its role on the intracellular side. Several lines of evidence suggest that the presence of inner leaflet SM is important in physiopathology. We are in a unique position to address more precisely the biological role of SM since genetic manipulation of identified proteins can alter the transbilayer distribution of SM. Together with overexpression of the cytosolic form of bSMase, we have new tools to study the function of SM. This project will study the effect of the alteration of SM asymmetry on membranes lipid content, composition and distribution. We will also clarify the effect on cytosolic nSMase-mediated exosome release. Our results will reveal the function of SM asymmetry in pathophysiology.

Reference: 1) Abe et al., (2021) Cell Rep 37, 109935. 2) Kobayashi (2023) Emerg Top Life Sci 7, 31-45. 3) Kobayashi and Menon (2018) Curr Biol 28, R386-R391. 4) Murate et al., (2015) J Cell Sci 128, 1627-1638. 5) Inaba et al., (2016) Proc Natl Acad Sci USA 113, 7834-7839.

3. Activities

➢ **Description of the research activities :**

- Choose, develop and adapt protocols for preparing and analyzing biological samples
- Conduct, by adapting the experimental conditions, a set of techniques (electrophoresis, immunological, histological techniques, genotyping, cloning, sequencing, PCR, microscopy, cytometry)
- Use and present the results of the analyses, guarantee their monitoring and quality
- Write experience or study reports, technical notes
- Manage and organize technical resources as part of a scientific project
- Operate the equipment dedicated to the approach and ensure its operation

- Train, internally and externally, in the principles and implementation of biological experimentation techniques
- Ensure the application of hygiene and safety principles and rules
- Ensure scientific and technological monitoring in its field of activity
- Participate in the dissemination and promotion of results in the form of oral presentations and publications

➢ **Related activities :** /

4. Skills

➢ **Qualifications/knowledge** :

- Strong background of molecular cell biology, membrane biophysics and lipid biology
- Health and safety regulations
- Legal and ethical framework
- Applied IT
- English language: B1 to B2 (common European framework of reference for languages)

➢ **Operational skills/expertise :**

- Implement biology techniques
- Use software specific to the activity
- Design experimental devices
- Write scientific documents
- Manage relationships with interlocutors

➢ **Personal qualities :**

- Analytical reasoning ability
- Sense of organization
- Relational sense

5. Environment and context of work

➢ **Presentation of the laboratory/unity :**

The LBP is composed of 81 persons, including 42 statutory agents. The Biophotonics of Molecular and Cellular Interactions (BIMC) team is made up of 31 persons, including 14 statutory agents.

The aim of the Laboratory of Bioimaging and Pathologies is to use multidisciplinary (biology/chemistry/physics) and multi-scale (from molecule to patient) approaches to study, at both fundamental and applied levels, the properties and roles of a limited number of key biomolecules involved in various pathological processes. Our approach is to develop new therapeutic and diagnostic approaches in oncology and microbiology based on information obtained at the fundamental level. A key feature of the unit is the parallel development and characterisation of innovative fluorescence-based tools, methods and techniques to answer these questions. This multidisciplinary approach, which combines the development of innovative fluorescence and imaging tools to address biological questions, is unique in the French scientific landscape.

- **Hierarchical relationship :**

The engineer will work under the joint supervision of Toshihide KOBAYASHI and Yves MELY, within the BIMC team.

- **Special conditions of practice :** /

To apply, please send your CV, cover letter and diploma to :

umr7021-bimc-recrutement@unistra.fr