Grenoble Alliance for Integrated Structural & Cell Biology

INTERNSHIP PROPOSAL

Institute and Group: Exploring the Dynamics of Proteomes (EDyP), Large Scale Biology Lab (BGE), Biosciences & Biotechnology Institute of Grenoble (BIG), CEA/Grenoble

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Research project title: Coupling surface acoustic wave nebulization (SAWN) with high resolution mass spectrometry for Integral Membrane Protein Characterization

5 Keywords to describe the project: integral membrane protein, native mass spectrometry, surface acoustic wave nebulization, top-down proteomics, and electron capture dissociation.

Description of the project (aims, experimental techniques, recommended background): 10 to 15 lines:

Integral membrane proteins (IMPs) have very unique and intricate structural features due to their interfacial position in cells, where they are located within the phospholipid bilayer. IMPs commonly adopt two structural architectures i. e., α helix transmembrane bundle or β-barrel. They perform diverse functions including signaling, immune response, transport, energy conversion, and drug transport. Around 70% of all drug candidates target IMPs. 20-40% of the sequences encoded in the human genome are thought to be IMPs. The most common problems associated with IMPs include their very hydrophobic nature, poor digestion efficiency, and the tendency to undergo rapid denaturation and aggregation after they are removed from the membrane environment. Therefore, a prime challenge in structural biology is not only to resolve new structures but improve the general understanding of IMP folding, dynamics, and function.

Due to the hydrophobic nature and lipid environment of IMPs, they are difficult to desorb and ionize them by conventional electrospray ionization (ESI). An alternative new method, surface acoustic wave nebulization (SAWN) technique would be appropriate to solve these problems as it can nebulize liquid samples placed on the surface of a piezoelectric lithium niobate wafer. In this internship, student will be trained to characterize membrane and hydrophobic proteins in the SAWN coupled high resolution FT-ICR mass spectrometer. Native and tandem top-down characterization of membrane protein by electron capture dissociation (ECD) and infrared multiphoton photodissocaiton (IRMPD) will also be investigated. This project will be appropriate for any student interested in biological mass spectrometry. No prior experiences in mass spectrometry or membrane protein is required for this position.

Justification that the internship's subject fits with the general theme of GRAL (3 lines):

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Understanding proteins structures and functions has great importance to develop therapeutic measures for various diseases. Thanks to their exposure at the cell surface, membrane proteins have high potential as therapeutic targets. Due to the difficulties in analyzing these proteins, it is crucial to enrich our fundamental knowledge of their behavior. This internship on the mass spectrometry characterization of integral membrane proteins (IMPs) by a new ionization technique is within the scope of method developments for structural biology.

Relevant publications of the team (3 max):

1. Surface Acoustic Wave Nebulization Facilitating Lipid Mass Spectrometric Analysis Sung Hwan Yoon, Yue Huang, J. Scott Edgar, Ying S. Ting, Scott R. Heron, Yuchieh Kao, Yanyan Li, **Christophe D. Masselon**, Robert K. Ernst, and David R. Goodlett. *Analytical Chemistry* 2012 *84* (15), 6530-6537. DOI: 10.1021/ac300807p

2. Surface Acoustic Wave Nebulization Produces Ions with Lower Internal Energy than Electrospray Ionization. Yue Huang, Sung Hwan Yoon, Scott R. Heron, **Christophe D. Masselon**, J. Scott Edgar, František Tureček, David R. Goodlett J. Am. Soc. Mass Spectrom. (2012) 23: 1062. https://doi.org/10.1007/s13361-012-0352-8

3. Combined Infrared Multiphoton Dissociation with Ultraviolet Photodissociation for Ubiquitin Characterization. **Mohammad A. Halim**, Marion Girod, Luke MacAleese, Jérôme Lemoine, Rodolphe Antoine, Philippe Dugourd, J. Am. Soc. Mass Spectrom. (2016) 27: 1435. https://doi.org/10.1007/s13361-016-1419-8