PhD position

Principles underlying the substrate specificity of the phospholipase iPLA$_2$-γ: neutron study of the effect of lipid composition in model membrane systems

UGA/ILL supervisor: Giovanna Fragneto (Chaire GIE at UGA, HdR)
Oxford University supervisor: Robert Jacobs

A 3-year PhD position is available for a highly motivated student with interest in neutrons and enzyme-lipid interactions at the ILL, Grenoble, France.

Project Description:

This project shall attempt to open new insights into the complexities underlying how glycerophospholipids (GPL) and the mitochondria-localized phospholipase, iPLA2-γ interact in a complex relationship. The enzyme, iPLA2-γ makes an impactful study since it is thought to play a key role in various cellular processes that include membrane remodelling and GPL homeostasis. In this study, we propose to use neutron reflectometry and complementary surface techniques to study the interaction of planar lipid bilayers formed by lipids of varying chain lengths and degree of unsaturation with 'iPLA$_2$-γ' thereby allowing us to shed light on the molecular dimensions of the catalytic active site of the enzyme in addition to other key factors that could regulate its substrate specificity. Thus unraveling these phenomena shall assist in studies (Molecular Dynamic simulations/molecular docking) attempting to design novel drugs/inhibitors targeting the enzyme.

The aims of this PhD study will be to:

- To develop and optimize a neutron reflectometry method to study protein-lipid interactions.
- To assess the contributions of efflux propensity and active site accommodation underlying the substrate specificity of iPLA2-γ.
- To study head group and acyl chain contributions that could regulate the activity of the recombinant enzyme.

What will you learn during the training:

Purification of recombinant proteins by FPLC, Gas Chromatography, HPLC, Mass Spectrometry (*within the lipid extraction activities of ILL under the supervision of Dr. K. Batchu*) as well as physics and physico-chemical methods like quartz crystal microbalance, ellipsometry and neutron reflectometry.

This project will adopt a multidisciplinary approach including neutrons, microbiology, lipidomics and biochemistry. The PhD student will benefit from the co-supervision of two scientists, one from ILL, Grenoble and one from Oxford University. The PhD student will be enrolled at the University of Grenoble and will be based at the Institut Laue-Langevin. ***Short stays at the University of Oxford are foreseen.***

We are looking for a highly motivated PhD student, who has a thorough understanding of Physical Chemistry and a strong interest in protein-lipid interaction studies. Applicants should hold a Master's degree in Physical Chemistry. A good knowledge of statistical data analysis would be of additional advantage.

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NEUTRONS FOR SOCIETY

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