TITRE du Stage: Influence of membrane curvature on protein dynamics

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Ce stage peut être poursuivi en thèse : OUI

Si oui, la thèse est-elle financée : NON

SUJET de la thèse: Effect of membrane mechanics on single membrane protein dynamics and diffusion

SUJET du stage :

Trans-membrane proteins are tightly embedded in fluid lipid bilayers where they diffuse laterally. Lipid membranes can be elastically stretched and bent, which can induce mechanical stresses onto the membrane proteins (Haswell et al., 2011; Tonnesen et al., 2014). Many membrane proteins are involved in the transport of ions or molecules through the membranes using different sources of energy (ATP hydrolysis, voltage, light, stretching etc…) that allow for conformational changes. How mechanical stresses on the membrane can affect these conformational changes and thus protein activity is still an open question. Moreover, our group showed that protein shape (conical versus cylindrical, for instance) has an effect on its lateral diffusion (Quemeneur et al., 2014). Our general objective is to **investigate the feedback between the physical properties of membranes, the functional conformational dynamics of membrane proteins and their diffusion**.

We will perform **single molecule experiments**, using a transporter of the ABC family, BmrA that transport drugs across membranes upon ATP hydrolysis. During the internship, we will use single molecule FRET on BmrA proteins reconstituted in liposomes of various diameters (between 40 to 200 nm) to study the effect of membrane curvature on the conformations of the protein, either active or passive. During her PhD thesis, A. Damm has already obtained evidences that high membrane curvature (higher than 1/30nm) induces an enhanced "opening" of the protein and also perturbs its activity, functionally and conformationally (Damm, 2019). The objective will be first to complete these data with new developments on the set-up. In the long-term, single molecule tracking experiments will allow to study BmrA diffusion in giant liposomes of controlled tension and in nanotubes of controlled curvature in order to decipher the effect of membrane mechanics on diffusion of passive and active proteins.

This project will be developed in close collaboration with D. Lévy (membrane protein expert) in the lab.

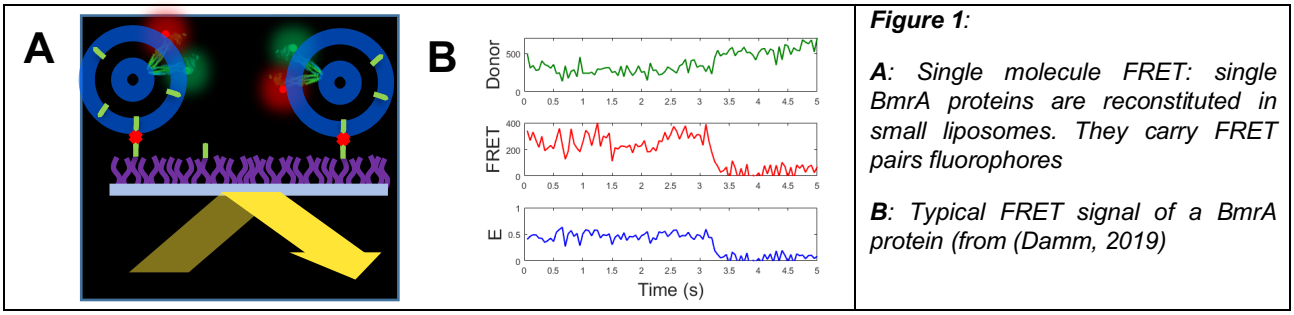

***Figure 1**:*

***A**: Single molecule FRET: single BmrA proteins are reconstituted in small liposomes. They carry FRET pairs fluorophores*

***B**: Typical FRET signal of a BmrA protein (from (Damm, 2019)*

Références

Damm, A. 2019. Interplay between the conformational dynamics of a transmembrane protein and the mechanical properties of its surrounding membrane. *PhD thesis.* Sorbonne Univsersité, Paris.

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Quemeneur, F., J.K. Sigurdsson, M. Renner, P.J. Atzberger*, P. Bassereau*, D. Lacoste*. 2014. *PNAS* 111 5083-5087.

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