IMPRS on Multiscale Biosystems

Title: Understanding Protein-Protein Interactions on Model Membranes
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Project description: Protein-protein interactions at the cell membrane play a fundamental role for the function and communication processes of cells. Eukaryotes can attach proteins to the cell membrane using complex glycosylphosphatidylinositol (GPIs) glycolipids, forming GPI-anchored proteins (GPI-APs), which participate in multiple events that are important part of the protection, regulation and activation of cells. However, studies of GPIs and GPI-APs have been hindered by the difficult isolation and production of these molecules in pure form.

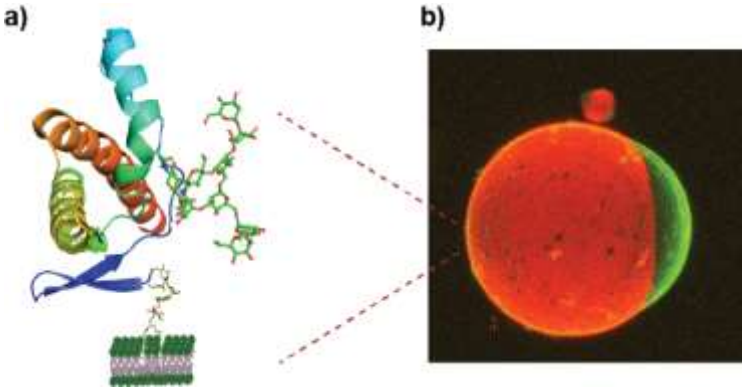

Figure 1. a) Schematic representation of a GPI-anchored protein b). A confocal 3D reconstruction of a giant vesicle (~35 μm in size) with phase separated membrane as observed from the distribution of the green and red fluorescent dyes.

In this project, we will employ a semi-synthetic strategy that involves expression of proteins and chemoselective attachment of synthetic GPI glycolipids to obtain well-defined GPI-APs (GFP and Thy-1), which we will use to investigate the properties and behaviour of GPI-APs and their interaction with other proteins on model membranes. The produced GPI-APs will have different glycolipid structures and lipid compositions. The GPIs alone and GPI-anchored proteins will be linked via the lipid part to vesicles of different size and composition and to surface plasmon resonance (SPR) chips coated with a lipid bilayer. The effect of the GPI-APs on the model membranes, their partitioning in membrane domains (see Figure), the formation of the protein complexes and the presence of protein-protein interactions and their inhibition with peptides will be studied using SPR and fluorescence microscopy techniques such as fluorescence resonance energy transfer (FRET) and fluorescence correlation spectroscopy.

Required background: The candidate should have a background in chemistry or biochemistry and be able of work in an international and multidisciplinary team. Knowledge and experience working with proteins or model membranes, especially in the preparation of protein conjugates would be an advantage.
Paper to read before the interview: Seeberger *et al. Angew. Chem. Int. Ed.* **2012**, 51(46), 11438-56, doi: 10.1002/anie.201203912; Dimova *et al.* R., *Biochimica et Biophysica Acta (BBA) – Biomembranes*, **2014**, 1838, 2036-45, doi: 10.1016/j.bbamem.2014.04.019
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