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). These proteins 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.

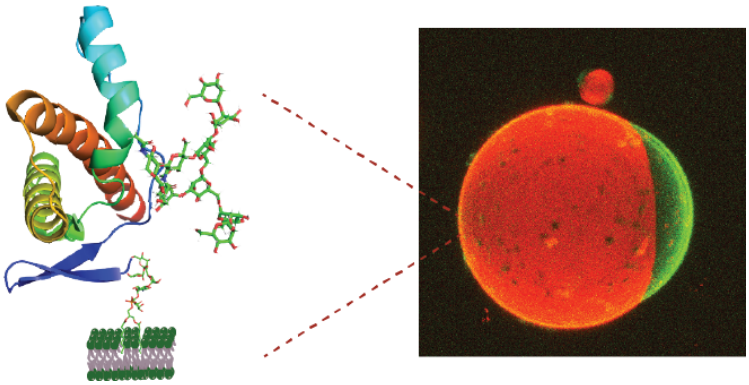

Figure 1. a) Schematic representation of a GPI-anchored protein (protein and membrane are not to scale). b) A confocal 3D reconstruction of a giant vesicle (~35 microns in size) with phase separated membrane as observed from the distribution of the green and red fluorescent dyes.

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 (e.g CD59 and Thy-1). Using these proteins, the role of GPIs on the properties and behaviour of GPI-APs will be investigated as well as their interaction with other proteins on model membranes. The GPIs alone and GPI-anchored proteins will be inserted into vesicles of different composition and size (including cell-sized giant vesicles, see Figure), and to chips coated with a lipid bilayer. Surface plasmon resonance (SPR) and fluorescence microscopy techniques such as fluorescence resonance energy transfer (FRET) and fluorescence correlation spectroscopy (FCS) will be employed to study the effect of the GPI-APs on the model membranes, their partitioning in membrane domains (see Figure), the formation of protein complexes, and the presence of protein-protein interactions and their inhibition.

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 modification of protein would be an advantage.
Papers to read before the interview: Seeberger *et al., Angew. Chem. Int. Ed.* **2012**, 51(46), 11438-56, doi: 10.1002/anie.201203912; Dimova R, *Annu. Rev. Biophys*. **2019**, 48, 93-119, doi: 10.1146/annurev-biophys-052118-115342
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