# Decoding secret conversations inside cells: Understanding how organelle interactions in human cells are regulated during the cell cycle

**Supervisory team:**
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**Host institution:** University of Exeter (Streatham)

**Project description:**
In this project you will carry out molecular cell biology studies on human cells to understand how a breakdown in internal cellular communication can lead to diseases such as Alzheimer's, ALS and other metabolic disorders.

The cell contains numerous organelles which are specialised to carry out a particular role but are also part of wider networks or production lines which requires cooperation with other organelles. This cooperation is crucial in the generation of specialised lipids found in neuronal membranes, which are partly metabolised in one organelle, such as peroxisomes or mitochondria, before being transferred to another such as the endoplasmic reticulum for further processing. This type of communication is also required for energy generation and activation of the cells recycling systems. The organelle contact site field is an exciting new research discipline and we still know relatively little about many fundamental aspects of this emerging area. Recent research revealed that organelles interact at membrane contact sites, points where apposing organelle membranes are in close proximity. Contact sites can be formed when proteins on different organelle membranes interact and numerous "tethering" complexes have now been identified. The next wave of research will focus on how membrane contact sites are regulated, how metabolites such as lipids are transferred and how contact site dysfunction is linked to disease. A long term aim is to pursue the modulation of organelle contact sites as a potential therapeutic approach.

The student will investigate how interaction between three organelles, the endoplasmic reticulum, peroxisomes and mitochondria is regulated in mammalian cells. This will build on preliminary evidence that post-translational modification of contact site proteins, which control organelle interactions, regulates their tethering function. They will also develop and utilise novel probes to track lipid movement between organelles using both microscopy and biochemical approaches.

They will receive training in mammalian cell culture, CRISPR, advanced microscopy and cell sorting techniques (novel fluorescent reporters and electron microscopy) as well as in protein characterisation techniques including TurboID, protein purification and ubiquitination assays and be involved in lipid synthesis and analysis. This project will benefit from the expertise of supervisors with experience in organelle contact sites, cell cycle, ubiquitin biology and lipid synthesis and from the cutting-edge and supportive research environments at the Universities of Exeter and Bath. The PhD student will receive training by a cross disciplinary team, providing a well-rounded PhD training and an excellent basis for starting a research career.

**Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.**