

## Regulation of membrane contact sites in mammalian cells

### Supervisory team:

**Main supervisor:** Dr Joseph Costello (University of Exeter)

**Second supervisor:** Dr Julien Licchesi (University of Bath)

Prof Michael Schrader (University of Exeter)

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

### Project description:

The cell contains numerous, distinct 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. For example, certain lipids are often 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 required for energy generation, the production of lipids required to build nerve cell membranes, and activation of the cells recycling systems.

The idea that organelles need to come together to communicate and collaborate is an exciting new field and we still know relatively little about how this works. Its importance was recently underlined by studies which observed alterations in organelle interactions in diseases such as Alzheimer's, Parkinson's and metabolic disorders. Disrupted organelle interactions have also been implicated in the ageing process and an emerging concept is the idea that organelle interactions impacts on reactive oxygen species (ROS) signalling and homeostasis.

Recent research revealed that organelles interact at membrane contact sites, points where apposing organelle membranes are in close proximity allowing metabolite and signal exchange. Contact sites can be formed when proteins on different organelle membranes interact and numerous "tethering" complexes have now been identified for different organelles. In this emerging and dynamic the next wave of research will focus on how membrane contact sites are regulated and how their dysfunction is linked to disease, which is currently unknown. A long term aim is to pursue the modulation of organelle contact sites as a potential therapeutic approach.

In this project, 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 receive training in mammalian cell culture, advanced microscopy techniques (using novel fluorescent reporters and electron microscopy) as well as in protein characterisation techniques including co-immunoprecipitation, protein purification and ubiquitination assays.

This project will benefit from the expertise of the two supervisors in both organelle contact site and ubiquitin biology and from the cutting-edge and supportive research environments at the Universities of Exeter and Bath. This will allow the student to receive excellent training and be equipped with all the essential skills to become a successful future scientist.