



PhD project: Regulation of membrane contact sites in mammalian cells

Main supervisor: Dr Joseph Costello (University of Exeter)

Second supervisor: Dr Julien Licchesi (University of Bath)

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 field 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 protein isolation and ubiquitination assays. This project will benefit from the expertise of supervisors in both organelle contact site and ubiquitin biology and from cutting-edge and supportive research environments at the Universities of Exeter and Bath.

Applications: Applicants must have obtained, or be about to obtain, a First or Upper Second Class UK Honours degree, or the equivalent qualifications outside the UK, in an appropriate area such as Cell biology or Biochemistry. Further studies and laboratory experience gained through a Master Degree would be highly advantageous. We encourage interested applicants to contact Dr Costello to discuss suitability prior to submitting an application. Applications are via the University of Exeter:

<http://www.exeter.ac.uk/doctorscollege/funding/fundedcentres/swbio/>

Funding notes: SWBio DTP funded studentship available for September 2020 entry. The studentship will provide funding of fees and a stipend (currently £15,009 per annum for 2019-20) plus research and training costs. These studentships are available to UK and EU nationals who have established UK residency (EU nationals must have ordinarily lived in the UK throughout the three years preceding the start of the studentship); a limited number of studentships may be available to EU applicants who do not meet the residency requirements. More details about the programme at:

<https://www.swbio.ac.uk/programme/projects-available/>

Deadline: Monday 2nd Dec 2019