Unravelling the molecular mechanisms of organelle communication in the regulation of cellular lipid metabolism and developmental processes

Supervisory team:
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Project description:
Research on organelle cooperation represents an exciting new field in modern cell biology and biomedical sciences because of its close relation to organelle functionality and its impact on developmental and physiological processes. Peroxisomes are multifunctional, oxidative organelles that are essential for human health and development and play vital cooperative roles in lipid synthesis and breakdown. Important roles for peroxisomes in signalling and the fine-tuning of cellular processes are emerging, which integrate them in a complex network of interacting cellular compartments (Silva BBA 2020, 1867:118800). Peroxisomal lipid metabolism requires coordination with the endoplasmic reticulum (ER), mediated via membrane contacts. Previously, we discovered that these peroxisome-ER contacts are important for inter-organelle lipid transfer, peroxisome formation and positioning, and are mediated by the acyl-CoA binding proteins ACBD4/5 present in the peroxisomal membrane (Costello 2017, JCB 216:331; Kors 2022, JCB 221:e202003143). Despite their importance to cellular lipid metabolism and human health, the physiological functions of many ACBD proteins remain unclear (Islinger BBA 1867:118675).

This multi-disciplinary project will therefore address fundamental questions related to the molecular mechanisms that regulate and coordinate organelle activities via inter-organelle communication. It will combine molecular cell biology approaches with omics and genetic approaches as well as new cellular and in vivo models and tools (zebrafish, fly). We will use molecular cell biology, developmental biology and in vivo approaches, as well as cutting edge imaging techniques, to elucidate how ACBD4/5 proteins orchestrate cellular lipid metabolism, organelle contacts and developmental processes. Our approaches will reveal the mechanisms and roles of ACBD4/5 proteins in orchestrating lipid metabolism and organelle communication networks at the molecular, cellular and physiological level. With this multi-disciplinary approach, we aim to obtain crucial new insights into the fundamental regulation of cellular lipid metabolism and organelle communication networks, which could ultimately reveal new strategies to treat age-related disorders where these processes are dysregulated.

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.