Targeted Project / AY 2024 -2025

How is endocytosis regulated in the malaria parasite?

Project Code: TRG-PATH-KA

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Research area: Plasmodium cell biology

BBSRC DTP main strategic theme: Understanding the rules of life

BBSRC DTP secondary strategic theme: Transformative technologies

Project outline:

Plasmodium, the parasite that causes malaria, survives by metabolising host haemoglobin. It does so through a process called endocytosis, whereby erythrocyte cytoplasm is taken up into vesicles, trafficked to the food vacuole, and digested to drive the parasite's growth. Although we know this pathway is essential to parasite survival, we understand very little about how it is mechanistically regulated, particularly since many of the molecular components that drive endocytosis in higher eukaryotes appear to be missing or incomplete in Plasmodium. There is increasing evidence that the ubiquitin pathway, endocytosis and drug resistance to front line antimalarials are interconnected. Seeing as ubiquitin signalling regulates endocytic events and trafficking in mammalian cells, the aim of this project will be to define how ubiquitin modification affects this pathway in Plasmodium falciparum, to characterise the enzymes involved and to inhibit them using constrained peptides. Ultimately, understanding the mechanisms of endocytosis in Plasmodium will not only reveal how to interfere with this pathway, thus defining novel targets for therapeutic intervention, but will also provide insight into the mechanisms underlying drug resistance.

This project will utilise biochemical and cell biological techniques, electron microscopy, parasite transgenesis, and enzyme inhibition assays.