Effector proteins in vector borne bacterial infection.

Project ID: 3735

Supervisory team

Main supervisor: Prof Paul Wigley (University of Bristol)
Second supervisor: Dr Ian Cadby (University of Bristol)
Other supervisors: Prof Andrew Preston (University of Bath) & Dr Suchitra Pradhan (University of Bristol)
Collaborators: Dr Mark Jepson (University of Bristol) & Prof Ben Makepeace (University of Liverpool)

Host institution: University of Bristol

Project description: Pathogenic bacteria spread by ticks cause a range of diseases in livestock, with major impacts on animal health, food production, and economies. Many tick-borne bacterial pathogens, such as Anaplasma, Ehrlichia, and Coxiella, infect and replicate inside phagocytic immune cells (macrophages and neutrophils) of their vertebrate hosts. To achieve this, these bacteria encode specialised secreted proteins called effectors, which reprogram host cell biology to convert host cells into a favourable niche for survival and proliferation. Effector proteins are essential for infection and are responsible for disrupting key phagocyte and innate immune functions, including cell migration, phagocytosis, vesicle trafficking, and apoptosis. Despite their importance, how effector proteins enable tick-borne bacterial infections remains poorly understood.This PhD project aims to address this knowledge gap by identifying how bacterial effector proteins facilitate intracellular survival and pathogenesis in tick-borne bacteria, and whether these effectors can be exploited as potential therapeutic targets.Specific objectives include:Identify the host targets of secreted effector proteins.Determine how effector proteins interact with, and influence the biochemistry of, their cognate host targets, whether proteins or other biomolecules.Explore the wider distribution, conservation, and evolutionary origins of similar effector proteins (in collaboration with Prof Preston, University of Bath).Assess the role of effectors in phagocyte reprogramming, and the impact of their targeted inhibition.Key approaches include immunoprecipitation and immunofluorescence microscopy in infected host cells; bioinformatics and genomics; interaction and protein structure-function analyses; and biomolecular and cellular assays.The student will work across two intracellular tick-borne bacteria — Anaplasma phagocytophilum and Ehrlichia chaffeensis — which infect neutrophils and macrophages and are representative of a wide range of animal and livestock pathogens. We have recently screened proteins from both bacteria and identified effectors targeting signalling pathways converging on apoptosis, cell migration, and central metabolism linked to phagocyte function.This project offers considerable flexibility, allowing the student to take ownership and shape its direction in line with their discoveries and interests. Our broad national and international collaborations offer extensive opportunities to train in cutting-edge approaches and develop as a researcher.

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.