Cytoskeletal subversion by the tick-borne pathogen Anaplasma phagocytophilum

Project ID: 3731

Supervisory team

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Host institution: University of Bristol

Project description: Anaplasma phagocytophilum is a zoonotic, tick-borne pathogen infecting a wide range of hosts, including livestock, wildlife, and humans, and causes tick-borne fever — a disease responsible for significant losses to global livestock economies. Infections are long-term and persistent; no licensed vaccines or targeted therapeutics exist; herd-level antibiotic treatment is a driving factor for antimicrobial resistance; and acaricides used to control tick vectors carry a significant environmental burden.Our group's current work focuses on how A. phagocytophilum interacts with the host and how its virulence factors facilitate infection (see short video here: https://www.youtube.com/watch?v=aa_GTkPq-RA), foundational information needed to develop novel pathogen- and host-directed therapeutics and vaccines. We recently discovered a new mechanism by which A. phagocytophilum manipulates host cell biology (manuscript here: https://www.biorxiv.org/content/10.64898/2026.07.31.742066v2): the secreted effector AnkA directly binds and modulates two regulators of the host cytoskeleton, the WAVE Regulatory Complex (WRC) and actin itself. Given the WRC's central role in innate immune functions (migration, endocytosis, signalling), and that AnkA and the WRC interact during both bacterial entry and exit from host immune cells (which A. phagocytophilum pacifies), we propose that AnkA–WRC interactions are essential for infection.In this project you will define this newly discovered mechanism of host subversion and uncover its role across the infective cycle. Suggested aims include:1. Determine how AnkA, the WRC, and other host signalling proteins are recruited throughout infection. Using immunofluorescence microscopy and immunoprecipitation to define how these interactions are orchestrated at key infection checkpoints.2. Discover the biochemical basis for cytoskeletal remodelling by AnkA during bacterial entry and exit, using protein structure-function approaches and binding/biochemical assays.3. Design ways to disrupt AnkA function and inhibit infection, via mutant protein expression in host cells, targeted pharmacological inhibition, and cell-penetrating peptides.This project affords considerable intellectual freedom, allowing you to tailor the research and specialise your training to your interests. You'll receive hands-on training from supervisors and our collaborator network, alongside a broad range of transferable skills, equipping you for diverse career paths in and beyond academia.Work in this area is currently supported by a £1.5 million UKRI Future Leaders Fellowship, providing extensive additional career development and training opportunities.This project will be primarily based at Bristol Veterinary School, Langford, nr Bristol.

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.