Establishment and Characterization of a Novel self-renewing, non-transformed Chicken Macrophage Cell Line for the Study of Innate Immunity

Supervisory team:
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Host institution: University of Bristol / University of Plymouth
Submit applications for this project to University of Bristol

Project description:
Macrophages are a heterogeneous population of immune cells critical for host defense against pathogens. Tissue macrophages are embryonic derived self renewing cells while bone marrow derived macrophages (BMDMs) are mostly inflammatory macrophages with a limited lifespan. While essential for understanding innate immunity, there is a paucity of suitable chicken macrophage models. Current models, such as BMDMs, exhibit limited lifespan and may not accurately reflect the phenotype of tissue-resident macrophages. Our preliminary data demonstrate the potential of generating self-renewing, non-transformed macrophages from chicken foetal liver, offering a promising tool to study the innate immune response.

Aims and Objectives
This studentship aims to comprehensively characterize a novel macrophage cell line derived from neonatal chicken hepatic stem cells. By comparing these cells to BMDMs, we will elucidate their differential phenotypic, functional, and molecular properties. The new, continuous macrophage line will contribute to the reduction of animal experimentation (3Rs).

Specific objectives include:

1. To comprehensively characterize novel macrophage cell lines: Conduct a comparative analysis of phenotypic, functional, and molecular properties between the novel hepatic-derived macrophage cell line and BMDMs. Utilize a battery of techniques, including flow cytometry, microscopy, ELISA, RNA-seq, RT-PCR, and proteomics, to assess lineage-specific markers, cytokine production, gene expression, and protein profiles, both in basal conditions and upon stimulation with pathogens and their ligands.
2. Functional validation of differentially expressed genes: Following the comparative analysis in Objective 1, the student will identify genes and proteins with significant expression differences between the cell lines. The data will be utilized to delineate signalling pathways and to investigate the functional roles of selected genes using RNA interference, lentiviral overexpression, and CRISPR/Cas9-mediated gene editing. Finally, the student will assess the impact of gene manipulation on the functional abilities of the macrophages, employing the same methods described in Objectives 1 and 3.
3. Evaluation of antimicrobial function: Assess the differential ability of the self-renewing macrophages and BMDMs to control Salmonella infection in vitro using the gentamicin protection assay. Determine the contribution of specific genes identified in objectives 1 and 2 to the antimicrobial response through CRISPR/Cas9-mediated gene manipulation.

This project offers an exceptional opportunity for the student to acquire a comprehensive skill set in both experimental methodologies and immunological concepts. By engaging in a comparative analysis of macrophage subtypes, the student will gain proficiency in a wide range of techniques, including flow cytometry, microscopy, ELISA, RNA-seq, RT-PCR, and proteomics. Furthermore, the project provides hands-on experience in gene editing technologies such as RNA interference, lentiviral overexpression, and CRISPR/Cas9. This multidisciplinary approach will equip the student with a strong foundation in immunology and prepare them for a successful career in research.

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.