Project Details	
Project Code	IIAR27Br Koh
Title	When immune memory becomes corrupted
Research Theme	Infection, Immunity & Antimicrobial Resistance
Project Type	Wet lab
Summary	Our immune system has a remarkable ability to "remember" infections and diseases, helping us respond more effectively to future threats. Exciting new research suggests that cancer can exploit this memory, reprogramming immune cells in ways that may help tumours grow. In this project, you will investigate how cancer hijack immune memory and uncover the consequences for disease development. Combining immunology, genomics, and data science, you will work with cutting-edge technologies to answer fundamental biological questions with the potential to inform future therapies.
Description	BACKGROUND The immune system protects the body from infections and diseases. Some immune cells can remember past threats and respond more effectively if they encounter them again. This feature is known as immune memory. For many years, immune memory was thought to be a unique property of adaptive immune cells such as T cells and B cells. However, recent research has shown that some innate immune cells, including monocytes and macrophages, can also develop a form of memory known as trained immunity. Following exposure to a stimulus, these cells can undergo long-lasting changes that alter how they respond to future challenges. Despite increasing interest in trained immunity, little is known about whether cancer cells can induce trained immune states in myeloid cells or how these changes affect anti-tumour immune responses. Understanding these processes could reveal new opportunities to improve cancer treatment by reprogramming the innate immune system. RESEARCH QUESTIONS This project aims to answer three questions: 1) Can cancer cells induce long-lasting trained immune states in myeloid cells? 2) How do cancer-trained myeloid cells influence T-cell responses against cancer? 3) Can cancer-trained myeloid cells be targeted to improve anti-cancer immunity? AIMS & OBJECTIVES Aim 1: Determine whether cancer cells induce trained immune states in myeloid cells Monocytes and macrophages are abundant in many tumours and play important roles in shaping immune responses. To investigate whether cancer cells can induce trained immune states, we will expose human monocytes to factors released by cancer cells, allow them to rest after removal of the stimulus, and then re-stimulate them. Then, we will examine whether prior exposure to cancer-derived signals causes long-lasting changes in myeloid cells. In collaboration with Prof Aled Clayton (Cardiff University) and Dr Nick Owens (Exeter University), we will use molecular profiling approaches, including analysis of tumour-derived

	secreted factors (secretomics) and gene expression profiling (transcriptomics), to identify proteins and pathways that establish these persistent changes. Key findings will be validated using more sophisticated models such as 3D co-cultures. Aim 1 will establish whether cancer cells can generate trained immune states in myeloid cells and identify the putative molecular mechanisms involved. Aim 2: Determine how cancer-trained myeloid cells affect T-cell function T cells are key mediators of anti-tumour immunity. To investigate the consequences of cancer-induced training, we will co-culture cancer-trained myeloid cells with T cells. In collaboration with Prof Christoph Wuelfing (University of Bristol), we will assess how these myeloid cells affect T-cell activation, proliferation, migration, and tumour-killing capacity. We will also examine whether cancer-trained myeloid cells enhance or suppress anti-tumour immune responses. Aim 2 will reveal how trained immune states in myeloid cells influence communication between the innate and adaptive immune systems in cancer. Aim 3: Explore strategies to target cancer-trained myeloid cells We will identify biological pathways that may be responsible for establishing or maintaining cancer-trained immune states. We will test whether targeting these pathways can alter myeloid cell behaviour and improve anti-tumour immune responses. Working with clinical partners, we will also assess the translational relevance of our findings using patient-derived specimens. Aim 3 will provide proof-of-concept evidence for therapeutic strategies that target cancer-trained myeloid cells to enhance anti-tumour immunity. STUDENT INVOLVEMENT Throughout the scholarship, the student will take an active role in shaping the direction of the project, supported by a multidisciplinary supervisory team. They will contribute to experimental design, data analysis, interpretation of results, and development of new hypotheses arising from the research. The project offers flexibility for the student to pursue specific mechanistic questions that emerge during the study. For example, depending on their results and interests, they may choose to investigate particular signalling pathways, secreted factors, metabolic changes, or other mechanisms associated with the identified immune states. The student will also co-design and optimise co-culture systems, select functional readouts, and evaluate therapeutic strategies. Collectively, this project will enable the student to gain training in immunology, cancer biology, systems biology, flow cytometry, omics technologies, and computational analysis. CONCLUSION In this project, you will investigate how cancer hijacks immune memory in myeloid cells and how these changes influence anti-tumour immune responses. By uncovering the mechanisms that underpin cancer-induced innate immune memory, the work may identify new ways to reprogramme the immune system and improve cancer treatment outcomes.

Can be completed part time?	Yes
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