EDITH COWAN UNIVERSITY

PROJECT DETAILS

Project Title:

Role of tertiary lymphoid structures in educating the anti-tumour response

Project Summary:

Summary: Immune checkpoint blockade (ICB) inhibits tumour immune escape and has significantly advanced cancer therapy, in particular for melanoma and lung cancer. However, ICB benefits only a minority of patients treated and may lead to many immune-related adverse events. Therefore, identifying factors that can predict treatment outcomes, enhance synergy with ICB, and mitigate immune-related adverse events is urgently needed.

Tertiary lymphoid structures (TLS) are ectopic lymphoid tissues that arise within or around a tumour and have been found to be associated with better prognosis and improved clinical outcomes after ICB therapy. TLS are dynamic structures where various immune cell subpopulations interact. These interactions can influence the overall immune response, either promoting or inhibiting tumour growth depending on the context. TLS facilitate the maturation of immune cells, including T cells and B cells, which are essential for mounting an effective anti-tumour response. However, the precise mechanisms and signals that initiate and regulate the formation of TLS are not fully understood. Moreover, although TLS are associated with better outcomes in immunotherapy, the exact ways they interact with different types of immunotherapies and how they can be manipulated to improve treatment responses need to be researched.

Our team has shown that a B-cell signature, referred, can be detected in the plasma of patients with improved clinical outcomes after ICB therapy, which overlaps with reported TLS gene expression signatures. The proposed PhD project will aim to:

1. To develop a murine model for the induction of TLS
2. To evaluate the evolution of the B-cell signature relative to TLS maturity
3. To analyse TLS and TME contexture, relative to B cell subpopulations and antigenic specificities.

Expected Outcomes and Impact: The results will underscore the aetiology of the B-cell signature observed in plasma relative to TLS formation and maturation. The study aims to uncover the role of B-cells in orchestrating the anti-tumour immune response and may reveal therapeutic strategies to enhance this response or enhance the activity of ICB.

Preferred Applicant Skillset:

We are seeking a highly motivated and diligent HDR applicant who has demonstrated the capacity to work independently. A background and interest in immunology and cancer research is required.

Highly desirable skills: Experience in working with animals and managing animal ethics, Experience in Windows and Linux operating systems, Experience with bioinformatics analysis using R, python and command line.

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