Project title: Development of ECM-targeting CAR-T Cell Therapy

Project Summary:

Chimeric Antigen Receptor (CAR)-T cell therapy has achieved transformative outcomes in hematologic malignancies, yet its efficacy in solid tumors remains limited due to immunosuppressive microenvironments and restricted T cell infiltration. Several cancers of unmet need exemplify these challenges including pancreatic cancer, lung cancer, mesothelioma and sarcomas. These are characterized by a dense and fibrotic extracellular matrix (ECM) that forms both a physical and biochemical barrier to immune engagement. Overcoming these stromal obstacles is essential to unlock the potential of CAR-T cell therapy in this setting.

This project aims to develop re-engineered CAR-T cells capable of targeting and modulating ECM components to enhance tumour access and cytotoxic function. By integrating transient and non-transient genetic modification strategies with advanced in vitro and in vivo cancer models, we will evaluate how ECM-directed CAR-T cells penetrate, persist, and exert antitumor activity within the tumour microenvironment. The transient nature of the introduced transgenes ensures precise temporal control of expression during the critical window of CAR-T trafficking and infiltration, while maintaining feasibility and translational relevance.

The proposed work constitutes the first systematic investigation of ECM-targeted CAR-T cell therapy. By addressing the fundamental barriers imposed by tumour stroma, this research is expected to yield mechanistic insights into immune cell–matrix interactions and define design principles for more effective CAR-T cell products in solid tumours. Ultimately, the project will advance a novel therapeutic paradigm with broad implications for the next generation of adoptive cell therapies in oncology.

Supervisory Team:

Primary Supervisor: Professor Paul Huang

Supervisory Team: Dr Astero Klampatsa, Professor Terry Rabbitts, Professot Robin Jones

Clinical Specialities:

Any relevant clinical speciality with an interest in cancer immunology including medical oncology, clinical oncology and pathology