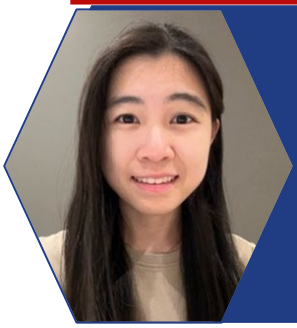
Singapore Immunology Network
SIgN

SIgN SEMINAR

Hosted by Dr Bei WANG



Kah Min YAP, PhD student

Peter MacCallum Cancer Centre
Melbourne, Australia

Identifying Optimal Tumour-specific Promoters for CRISPR/Cas9 Engineering of Armoured CAR T Cells with Enhanced Safety and Efficacy

The efficacy of chimeric antigen receptor (CAR) T cell therapy in solid tumors is limited by immunosuppression and antigen heterogeneity. To overcome these barriers, “armored” CAR T cells, which secrete proinflammatory cytokines, have been developed. However, their clinical application has been limited due to toxicities related to peripheral expression of the armoring transgene. Here, we developed a CRISPR knock-in strategy that leverages the regulatory mechanisms of endogenous genes to drive transgene expression in a tumor-localized manner. By screening endogenous genes with tumor-restricted expression, the *NR4A2* and *RGS16* promoters were identified to support the delivery of cytokines such as IL-12 and IL-2 directly to the tumor site, leading to enhanced anti-tumor efficacy and long-term survival of mice in both syngeneic and xenogeneic models. This was concomitant with improved CAR T cell polyfunctionality, activation of endogenous anti-tumor immunity, a favorable safety profile, and was applicable using CAR T cells from patients.

18 November 2024 (Monday)
10 AM – 11 AM (Singapore Time)
SIgN Seminar Room
8A Biomedical Grove, Immunos, #04-06
Singapore 138648

Seminar is open for all to attend.

Registration is not required.