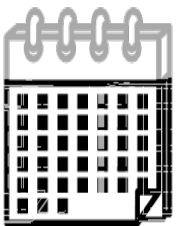


The efficacy of chimeric antigen receptor (CAR) T cell therapy in solid tumors is limited by immunosuppression and antigen heterogeneity. To overcome these barriers, “armored” CAR T cells, which secrete proinflammatory cytokines, have been developed. However, their clinical application has been limited 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. Our findings provide a novel approach to improve CAR T cell therapy for solid tumors.



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

