Singapore Immunology Network
SIgN

SIgN SEMINAR

Hosted by Dr Cheng-I WANG

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Combining Adoptive T cell Therapy with Tumour-Localized BiTEs for Treating Heterogeneous Solid Tumours

Chimeric Antigen Receptor (CAR) T cells and Bispecific T Cell Engagers (BiTEs) are potent immunotherapies that redirect T cells to target and kill tumour cells. CAR T cells are genetically engineered for sustained, antigen-specific cytotoxicity, while BiTEs are synthetic antibodies that transiently link T cells to tumour cells via CD3, enabling rapid activation without genetic modification. However, both approaches face challenges in treating solid tumours, particularly due to heterogeneous antigen expression. To address this, we combined CAR T cell therapy with BiTE secretion in an immunocompetent mouse model. T cells were engineered to secrete HER2-targeting BiTEs either (1) constitutively via retroviral transduction or (2) tumour site-specifically using a CRISPR/HDR knock-in system regulated by the NR4A2 promoter, which is activated only upon T cell stimulation. CAR T and OT1 T cells were tested in tumours expressing HER2 and/or OVA. BiTE-expressing T cells enhanced anti-tumour efficacy and T cell activation. However, 30% of mice receiving constitutive BiTE-expressing cells experienced rapid weight loss. This toxicity was eliminated when HER2 BiTE expression was regulated by the NR4A2 promoter. These results suggest tumour-specific BiTE delivery as a safer, effective strategy to overcome antigen heterogeneity and improve outcomes in solid tumour immunotherapy.

22 July 2025 (Tuesday)
10 – 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.