

SigN VIRTUAL SEMINAR

hosted by Dr Ng Lai Guan

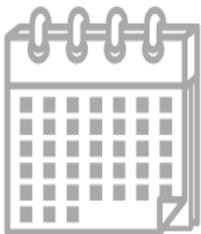


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Overcoming tumour heterogeneity by engaging host immunity to enhance chimeric antigen receptor T cell therapy of solid cancers

Adoptive cell therapy (ACT) using chimeric antigen receptor (CAR) T cells is an emerging form of immunotherapy that redirect T cells to specifically target cancer. While CAR T cell therapy has achieved a significant impact in some haematological malignancies, its efficacy in solid cancers has remained limited to date. One confounding issue is the variable expression of target antigens on solid tumours (i.e. tumour antigen heterogeneity). CAR T cells may eliminate antigen-expressing but not antigen-negative tumour cells, which can consequently lead to disease relapse involving the latter. Dendritic cells (DCs) are professional antigen-presenting cells specialised in the priming and activation of T cells. We hypothesised that engaging the host immune system by enhancing DCs will improve host T cell anti-tumour responses and overcome tumour heterogeneity in ACT. To this end, we engineered T cells to secrete the DC growth factor Fms-like tyrosine kinase 3 ligand (FL). Administration of FL-secreting T cells showed expanded host intratumoural DC and T cell numbers in preclinical models. Combination of FL-secreting T cells with immune-stimulatory adjuvants further inhibited tumour growth in both models of ACT and CAR T cell therapy in a host DC and T cell-dependent manner. Importantly, combination therapy was associated with a significant increase in host anti-tumour T cells recognising antigens beyond those targeted by the adoptively transferred T cells (epitope spreading). Our data suggest that augmenting endogenous DCs and host anti-tumour immunity represent a promising strategy to overcome the clinical problem of antigen-negative tumour escape following ACT.



9th February 2021 (Tuesday)

10:00am – 11:00am

Join Zoom Meeting: [LINK](#)

Meeting ID: 953 9606 9933

Passcode: 759840

*Seminar is
open for all
to attend.*

*Registration
is not
required.*

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