Singapore Immunology Network
SIgN

SIgN SEMINAR

Hosted by Dr Melissa Ng

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Overexpression of constitutively active Foxo1 enhances CAR T cell polyfunctionality and efficacy against solid tumors

Chimeric antigen receptor (CAR) T cell therapy is a form of immunotherapy that involves genetically engineering a patient's T cells to target a defined cancer antigen. CAR T cells are effective in some haematological cancers but challenges remain in the treatment of solid tumors due to tumor-mediated immunosuppression and CAR T cell exhaustion. Clinical data indicates that less differentiated CAR T cells have improved persistence and therapeutic efficacy. These cells have a unique transcriptional profile defined by the expression of several pro-memory transcription factors (TFs). In this study, we compared the efficacy of CAR T cells overexpressing various pro-memory TFs including we obtained a strong gene signature for the transcription factor, forkhead box protein O1 (Foxo1), for which a strong signature was observed in memory-like CAR T cells. CAR T cells expressing a constitutively active variant of Foxo1 exhibited improved *in vivo* therapeutic efficacy in a syngeneic orthotopic mammary fat pad model of breast cancer and a subcutaneous colon carcinoma model. Remarkably, Foxo1-ADA overexpression enhanced CAR T cells polyfunctionality, persistence and mitochondrial fitness with therapeutic effects dependent on their enhanced capacity to secrete inflammatory cytokines. Our data suggests that overexpression of Foxo1 in CAR T cells is a promising strategy for overcoming the hurdles of limited CAR T cell persistence and immunosuppression, particularly in the context of treating solid cancers.

10th October 2022 (Monday)
10 AM – 11 AM (Singapore Time)
SIgN Seminar Room, Immunos, Level 4

8A Biomedical Grove, Immunos, #04-06, Singapore 138648

Seminar is open for all to attend.

Registration is not required.