Singapore Immunology Network
SIgN

SIgN VIRTUAL SEMINAR

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An IL-2 Partial Agonist Promotes CD8+ T Cell Stemness

Adoptive cell transfer of antigen specific T cells represents a major advance in cancer immunotherapy, with robust clinical outcomes in a subset of patients. To achieve effective responses, both the number of transferred T cells and their cell differentiation state are critical determinants. T cells can be expanded with T cell receptor (TCR)-mediated stimulation and IL-2, but this can also lead to T cell differentiation into effector T cells and lower their therapeutic efficacy, whereas maintenance of a more stem-like state prior to adoptive transfer is beneficial. Here, we show that an engineered IL-2 partial agonist promoted T-cell expansion without driving terminal differentiation. The partial agonist exhibited altered signaling and mediated activated distinctive downstream transcriptional, epigenetic, and metabolic programs. Moreover, it sustained expression of T cell transcription factor 1 (TCF-1) and promoted mitochondrial fitness, facilitating the maintenance of a stem cell-like state. Accordingly, TCR transgenic and CAR-modified CD8+ T cells expanded with this engineered molecule displayed robust anti-tumor activity in vivo in established mouse models of melanoma and acute lymphoblastic leukemia. Thus, tempering cytokine signaling with the IL-2 partial agonist provides a strategy for enhancing therapeutic efficacy by limiting exhaustion while preserving stemness in cell therapy. Moreover, our findings demonstrate the translational potential of engineered cytokine partial agonists in immunotherapies.

7th September 2021 (Tuesday)
9:30AM – 10:30AM (Singapore Time)
Join Zoom: LINK or Scan QR Code
Meeting ID: 921 3498 8419
Passcode: 808935

Seminar is open for all to attend.

Registration is not required.

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