

# SigN VIRTUAL SEMINAR



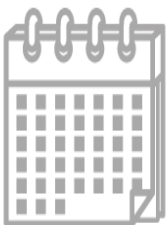
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## An IL-2 Partial Agonist Promotes CD8+ T Cell Stemness

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.



**7<sup>th</sup> 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  
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*Registration  
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