1033 ID3 AND C-KIT DEFINE THE STEM-LIKE POTENTIAL OF T CELLS AND THEIR RESPONSE TO CHRONIC INFECTION AND CANCER

[1]Amania A Sheikh, [2]Dane M Newman, [2]Ricky W Johnstone, [1]Axel Kallies, [1]Daniel Utzschneider*. [1]*The Peter Doherty Institute for Infection and Immunity and The University of Melbourne, Melbourne, VIC, Australia*; [2]*Peter MacCallum Cancer Centre, Melbourne, VIC, Australia*

Background CD8+ T cell responses to chronic infection and cancer are sustained by stem-like precursors of exhausted T (Tpex) cells that express high levels of memory-related transcriptional regulators including TCF1 and ID3.

Methods Here, we take advantage of the murine acute and chronic Lymphocytic Choriomengitis Virus (LCMV) as well as B16F10 cancer model to address the role of ID3 in exhausted T cells.

Results We identify a critical role for ID3 in promoting continuous differentiation of Tpex cells to sustain ongoing T cell responses in chronic infection. Mechanistically, we show that ID3 regulates the developmental progression of stem-like Tpex cells expressing CD62L and MYB to Tpex cells marked by expression of the tyrosine-protein kinase c-Kit, which itself promoted T cell expansion and effector differentiation. Finally, we demonstrate that ID3 expression in memory T cells that develop after acute infection or T cells activated in the presence of IL-18 promoted the generation of Tpex cells and thus superior T cell responses when challenged with chronic infection or cancer.

Conclusions Thus, we identify a critical role for ID3 in promoting functional and long-lasting T cell responses in chronic infection and cancer.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1033