The Journal of Immunology

ABSTRACT | MAY 01 2023

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J Immunol (2023) 210 (1_Supplement): 77.07.
https://doi.org/10.4049/jimmunol.210.Supp.77.07

Regulation of CD4 T-cell immunity by eukaryotic Elongation Factor 2 Kinase

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CD4 T cells are a major source of inflammatory cytokines to manage the immune responses, and there is evidence showing that IL-17-secreting helper CD4 T cells (Th17 cells), play a critical role in autoimmune diseases. Eukaryotic Elongation Factor 2 Kinase (eEF2K) is a protein kinase that negatively regulates the elongation step of protein synthesis. eEF2K regulates vascular inflammatory responses and hypertension development, yet a complete immunologic characterization of eEF2K, particularly in CD4 T cells and autoimmune diseases, remains obscure. Defining eEF2K-mediated CD4 T cell activities, including CD4 T cell inflammation and metabolism, will significantly enhance our knowledge toward the goal of improving health span. Here, we reported that eEF2K is essential for the survival and proliferative capacity of CD4 T cells. eEF2K deficient mice displayed a higher metabolic profile and increased production of inflammatory cytokines. By analyzing CD4 T cells from the wild type (WT) and eEF2K deficient mice, we revealed that eEF2K regulates mitochondrial stress capacity and the production of reactive oxygen species (ROS) through the master transcription factor, STAT3. Depletion of eEF2K agitated Th17-related autoimmune diseases, including arthritis and colitis. A STAT3 inhibitor, C188-9, attenuated Th17 cell-mediated autoimmune colitis by reducing inflammation in the murine colitis model that received eEF2K deficient CD4 T cells. Our findings provide insights into the regulation of CD4 T cells and autoimmunity by eEF2K, and further investigations would help design novel strategies by targeting eEF2K-based immunotherapy in autoimmune diseases.