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Post-transcriptional regulation of cytokine expression and T cell development

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Cytokines produced by innate immune cells, especially IL-12 family cytokines, play essential roles in the development of specific adaptive immunity against invading pathogen. IL-12 is essential for the differentiation and proliferation of Th1 cells important for protection against intracellular infection, while IL-23 plays an important role for Th17 cell survival and expansion important for host defense against extracellular infection. Transcriptional regulation of these cytokines has been intensively studied for the past decades. Posttranscriptional regulation of these cytokines, however, remains largely elusive, due probably to technique barriers. Posttranscriptional regulation of many cytokines occurs by modulation of their mRNA stability through AREs in the 3'UTR. One of the best characterized ARE-associated RNA binding decay proteins is tristetraprolin (TTP). TTP is a member of CCCH tandem zinc finger proteins and involved in the regulation of inflammatory responses at the posttranscriptional level. TTP binds to AREs within the 3'UTR causing destabilization of mRNAs encoding tumor necrosis factor-alpha (TNF-α), granulocyte-macrophage colony-stimulating factor (GM-CSF), cyclooxygenase 2, interleukin-2, interleukin-10 and the chemokine CXCL1. We have recently found that mice deficient of TTP show increased IL-12 and IL-23 expression. The suppression of IL-12 and IL-23 expression by TTP is mediated through different mechanisms. As a result of IL-12 and IL-23 suppression, Th1 and Th17 cells are increased in mice deficient of TTP. Our date indicate that TTP is a critical protein involved in the control of inflammation and maintenance of homeostasis via affecting pro-inflammatory cytokine expression and subsequent T help cell development.

Biography

Jianguo Liu has completed his postdoctoral training at the Weill Medical College of Cornell University. He is currently a tenure-track assistant professor at Saint Louis University School of Medicine. He has published more than 40 peer-reviewed papers in reputed journals. His primary research interest focuses on cytokine regulation in macrophages and its effects on T cell development in tumor and autoimmune disease.

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