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New mechanism of CD8 T cell differentiation upon combinatorial activation by antigen and cytokine

Yutaka Tagaya
Institute of Human Virology, University of Maryland School of Medicine, USA

CD 4 T cell differentiation is complex and is dictated by unique transcriptional networks. In contrast, only T-bet and eomesdermin have been extensively studied in the differentiation of peripheral CD8 T cells. Some years ago, we demonstrated a critical requirement of γc-signaling for CD8 T cell differentiation into effector cells using a mouse model of GvHD (Miyagawa et al. J. Immunol. 2008 181: 1109). This study prompted us to ask if two modes of CD8 T cell activation exist, namely one by a high dose-antigen and the other by suboptimal dose-antigen + a γc-cytokine signaling. We then postulated that these two modes of CD8 T cell activation may require different transcriptional networks and conducted transcriptome profiling representing each mode of activation. Globally, cytokine or antigen alone only transiently induced genes which quickly declined to quiescence. In contrast, the combinatorial (cytokine + antigen) stimulation led to a stabilized and more versatile gene induction. We sought after a unique transcription factor that is only found in the gene pool from the combinatorial stimulation and identified IRF-8. Subsequent analyses demonstrated that IRF8 is not required for the early stages of T cell differentiation, but the abrogation of IRF8 activity efficiently cripples the effector differentiation of peripheral CD8 T cells, even in the presence of T-bet/eomesdermin. Several reports demonstrate an efficient adjuvant effect of various γc-cytokines in vaccination. Our study seems to provide a mechanistic explanation for these findings and may shed new light on the enhancement of existing protocols.

Biography

Dr. Tagaya has acquired M.D., and Ph.D. from the Kyoto University Medical School, and completed postdoctoral studies at the National Cancer Institute. He is currently the head of the Cell Biology Lab, Institute of Human Virology at the University of Maryland School of Medicine. His bibliography contains more than 60 publications in reputed journals in the field of cytokine biology, molecular and cellular immunology.

YTagaya@som.umaryland.edu