Transcription factors regulating duration of T cell immune responses and host protection through metabolic regulation

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Although cMyc is an essential transcription factor that establishes a metabolically active and proliferative state in T lymphocytes after antigen priming, its expression does not persist during the entire period of T cell immune responses. To date, it remains unknown how T cell activation is maintained after cMyc down-regulation. Here, we identify AP4, encoded by the gene Tfap4, as the transcription factor that sustains activation of antigen-specific CD8+ T cells and maximizes the magnitude of clonal expansion. Despite normal priming, Tfap4$^{-/-}$ CD8^{+} T cells fail to continue transcription of a broad metabolic program necessary for sustained proliferation. The physiological importance is highlighted by the enhanced susceptibility of mice that specifically lack AP4 only in CD8^{+} T cells to virus infection. Genome-wide analysis suggests that many activation-induced metabolic genes are shared targets of cMyc and AP4. Thus, AP4 maintains Myc-initiated cellular metabolic programs in CD8^{+} T cells to control microbial infections.