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Deciphering the Novel Intrinsic System in T cells

Abstract

T cells are fated to firmly maintain the quiescent state prior to activation; however, little is known about the biology and factors that underlie this phenomenon. For decades, T cell studies have solely focused on activation, differentiation, and effector function. The research efforts have revealed the key Cell-Extrinsic Cues (*CEC*) system such as Signal 1, 2 and 3 that accounts for the initiation of T cell activation and differentiation. However, this *CEC* mechanism is insufficient to illustrate how T cells sustain quiescence while inhibiting spontaneous activation. We propose that quiescent T cells underlie a self-suppressed, but actively prepared ground state, which is primarily governed by intrinsic system. To identify key intrinsic factors responsible for regulating the quiescence program in T cells, we developed "*Super-Enhancer based Screening"* that led to critical candidates. Among the candidates, we found that intrinsic factors BTG1/2 constantly destabilize mRNA in a global manner by inducing deadenylation to minimize total mRNA abundance in quiescent T cells thus actively maintaining a ground state. We also identified that novel transcription factor FOX family maintains the quiescent state via repressing ciliary gene expression that controls immunological synapse formation.