

Special Issue

T Cell Ca²⁺ Signal Dynamics: An Emerging Landscape for Therapeutic Strategies

Message from the Guest Editors

T lymphocytes have evolved a considerable reliance on the induction and management of the intracellular Ca²⁺ signal. The foundation of the adaptive immune response is critically dependent on the T cell's recognition of an antigen and the immediate transduction of antigen recognition via the T cell receptor's recruitment of a multiplex Ca²⁺ signal. T cell-activated Ca²⁺ signals then proceed according to a complex trajectory, with an initial increase in cytoplasmic Ca²⁺ due to inositol 1,4,5-trisphosphate-mediated release from internal Ca²⁺ stores, followed by a Ca²⁺ influx phase due to the activation of plasma membrane-localized Orai Ca²⁺ channels gated by ER Ca²⁺ store depletion signals. Importantly, in the absence of the successful deployment of the Ca²⁺ influx signal, which can occur over protracted periods of T cell engagement with antigen-presenting cells, T cells fail to be adequately activated, resulting in impaired immune function. Thus, there are several key points where the regulation of the T cell Ca²⁺ signal is important, from the management of ER Ca²⁺ store status to pathways linked to PM Ca²⁺ channel activation, all of which warrant closer examination.

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