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Review

cAMP: a multifaceted modulator of immune synapse assembly and T cell activation

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Abstract

T Lymphocyte activation involves a substantial reorganization of the membranous and intracellular compartments. Signaling complexes assemble and dismantle in a highly ordered fashion in both compartments and orchestrate the activation of T cells with high sensitivity and specificity. TCR ligation leads to a short burst of cAMP production, which is centrally required for T cell activation; however, sustained elevations in intracellular cAMP concentrations are immunosuppressive. Emerging evidence of the existence of local cAMP pools gleaned from studies on other cell types suggests that cAMP compartmentalization may account, in part, for these opposing effects. Whereas cAMP compartmentalization has been identified as a central factor in the control of the cAMP - dependent processes in other cell types, this has, as yet, not been addressed in T lymphocytes. In this review, we discuss the role of cAMP in T cell activation and differentiation, with an emphasis on the effects mediated by the cAMP effectors, protein kinase A (PKA) and exchange protein activated by cAMP (EPAC)1, and on the regulatory proteins that may control the generation of local cAMP pools in T cells. We also present an overview of the available tools to image cAMP production at the subcellular level and discuss how bacterial adenylate cyclase (AC) toxins that are known to generate local cAMP pools can be exploited to address the role of cAMP compartmentalization in T cell activation.

Citing Literature

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