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Titel des Beitrags: The cGMP/protein kinase G pathway contributes to dihydropyridine-sensitive calcium response and cytokine production in TH2 lymphocytes.

Abstract:
Th2 lymphocytes differ from other CD4+ T lymphocytes not only by their effector tasks but also by their T cell receptor (TCR)-dependent signaling pathways. We previously showed that dihydropyridine receptors (DHPR) involved in TCR-induced calcium inflow were selectively expressed in Th2 cells. In this report, we studied whether cGMP-dependent protein kinase G (PKG) activation was implicated in the regulation of DHPR-dependent calcium response and cytokine production in Th2 lymphocytes. The contribution of cGMP in Th2 signaling was supported by the following results: 1) TCR activation elicited cGMP production, which triggered calcium increase responsible for nuclear factor of activated T cell translocation and Il4 gene expression; 2) guanylate cyclase activation by nitric oxide donors increased intracellular cGMP concentration and induced calcium inflow and IL-4 production; 3) reciprocally, guanylate cyclase inhibition reduced calcium response and Th2 cytokine production associated with TCR activation. In addition, DHPR blockade abolished cGMP-induced [Ca2+]i increase, indicating that TCR-induced DHPR-sensitive calcium inflow is dependent on cGMP in Th2 cells. Th2 lymphocytes from PKG1-deficient mice displayed impaired calcium
signaling and IL-4 production, as did wild-type Th2 cells treated with PKG inhibitors. Altogether, our data indicate that, in Th2 cells, cGMP is produced upon TCR engagement and activates PKG, which controls DHP-sensitive calcium inflow and Th2 cytokine production.