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Vitamin D controls T cell antigen receptor signaling and activation of human T cells

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Abstract

Phospholipase C (PLC) isozymes are key signaling proteins downstream of many extracellular stimuli. Here we show that naive human T cells had very low expression of PLC-γ1 and that this correlated with low T cell antigen receptor (TCR) responsiveness in naive T cells. However, TCR triggering led to an upregulation of ~75-fold in PLC-γ1 expression, which correlated with greater TCR responsiveness. Induction of PLC-γ1 was dependent on vitamin D and expression of the vitamin D receptor (VDR). Naive T cells did not express VDR, but VDR expression was induced by TCR signaling via the alternative mitogen-activated protein kinase p38 pathway. Thus, initial TCR signaling via p38 leads to successive induction of VDR and PLC-γ1, which are required for subsequent classical TCR signaling and T cell activation.

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Contributions

M.R.v.E. did most of the experiments, analyzed data and contributed to the writing of the manuscript; M.K. and P.S. contributed to the ketoconazole and mRNA experiments; K.O. contributed to the planning and analyses of studies involving patients; N.Ø. contributed to the design and analysis of some of the experiments; and C.G. conceptualized the research, directed the study, analyzed data and wrote the manuscript.

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Ethics declarations

Competing interests

The authors declare no competing financial interests.

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