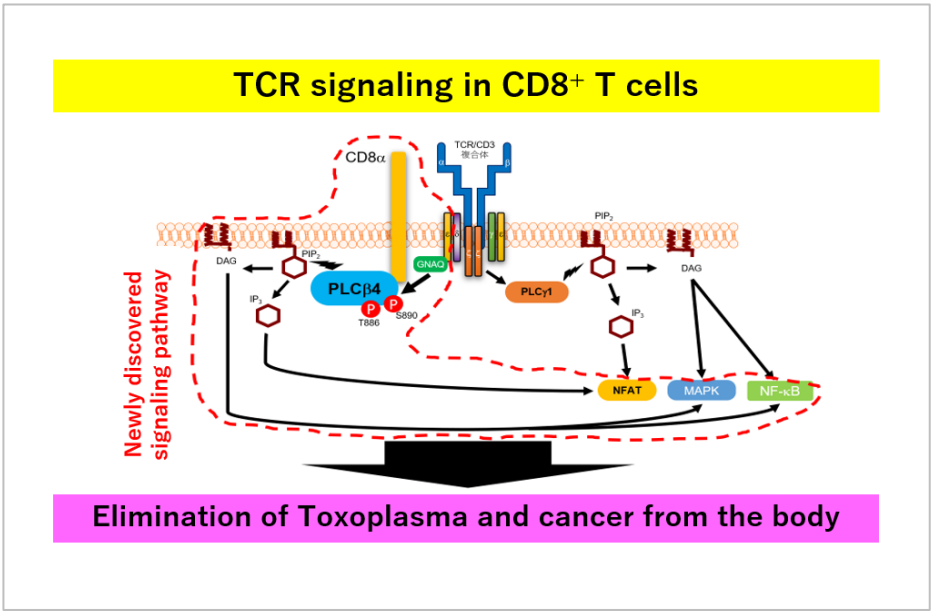
A novel role of PLCβ4 in selectively mediating TCR signaling in CD8⁺ but not CD4⁺ T cells

Keywords: toxoplasma, cancer immunity, CTLC, PLCβ4

Because of their common signaling molecules, the main T cell receptor (TCR) signaling cascades in CD4⁺ and CD8⁺ T cells are considered qualitatively identical. Masahiro Yamamoto and his research group show that TCR signaling in CD8⁺ T cells is qualitatively different from that in CD4⁺ T cells, since CD8α ignites another cardinal signaling cascade involving phospholipase C β4 (PLCβ4). TCR-mediated responses were severely impaired in PLCβ4-deficient CD8⁺ T cells, whereas those in CD4⁺ T cells were intact. PLCβ4-deficient CD8⁺ T cells showed perturbed activation of peripheral TCR signaling pathways downstream of IP3 generation. Binding of PLCβ4 to the cytoplasmic tail of CD8α was important for CD8⁺ T cell activation. Furthermore, GNAQ interacted with PLCβ4, mediated double phosphorylation on threonine 886 and serine 890 positions of PLCβ4, and activated CD8⁺ T cells in a PLCβ4-dependent fashion. PLCβ4-deficient mice exhibited defective antiparasitic host defense and antitumor immune responses. Altogether, PLCβ4 differentiates TCR signaling in CD4⁺ and CD8⁺ T cells and selectively promotes CD8⁺ T cell–dependent adaptive immunity.



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