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SUMMARY/ABSTRACT The goal of this study is to understand the molecular mechanism of how cAMP binds to its receptor and how GPCR signaling is coupled to cAMP production. Mammals express four G-protein coupled receptors for cAMP, GPCR13, GPCR11, GPCR13, and GPCR12, but their functions have not been fully understood. We recently demonstrated that GPCR13 is essential for the development and function of spleen and thymus. Loss of GPCR13 leads to a severe defect in T-cell development in the thymus and impairs the production of peripheral T cells in the spleen. These phenotypes are recapitulated by gene ablation of adenylyl cyclase 1 (AC1), which encodes the enzyme that converts ATP into cAMP.

Consistently, treatment of mice with an AC1 inhibitor or exposure of bone marrow cells to adenosine induces similar defects in T-cell development and function. Intriguingly, our preliminary data suggest that AC1 is required for the activation of GPCR13. In this grant application, we propose to study how AC1 activates GPCR13. We will determine the mechanisms of AC1 activation by GPCR13. We will study the role of AC1 in the function of thymus and spleen by creating a GPCR13/AC1 double knockout mouse. The information obtained will advance our understanding of the function of GPCR13 and provide new insights into the molecular mechanism of GPCR activation.Q: PHP cURL response charset I've been trying to find out how to set the charset of a cURL response but it's 3e33713323

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