論文の内容の要旨

論文題目　Functional analysis of an opioid precursor gene expressed in regulatory T cells

（制御性 T 細胞で発現するオピオイド前駆体遺伝子の機能解析）

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The net outcome of a complex series of stimulatory and inhibitory cues defines the intensity and dynamics of immune responses. Their disbalance can result in autoimmunity as suggested by accumulating evidence. A better understanding of these regulatory mechanisms will open new avenues for the treatment of autoimmune diseases. In this study we found that genetic deletion of proenkephalin (Penk) in mice resulted in experimental autoimmune encephalomyelitis (EAE) amelioration. We found that Penk, a classically defined opioid gene known to be expressed in the nervous and neuroendocrine systems, is expressed mainly in regulatory T cells (Tregs) among immune cells and that its expression was upregulated in Tregs infiltrated into the spinal cord of mice with EAE. We generated Penk floxed mice and crossed them with Treg-specific Cre line (FoxP3-Cre) to obtain mice lacking Penk specifically in Tregs. These conditional knock-out (cKO) mice could recapitulate EAE amelioration seen in Penk total KO mice indicating that loss of Penk function in Tregs is responsible for amelioration of chronic autoimmunity. Thus, our findings suggest a novel negative feedback loop in regulatory T cells to counterbalance the suppression of immune responses.