［課程－２］

審査の結果の要旨

氏名リヤン ベンラリビ

A disbalance between stimulatory and inhibitory cues can result in autoimmunity, in order to add to the bigger picture of the mechanisms controlling the intensity and dynamics of immune responses, this study addresses the role of an opioid precursor gene in the course of autoimmune demyelinating inflammation of the central nervous system. Here, using single-cell RNA sequencing reanalysis and CRISPR–Cas9-based cell-specific in vivo genetic perturbations in mice, we identified a novel signal molecule expressed in regulatory T cells that limits the suppression of chronic immune responses. We found that total genetic inactivation of proenkephalin (Penk) resulted in an amelioration of experimental autoimmune encephalomyelitis (EAE) symptoms during the chronic phase. We identified regulatory T cells (Tregs) as the main immune cell expressing Penk in homeostasis and in the course of EAE. We found that the specific deletion of Penk in Tregs recapitulated EAE amelioration seen in Penk total KO mice with the same amplitude, indicating that loss of Penk function in Tregs is responsible for the amelioration of chronic autoimmunity. Thus, our findings suggest a novel negative feedback loop in Tregs to counterbalance the suppression of immune responses. The findings in this study are thought to open new avenues for the treatment of autoimmune diseases.

よって本論文は博士（ 医学 ）の学位請求論文として合格と認められる。