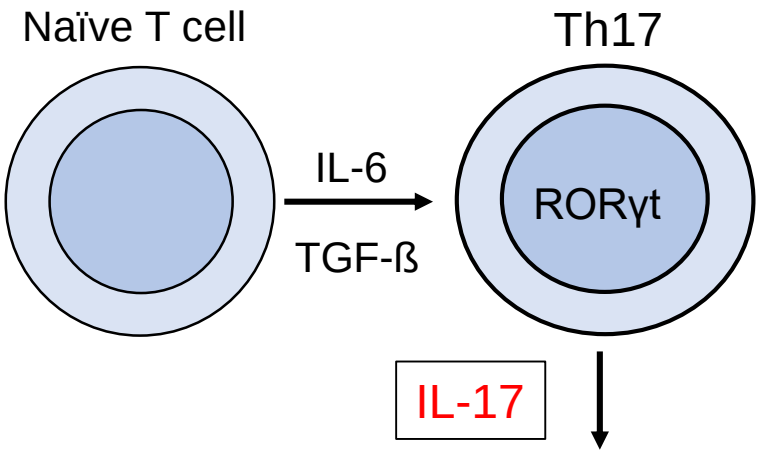
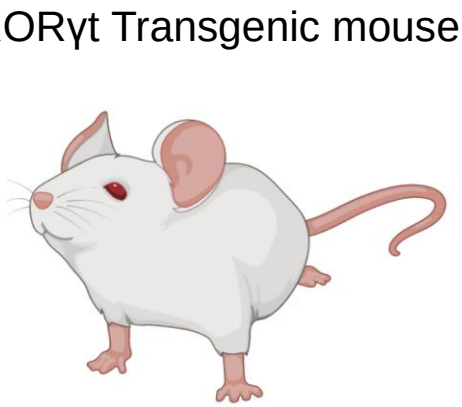
From Department of Anatomy and Neuroscience

Effects of RORγt overexpression on the murine central nervous system

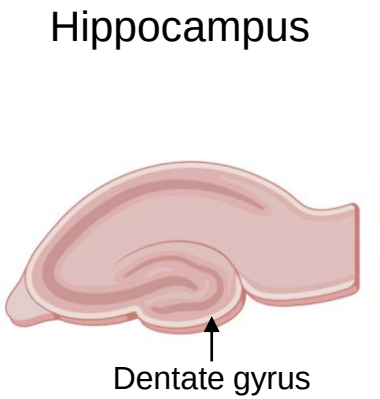


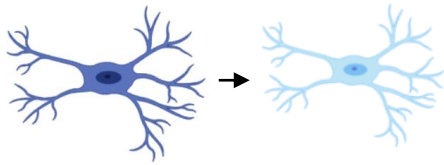
Fungal and extracellular pathogenic bacteria elimination
Cytotoxicity, autoimmunity
Neuropsychiatric disorders ?



RORγt overexpression

Excess Th17 cells





The activity and density of Iba1^{+} microglia ↓

T-helper 17 (Th17) cells are a subset of CD4^{+} T cells that produce interleukin (IL)-17A. Recent studies showed that an increase in circulating IL-17A causes cognitive dysfunction, although it is unknown how increased systemic IL-17A affects brain function. Using transgenic mice overexpressing RORγt, a transcription factor essential for differentiation of Th17 cells (RORγt Tg mice), we examined changes in the brain caused by chronically increased IL-17A resulting from excessive activation of Th17 cells. RORγt Tg mice exhibited elevated *Rorc* and *IL-17A* mRNA expression in the colon, as well as a chronic increase in circulating IL-17A. We found that the immunoreactivity of Iba1 and density of microglia were lower in the dentate gyrus of RORγt Tg mice compared with wild-type mice. However, GFAP^{+} astrocytes were unchanged in the hippocampi of RORγt Tg mice. Levels of synaptic proteins were not significantly different between RORγt Tg and wild-type mouse brains. In addition, novel object location test results indicated no difference in preference between these mice. Our findings indicate that a continuous increase of IL-17A in response to RORγt overexpression resulted in decreased microglia activity in the dentate gyrus.

References: Sasaki, Nagata, Takahashi, Takei., Neuropsychopharmacology Reports. 2021. *in press*. Contact: Assist. Prof. Sasaki and Prof. Takei