

Regulation of inflammatory cytokine response by aquaporin 5 and its pathophysiological significance in AQP5 transgenic mice

Keisuke Osada, Yuko Kikusima, Shingo Matsuyama, Yoichiro Isohama

Lab. appl. Pharmacol., Facul. of Pharm. Sci., Tokyo Univ. of Sci.

Aquaporin-5 (AQP5) is a water-selective channel protein expressed in alveolar epithelial and submucosal gland cells, and plays an important role to maintain water homeostasis in the lung. Recently, several lines of evidence indicated that AQPs regulate not only plasma membrane water permeability, but also various cellular functions, such as cell migration and growth. In our previous study, we have found that AQP5 potentiated TNF- α -induced cytokine expression, whereas it attenuated Th2 cytokine-induced response. In the present study, we first examined the underlying mechanisms involved in the attenuation by AQP5 in Th2 cytokine signaling. In AQP5-expressing cells, the IL-13-induced phosphorylation of STAT6 was lower than that in control cells. Consistent with this, phosphorylation of JAK1 and TYK2 by IL-13 in AQP5 expressing cells were considerably lower than those in control cells, suggesting that AQP5 inhibits IL-13 and tyrosine kinase complex. In addition, we have established transgenic mouse in which AQP5 is highly expressed in the lung, to investigate the pathophysiological role of modification of cytokine signaling by AQP5. The phenotypes of this transgenic mice will be also shown this presentation.