Hypoxia increases $K_{2P}5.1$ K^+ channel expression in $CD4^+$ T cells of the mouse IBD model

Kyoko Endo[1], Hiroaki Kito[2], Ryo Tanaka[1], Junko Kajikuri[2], Satoshi Tanaka[1], Takayoshi Suzuki[3], Susumu Ohya[2]

[1]Dept.Pharmacol., Div. Pathol. Sci., Kyoto Pharmaceut. Univ., [2]Dept. Pharmacol., Grad. Sch. Med. Sci., Nagoya City Univ., [3]Dept. Compl. Mol. Chem., Inst. Sci. Indust. Res., Osaka Univ.

Several studies have shown that up-regulation of $K_{2P}5.1$ K^+ channel in $CD4^+$ T cells of patients with multiple sclerosis (MS) and rheumatoid arthritis (RA) and a mouse model of inflammatory bowel disease (IBD). However, the underlying mechanism of $K_{2P}5.1$ up-regulation in T cells remains to be elucidated. Inflammation-associated hypoxia is involved in the pathogenesis of autoimmune diseases, and T cells are exposed to hypoxic environment during recruitment from the inflamed tissues to secondary lymphoid tissues. Here we explored whether inflammation-associated hypoxia is attributable to increased expression and activity of $K_{2P}5.1$ in splenic $CD4^+$ T cells of chemically-induced IBD model mice. Significant increase in hypoxia-inducible factor (HIF)-1α transcripts and proteins was found in splenic $CD4^+$ T cells of IBD model. In activated splenic $CD4^+$ T cells, hypoxia (1.5% O_2) increased $K_{2P}5.1$ expression and activity, whereas, the treatment with the HIFα subunit inhibitor, FM19G11 decreased them. Together, these results provide the possible mechanism for $K_{2P}5.1$ up-regulation via HIF-1α signal activation in $CD4^+$ T cells of IBD model.