GS01-1 **Role of two-pore domain K^+ channel $K_{2P}5.1$ and effect of pre-mRNA splicing inhibitor on $K_{2P}5.1$ expression and activity by pre-mRNA inhibitor**

○Kyoko ENDO[1], Hiroaki KITO[1,2], Masanori FUJII[1], Susumu OHYA[1,2]
[1]Kyoto Pharmaceut. Univ., [2]Grad. Sch. Med. Sci., Nagoya City Univ.

Two-pore domain K^+ channel $K_{2P}5.1$ plays an important role in the regulation of Ca^{2+} signaling, and contributes to various cell functions such as proliferation, differentiation and cytokine production in T cells. We have reported that $K_{2P}5.1$ is upregulated in $CD4^+$ T cells of the inflammatory bowel disease (IBD) model mice and the knockout of $K_{2P}5.1$ in mice suppressed the disease responses implicated in the IBD model. We identified a novel splicing isoform of $K_{2P}5.1$, $K_{2P}5.1B$ lacking the N-terminus of full-length $K_{2P}5.1A$ from human and murine lymphoid tissues. Overexpression of $K_{2P}5.1B$ suppressed $K_{2P}5.1$ activity by inhibition of $K_{2P}5.1A$ membrane trafficking in HEK293 cells. The pre-mRNA splicing inhibitor, Pladienolide B (PB) upregulated $K_{2P}5.1B$ expression, resulting in decrease in the $K_{2P}5.1$ activity in human leukemia K562 cells. In mouse splenic $CD4^+$ T cells stimulated by concanavalin A, PB significantly inhibited $K_{2P}5.1$ activity by preventing $K_{2P}5.1A$ transcription, resulting in decrease in inflammatory cytokine production. These findings may provide a novel insight into therapeutic strategy for treating $K_{2P}5.1$-related diseases like autoimmune diseases.