1-YIA-23 YIA

GPR143, a L-DOPA receptor, is involved in monocrotaline-induced pulmonary hypertension in rats

Masayuki Nakano[1,3], Tatsuo Hashimoto[1,3], Motokazu Koga[2], Daiki Masukawa[1], Shinya Oku[2], Yusuke Mizuno[2], Takahisa Goto[2], Kouichi Tamura[3], Yoshio Goshima[1]

[1]Dept. Mol. Pharmacol. Neurobiol., Yokohama City Univ. Grad. Sch. Med., [2]Dept. Anesthesiology Crit. Care Med., Yokohama City Univ., Sch. Med., [3]Dept. Medical Science and Cardiorenal Medicine, Yokohama City Univ., Sch. Med.

We previously demonstrated that L-DOPA modulated the vascular α1-adrenergic receptor through GPR143, a G-protein coupled receptor, and sensitized vasomotor tone. The purpose of this study is to clarify the involvement of GPR143, in pulmonary hypertension (PH). We generated GPR143 gene-deficient (KO) rats and comparatively studied monocrotaline (MCT) -induced PH in wild type (WT) and *Gpr143*-KO rats. We evaluated the interaction between L-DOPA and adrenergic α1 receptor by contractile force of rat isolated pulmonary arteries. The degree of PH was evaluated by right ventricular systolic pressure (RVSP) and right ventricular to body weight ratio (RV/BW). In isolated pulmonary arteries, L-DOPA (1 μM) augmented contractile response to phenylephrine, an α1 adrenergic receptor agonist. One month after injection subcutaneously with MCT (60 mg/kg), the RVSP was attenuated in *Gpr143*-KO rats as compared to the WT rats (49.7 +/- 1.1 mmHg and 41.1 +/- 1.4 mmHg in WT and *Gpr143*-KO, $p<0.01$, N=5). Coordinately, the RV/BW was also reduced in *Gpr143*-KO rats compared to the WT rats ($5.8 +/- 0.3 \times 10^{-4}$ and $4.9 +/- 0.2 \times 10^{-4}$ in WT and *Gpr143*-KO, $p<0.05$, N=7). We here provide evidence that GPR143 is involved in MCT-induced PH in rats. Further studies are needed to elucidate detailed mechanisms.