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

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We previously demonstrated that L-DOPA modulated the vascular $\alpha 1$ -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 $\alpha 1$ 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 ($1 \mu\text{M}$) augmented contractile response to phenylephrine, an $\alpha 1$ 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 $\pm$ 1.1 mmHg and 41.1 $\pm$ 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 $\pm$ 0.3 $\times 10^{-4}$ and 4.9 $\pm$ 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.