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Pharmacological profile of fingolimod for pulmonary arterial hypertension

Moe Fujiwara[1], Aya Yamamura[2], Yoshiaki Suzuki[1], Hisao Yamamura[1]

[1]Dept. Mol. Cell. Pharmacol., Grad. Sch. Pharmaceut. Sci., Nagoya City Univ., [2]Dept. Physiol., Aichi Med. Univ.

Pulmonary arterial hypertension (PAH) is pathophysiologically characterized by vasoconstriction and vascular remodeling of the pulmonary artery. Pulmonary vascular remodeling is mainly mediated by the enhanced cell proliferation of pulmonary arterial smooth muscle cells (PASMCs). In this study, we examined the pharmacological effects of fingolimod on the development of PAH. The proliferation rate of PASMCs from idiopathic PAH (IPAH) patients was much higher than that of PASMCs from normal subjects. In normal-PASMCs, fingolimod at low concentrations did not affect the cell proliferation, whereas higher concentrations partly reduced the cell proliferation. On the other hand, the application of fingolimod clearly inhibited the proliferation of IPAH-PASMCs and the inhibitory effect was in a concentration-dependent manner. In monocrotaline-induced pulmonary hypertensive rats, intraperitoneal administration of fingolimod ameliorated both pulmonary vascular remodeling and right ventricular hypertrophy. In addition, fingolimod improved the mortality rate. Our results suggest that fingolimod blocks the development of PAH through inhibiting the excessive proliferation of PASMCs. Fingolimod may be a novel option for the treatment of PAH.