1. No.
   2021Y003

2. Title
   Involvement of hypoxic dysfunction of pulmonary vessels on chronic respiratory diseases

3. Period
   2021-2023

4. Summary

   Smoking causes vasoconstriction (spasm) and vascular remodeling (thickening, fibrosis, and inflammation) under hypoxic conditions. These hypoxic responses are similar to the pathophysiological features of pulmonary arterial hypertension (PAH). In the present study, the expression and activity of nicotinic acetylcholine receptors (nAChR) were examined in pulmonary arterial smooth muscle cells (PASMCs) from normal subjects (Normal) and patients with idiopathic pulmonary arterial hypertension (IPAH). In Normal-PASMCs, nicotine induced inward currents and cytosolic Ca^{2+} increases, which were mediated by nAChRα5. In addition, the expression of nAChRα7 was upregulated by exposure to hypoxia (1% O_2) in Normal-PASMCs. On the other hand, in IPAH-PASMCs, nicotine caused inward currents and cytosolic Ca^{2+} increases, which were responsible for upregulated expression of nAChRα1 and nAChRα7. The increased expression of nAChRα1 was also detected in PASMCs from monocrotaline-induced PAH rats. The activation of nAChRα7 facilitated JAK2 and JNK signaling pathways in IPAH-PASMCs, resulting in the excessive proliferation of IPAH-PASMCs. In conclusion, the activity of nAChRα5 is attributed to the physiological role in PASMCs. On the other hand, the activity of nAChRα7 is involved in the development and progression of PAH. These results strongly suggest that the expression and activity of nAChRα1, nAChRα5, and nAChRα7 were involved in the molecular mechanism of chronic respiratory diseases including PAH.