Calcium Signaling Abnormality in Pulmonary Arterial Hypertension

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Abstract

Pulmonary arterial hypertension (PAH) is a severe and progressive disease that causes right heart failure when the condition progresses after being neglected in an early stage. The pathogenesis of PAH is generally characterized by vasoconstriction, dysregulated apoptosis, upregulated proliferation, migration, and pulmonary vascular remodeling in lung tissue. Although several vasodilating drugs are currently used for preventing the elevation of pulmonary arterial pressure, their therapeutic effects are still insufficient. Thus, there is an urgent need for novel therapeutic targets and drugs. In the past decades, the analysis of patients with idiopathic and familial PAH has revealed several genetic abnormalities that may cooperate with each other to cause pulmonary vascular proliferation and remodeling. On the other hand, recent studies that have employed genetic analyses and experimental models have suggested that the hypercontraction of the pulmonary artery induced by Ca^{2+} signaling abnormality may be involved in the pathogenesis of PAH. This review suggests the critical role of Ca^{2+} signaling abnormality in the development and progression of PAH, and the possibility that Ca^{2+}-permeable channels/transporters may represent novel therapeutic targets.

Key words: Pulmonary hypertension, Ca^{2+} signaling, Ion transporter, Vasoconstriction, Smooth muscle cell proliferation