

Journal club

Protein kinase G dysfunction is an important factor in induced pulmonary hypertension in mice

In this preclinical study, the authors hypothesised that deficiency of protein kinase G-1 (PKG-1), a serine/threonine kinase, would induce pulmonary hypertension (PH) in mice through Rho A/Rho kinase activation.

Protein kinase G-1- knockout (Prkg1^{-/-}) mice had decreased PKG-1 and increased pulmonary artery systolic pressure compared to wild type mice. Prkg1^{-/-} mice had marked microvascular remodelling and precapillary occlusion in the lung, suggesting the two mechanisms cause PH in Prkg1^{-/-} mice. The increased pulmonary artery pressure was independent of left-sided heart disease and systemic hypertension at day 45 in Prkg1^{-/-} mice. Furthermore, the western blot of Prkg1^{-/-} mice showed decreased phosphorylation of Rho A Ser188 and increased activation of Rho A. After fasudil (a Rho kinase inhibitor) treatment, a significant decrease in pulmonary artery pressure was noted in Prkg1^{-/-} mice.

In this study, the authors showed that PKG-1 deficiency results in activation of Rho A-Rho kinase signalling, which causes vascular remodelling and vasoconstriction, leading to PH. Short term inhibition of Rho kinase by fasudil decreased pulmonary pressure in Prkg1^{-/-} mice. Thus, based on the mouse model, PKG-1 deficiency should be one of the important key mechanisms inducing pulmonary artery pressure in Prkg1^{-/-} mice. However, extrapolating this evidence from Prkg1^{-/-} mice to PH human population will require further study.

► Zhao YD, Cai L, Mirza MK, *et al*. Protein Kinase G-1 deficiency induces pulmonary hypertension through Rho A/Rho kinase activation. *Am J Pathol* 2012 Jun 180(6); 2268–75.

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