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.

En-Ting Chang

Correspondence to Dr En-Ting Chang, Department of Chest Medicine, Buddhist Tzu Chi General Hospital, 707, Sec 3, Chung-Yang Rd., Hualien 970, Taiwan; evan19760202@yahoo.com.tw

Competing interests None.

Provenance and peer review Not commissioned; internally peer reviewed.

To cite Chang E-T. *Thorax* 2013;**68**:564.

Published Online First 24 August 2012

Thorax 2013;**68**:564. doi:10.1136/thoraxjnl-2012-202517