Acta Cardiologia Indonesiana (Vol. 3 No. 2) 2017 [supplement]: S10

Identification of a Novel Gene That is Involved in the Development of Pulmonary Arterial Hypertension

Gusti Rizky Teguh Ryanto[1,*], Koji Ikeda[2], Kazuya Miyagawa[2], Keiko Yagi[2], Yoko Suzuki[2], Noriaki Emoto[1,2]
[1]Cardiovascular Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine, Kobe, Japan
[2]Clinical Pharmacy, Kobe Pharmaceutical University, Kobe, Japan
*correspondence: waniqmatun@yahoo.com

Abstract

Introduction: Pulmonary arterial hypertension (PAH) is a rare but potentially fatal disease affecting 1-2 person/millions of population. Pulmonary artery remodeling has been established as a culprit in PAH development, and endothelial dysfunction is critically involved in the pathologic pulmonary artery remodeling; however, mechanisms underlying these pathologies remain unclear. In this study, we searched for genes preferentially expressed in the lung microvasculature that are potentially important for PAH development.
Aim: To identify specific, potentially important genes in PAH pathogenesis and elucidate its mechanism.
Method: We performed DNA microarray analysis using RNAs of human endothelial cells (ECs) from various vascular beds as well as RNAs isolated from various organs including the lungs. After finding a candidate gene, we analyzed its effect on pulmonary artery ECs (hPAECs) functions through gene transfection using retrovirus. We also generated mice with targeted activation of the gene in ECs, and then produced PAH model through chronic exposure to hypoxia (10% O_2 hypoxia for 3 weeks).
Results: Through the microarray analysis, we identified one gene (gene-X) that is highly and preferentially expressed in human lung microvascular ECs. Overexpression of gene-X substantially reduced migration and tube formation capacities in hPAECs, while it enhanced endothelial apoptosis. Targeted activation of gene-X in ECs caused higher pulmonary arterial pressure even under normoxic condition, while hypoxia-induced PAH was exacerbated in these mice.
Conclusion: Our data strongly suggest that gene-X plays a crucial role in PAH pathologies, and thus gene-X has a therapeutic potential for the treatment of PAH.

Keywords: pulmonary arterial hypertension; angiogenesis