Pulmonary vascular stiffness and remodeling are the key factors in generating pulmonary arterial hypertension (PAH). Elastin is critical in conferring vascular distensibility and in suppressing abnormal vascular cell growth. Previously studies have shown that increase in cathepsin production cause a decrease in cellular tropoelastin protein levels during atherosclerosis. Cathepsin K and cathepsin S are both strong elastase which could degrade elastin. In addition, degradation and susceptibility of elastin by elastases are key determinants of vascular stiffness of pulmonary arterial hypertension (PAH). However the relationship between tropoelastin and elastase (cathepsin S and cathepsin K) in the progress of PAH arterial stiffness has not been clarified. We therefore hypothesize that induction of elastase (cathepsin S and cathepsin K) may lead to reduction of tropoelastin protein levels and affect the progress of PAH arterial stiffness.

Methods

The monocrotamine-induced PAH animal model in addition to the harvest and culture of proximal pulmonary arterial smooth muscle (PASMC) were used to test the hypothesis. The migration and proliferation ability of proximal PASMC was assessed by MTT assay and migration chamber assay. To evaluate the downregulation of tropoelastin and upregulation of cathepsin in experimental pulmonary arterial hypertension (PAH), the tropoelastin and cathepsin S, K mRNA levels in the proximal PASMC were assessed by qRT-PCR. To observe the protein level of tropoelastin and cathepsin, we utilized western blotting to compare PASMC from PAH and control rat. Furthermore, we observed the elastin assembly in the pulmonary artery from experimental PAH by immunofluorescence.

Support: This work was supported by NMRPD1B1232 (NSC 101-2314-B-182-076-MY3) and CMRPD 1B0013.