学 位 論 文 の 要 旨

所　　属	三重大学大学院医学系研究科 生命医科学専攻　病態解明医学講座	氏　　名	秦　利強

主論文の題名

Pulmonary hypertension is ameliorated in mice deficient in thrombin-activatable fibrinolysis inhibitor

主論文の要旨

Background: The fibrinolytic system has been implicated in the pathogenesis of pulmonary hypertension (PH). Thrombin-activatable fibrinolysis inhibitor (TAFI) inhibits fibrinolysis and its absence would therefore be expected to increase fibrinolysis and ameliorate PH.

Objective: The objective of the present study was to evaluate the effect of TAFI deficiency on pulmonary hypertension in the mouse.

Methods and Results: PH was induced in C57/BL6 wild type (WT) or TAFI-deficient (KO) mice by weekly subcutaneous treatment with 600 mg/kg monocrotaline (MCT) for 8 weeks. Pulmonary hypertension was inferred from right heart hypertrophy measured by the ratio of right ventricle-to-left ventricle-plus-septum weight (RV/(LV+S)). Pulmonary vascular remodeling was analyzed by morphometry. TAFI-deficient MCT-treated and wild type MCT-treated mice suffered similar weight loss. TAFI-deficient MCT-treated mice had reduced levels of total protein and TNF-α, IL-6 and MCP-1 in bronchial alveolar lavage compared with wild type MCT-treated mice. The ratio of RV to (LV+S) weight was significantly higher in WT/MCT than in KO/MCT mice. Pulmonary artery wall area and vascular stenosis were both greater in MCT-treated WT mice compared to MCT-treated TAFI-deficient mice.

Conclusions: TAFI-deficient MCT-treated mice have less pulmonary hypertension, vascular remodeling and reduced levels of cytokines compared to MCT-treated WT animals, possibly due to reduced coagulation activation.

（注）２，０００字以内にまとめて記入すること。