

Chronic Obstructive Pulmonary Disease

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Plasma uric acid as a protective factor of respiratory dysfunction and emphysema in female mice and human with obstructive pulmonary diseases

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One of the major pathophysiological hallmarks of COPD is oxidative stress. Our microarray analysis using the lung tissue of COPD like murine models (β ENaC-transgenic mice) suggested an imbalance between oxidants and antioxidants. Uric acid (UA), a product of purine metabolism, is one of the strongest endogenous antioxidants in the body. Interestingly, recent cohort studies showed that low levels of serum UA are associated with higher rates of COPD. However, the experimental evidence remains inconclusive. To clarify how serum UA levels affect pulmonary phenotypes of COPD, we treated β ENaC-Tg mice with oxonate, a pharmacological inhibitor of uricase, which is an enzyme that oxidizes UA to allantoin, to increase blood concentration of UA in the mice. Notably, oxonate treatment (500 mg/kg/day, p.o., 4-5 weeks) in β ENaC-Tg mice revealed that typical phenotypes of COPD, such as emphysema demonstrated by an alteration of the mean linear intercept (MLI) and pulmonary function (FEV 0.1%) determined by the ventilator based flexiVent system, tended to be improved in oxonate treated β ENaC-Tg female but not male mice. Moreover, a cross sectional study and a retrospective longitudinal study with Japanese participants in a health screening program also demonstrated the association between plasma UA level and pulmonary function in a female specific manner. Thus, our studies demonstrate plasma UA as a protective factor of respiratory dysfunction and emphysema in female mice and human with obstructive pulmonary diseases.

Biography

Haruka Fujikawa has completed her undergraduate degree from the School of Pharmacy, Kumamoto University (2011-2014) and she was a Laboratory Student at the Department of Molecular Medicine in School of Pharmacy, Kumamoto University, Japan (2013-2014). She is currently pursuing Master's course at the Department of Molecular Medicine, Graduate School of Pharmaceutical Sciences of Kumamoto University, Japan.

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