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Extended Abstract
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# COPD 2016: Plasma uric acid as a protective factor of respiratory dysfunction and emphysema in female mice and human with obstructive pulmonary diseases_ Haruka Fujikawa_Kumamoto University, Japan

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One of the main pathophysiological features of COPD is oxidative stress. Our DNA microarray analysis using COPD lung tissue as mouse models (□ENaC transgenic mice) suggested an imbalance between oxidants and antioxidants. Uric acid (UA), a product of purine metabolism, is one of the most powerful endogenous antioxidants in the body. Interestingly, recent cohort studies have shown that low serum AU levels are associated with higher levels of COPD. However, the experimental evidence remains inconclusive. To clarify how serum DU levels affect pulmonary COPD phenotypes, we treated □ENaC-Tg mice with oxonate, a pharmacological inhibitor of uricase, which is an enzyme that oxidizes DU in allantoin, to increase the blood concentration of UA in mice. In particular, treatment with oxonate (500 mg / kg / day, po, 4-5 weeks) in □ENaC-Tg mice revealed that the phenotypes typical of COPD, such as emphysema, have been demonstrated by a alteration in mean linear interception (MLI) and lung function (FEV 0.1%), determined by the ventilator-based FlexiVent system, tended to be improved in female but non-male mice treated with oxenate □ENaC-Tg. In addition, 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 lung function in a women-specific manner. We, our studies demonstrate plasma UA as a protective factor for respiratory dysfunction and emphysema in female mice and humans with obstructive pulmonary disease.

Respiratory dysfunction affects quality of life and facilitates the development of chronic non-communicable lung disease such as chronic obstructive pulmonary disease (COPD), a condition characterized by symptoms such as an increase in the average size of the airspace, a decrease in elasticity and a decrease in forced expiratory volume in one second (FEV1) / forced vital capacity (CVF). In general, respiratory dysfunction is associated with the accumulation of oxidative stress, a condition of imbalance between the formation of reactive oxygen species (ROS) and cellular antioxidant capacity due to the increased generation of ROS and / or dysfunction of the antioxidant system, indicating that a decrease in oxidative stress is crucial for the maintenance of pulmonary homeostasis. Consistently, some epidemiological studies have shown that dietary intake of antioxidants delays the decline in lung function in healthy adults. Among the endogenous antioxidants in the epithelial coating fluid (ELF), uric acid (UA) exists in higher concentrations and has the potential role of trapping ROS (e.g., singlet oxygen and hydroxyl radicals). Although DU is a terminal product of purine metabolism in humans and great apes, this is not the case for most mammals; great apes and great apes have lost the enzymatic activity of urate oxidase, or uricase (Uox), which converts AU to allantoin, due to a loss of function during evolution. As a result, the levels of UA in human blood are much higher than in other mammals, such as mice. UA is known as an antioxidant abundant in human blood. In fact, high levels of UA have been reported to be beneficial for central nervous system (CNS) disorders related to oxidative damage. Paradoxically, high plasma AU levels are detrimental to the host due to its ability to be pro-oxidant under certain conditions, thereby increasing not only the risk of gout, but also many diseases linked to oxidative stress. The paradox of AU in respiratory diseases, particularly in COPD, is often discussed in epidemiological studies, but the conclusions are controversial. Horsfall et al. claimed lower AU blood levels were associated with risk of COPD, while others showed higher AU blood levels correlated with exacerbation of COPD

**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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