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Extended Abstract
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COPD 2016: Mechanisms of chronic obstructive pulmonary disease and airway smooth muscle remodeling: Potential roles of ABHD2_Shoude Jin_The Fourth Hospital of Harbin Medical University, China

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Chronic obstructive pulmonary disease (COPD) is a complex multifactorial disease involving both genetic and environmental factors and is one of the leading causes of death worldwide. Although considerable improvements have been made in controlling environmental factors, the morbidity and mortality of COPD continues to increase. In recent years, we have focused on the genetic factors contributing to COPD, starting with the ABHD2 mutations. We found that the ABHD2 gene trap mice spontaneously developed into emphysema. These results strongly suggest the role of ABHD2 mutations in the development of COPD, but the exact mechanisms and whether ABHD2 mutations can be used as warning markers for COPD remain largely unknown. Based on the results according to which ABHD2 is expressed in smooth muscle cells of the respiratory tract, in the next research project, we propose to test our hypothesis that ABHD2 regulates apoptosis of alveolar epithelial type cells at the cellular level and animal and elucidate the effects of specific mutations of ABHD2 on COPD, and use ovalbumin to stimulate ABHD2-deficient mice with a genetic background of COPD and trigger asthma attacks. The goal is to clarify the function and structure of changes in smooth muscle cells in the airways to promote inflammation and remodeling, making it easier for COPD to develop ACOS in mice deficient in Abhd2. Finally, we hope to provide a theoretical basis and potential key drug targets for early detection and early intervention for people at high risk for COPD and identify potential key drug targets and provide new strategies for precise clinical treatment.

The protein 2 gene containing the human □ / □ hydrolase domain (ABHD2) plays an essential role in pulmonary emphysema, a major subset of the clinical entity known as chronic obstructive pulmonary disease (COPD). Here, we evaluated the genetic variation of the ABHD2 gene in a Han Chinese population of 286 COPD patients and 326 control subjects. The rs12442260 CT / CC genotype has been associated with COPD (P <0.001) in a dominant model. In the group of ex-smokers, the rs12442260 TT genotype was associated with a reduced risk of developing COPD after adjustment for age, sex and years of conditioning (p = 0.012). Rs12442260 was also associated with pre-FEV1 (the forced bronchodilator expiratory volume expected in the first second) in the controls (P = 0.027), but with the FEV1 / forced vital capacity (CVF) ratios only in patients with COPD (P = 0.012) under a dominant model. The results of the present study suggest that polymorphisms of the ABHD2 gene contribute to sensitivity to COPD in the Han Chinese population.

The protein 2 gene containing the □ / □ hydrolase domain (ABHD2, MIM612196) is located at 15q26.1 and is a member of the □ / □ hydrolase superfamily which has been identified in a genetic screen of human emphysematous tissue. ABHD2 codes for a protein containing a fold of alpha / beta hydrolase, which serves as a catalytic domain in a wide range of enzymes. Thus, human ABHD2 should have multiple functions in maintaining the structural integrity of the lungs, as observed with mouse Abhd2.

The results of the previous study revealed that the Abhd2 mouse is expressed in vascular smooth muscle cells (SMC) and that increased migration occurs with cultured vascular SMCs from mice deficient in Abhd2. Improved neointimal hyperplasia was observed in mice deficient in Abhd2, using an experimental model of vascular cuff placement injury. Previously, we have used Abhd2-deficient mice obtained by gene trap mutagenesis to examine the role (s) of Abhd2 in the lungs of mice. Our results showed that the disruption of the alveolar metabolism of phospholipids could induce emphysema and that Abhd2 plays an essential role in maintaining pulmonary structural integrity. Recently, Tsuyoshi Yoshida et al. have reported an association between the human ABHD2 gene and colorectal cancer, although the molecular function of ABHD2 in the conduct of colorectal cancer remains unclear. Maryam Shahdoust et al. recruited 13 normal smokers and 9 non-smokers to identify the genes differentially expressed between 2 groups and evaluated the effects of smoking on epithelial cells of the large respiratory tract. Their results showed that ABHD2 was more strongly expressed in smokers than in a control group composed of non-smokers.

The aim of the present study was to investigate whether the mononucleotide polymorphisms (SNPs) in the ABHD2 gene are linked to COPD in the Han Chinese population using a large panel of samples from COPD patients and control subjects.

Biography

Shoude Jin has completed her PhD in 2009 from Chinese Medicine University. She is the Director of the Department of Respiratory Medicine, Academic Leader, Professor and a Tutor of graduate students. Her research direction is chronic obstructive pulmonary disease pathogenesis, diagnosis and treatment of respiratory critical care. She has published more than 20 papers as the first or corresponding author in reputed journals including 8 papers of SCI.

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