Air Pollution Related COPD and the Molecular Mechanism

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Air pollution is the second risk factor, following cigarette smoking, of COPD. In addition to inducing acute exacerbation by acute exposure, long-term exposure to ambient air pollution, particularly fine particulate matter (PM2.5), has been linked to lung function reduction and increased risk of emphysema and COPD. Nevertheless, the underlying mechanisms are poorly understood. Oxidative stress-induced lung inflammation and apoptosis of alveolar and bronchial epithelial cells have been implicated in this process. By using animal models, including an ambient air exposure chamber, we establish the pathogenetic role of PM in inducing emphysema – chronic exposure to PM for 6 months by itself could induce emphysema and airflow limitation. Currently, we provided clinical evidence using our cohorts to show the association of PM exposure with quantitative HRCT-defined emphysema. Through unbiased proteomics studies using the serum, we identified several COPD related molecules, such as inter-alpha-trypsin inhibitor heavy chain 4 (ITIH4), Proteoglycan 4 (PRG4) and beclin 1. Interestingly, ITIH4 was closely associated with air pollution exposure. Our clinical data showed that reduction of ITIH4 in the serum and in the lung tissue were linked to the severity of emphysema. In primary respiratory airway epithelial cells, we found a protective role of ITIH4 in response to air pollution exposure. Reduction of ITIH4 in COPD causes the lung more vulnerable to air pollution- and other environmental stress-induced damage, through JNK-dependent and JNK-independent signaling, leading to excessive bronchial and alveolar cells apoptosis and impairment in lung tissue repair. Through the understanding of the pathogenesis of PM-related COPD, we could establish an insight into the phenotype of PM-related COPD and direct to novel precision therapy.