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Comparison and evaluation of two different methods to establish the cigarette smoke exposure mouse model of COPD

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Animal model of cigarette smoke (CS) –induced chronic obstructive pulmonary disease (COPD) is the primary testing methodology for drug therapies and studies on pathogenic mechanisms of disease. However, researchers have rarely run simultaneous or side-by-side tests of whole-body and nose-only CS exposure in building their mouse models of COPD. We compared and evaluated these two different methods of CS exposure, plus airway Lipopolysaccharides (LPS) inhalation, in building our COPD mouse model. Compared with the control group, CS exposed mice showed significant increased inspiratory resistance, functional residual capacity, right ventricular hypertrophy index, and total cell count in BALF. Moreover, histological staining exhibited goblet cell hyperplasia, lung inflammation, thickening of smooth muscle layer on bronchia, and lung angiogenesis in both methods of CS exposure. Our data indicated that a viable mouse model of COPD can be established by combining the results from whole-body CS exposure, nose-only CS exposure, and airway LPS inhalation testing. However, in our study, we also found that, given the same amount of particulate intake, changes in right ventricular pressure and intimal thickening of pulmonary small artery are a little more serious in nose-only CS exposure method than changes in the whole-body CS exposure method.

Chronic Obstructive Pulmonary Disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation, is usually progressive, and is associated with an enhanced chronic inflammatory response to noxious particles or gases in the airways and the lung. Exacerbations and comorbidities contribute to the overall severity in individual patients[1]. COPD, which is the fourth leading cause of death in the world, now becomes an increasingly important public health challenge. COPD causes fateful chronic morbidity and mortality throughout the world, with many suffering for several decades, and dying prematurely from it, or its complications. Throughout the world, cigarette smoking is the most common risk factor for COPD[1]. Cigarette smokers are far more susceptible to the respiratory symptoms and lung function abnormalities than non-smokers[2].

Pulmonary hypertension (PH) may develop late in the progression of COPD, and its severity is an important factor impacting on the prognosis of patients[3]. As one of the common complications of COPD, PH is mainly due to hypoxic vasoconstriction of small pulmonary arteries, eventually resulting in pathologic changes in structure, including intimal hyperplasia, and later, smooth muscle hypertrophy/hyperplasia[4]. COPD morbidity and mortality are significantly increased by the common occurrence of pulmonary hypertension associated with cigarette smoke[5]. The loss of the pulmonary capillary bed in emphysema may also contribute to the increased pressure in pulmonary circulation[6]. Progressive pulmonary hypertension may lead to right ventricular hypertrophy, and ultimately to right ventricular failure and even death[7].

Cigarette smoke (CS) is the main preventable cause of COPD, resulting in progressive proteolytic inflammatory and pulmonary hypertension. Currently, animal CS exposure models are the most appropriate method for

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