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۴۰ درصد تخفیف نوروزی ویژه کارگاه‌ها و فیلم‌های آموزشی



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Limitation of COPD Studies in Animal Modeling

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Chronic obstructive pulmonary disease (COPD) is a major health problem and cigarette smoke is the main risk factor for the development of COPD. The characteristic changes in airway morphology, inflammatory cell infiltration and mediator expression in COPD may result from direct effects of cigarette smoke (CS) on airway cells. CS causes lung damage through oxidative stress either by itself or due to oxidants released by inflammatory cells that are recruited as a result of smoke-induced injury. CS is a major source of oxidants/free radicals and a complex of over 4,700 chemical compounds. This huge amount of oxidants from CS and those formed endogenously cause an imbalance between oxidants and antioxidants which are considered to be important in the pathogenesis of COPD.

Animal models of disease over many years has contributed much to our understanding of immune and inflammatory mechanisms; however, this research has often failed to translate into man with drugs that are effective in animal models failing in Phase II trials. With this in mind we have to consider how effective the CS model of COPD may be. For example, since mice do not produce mucus in their bronchial tract they cannot represent this aspect of COPD. In addition, in contrast to the variable pathology and different stages of COPD severity in humans, current available animal models of COPD are restricted to mimicking a limited number of characteristic features of COPD which must be born in mind when assessing the clinical utility of these models. Animal models need to be precisely evaluated and conclusions should be drawn based on whether they agree with features of human COPD in order to advance the understanding of mechanisms involved in human COPD.

To date, three major experimental approaches have been described to mimic COPD by inhalation of noxious stimuli, tracheal instillation of tissue-degrading enzymes to induce emphysema-like lesions and gene-modifying techniques leading to a COPD-like phenotype.

The challenge is in the measurement of lung function in very small mammals such as mice. The use of the enhanced pause (Penh) in conscious mice as an indicator of airflow obstruction is not ideal and invasive methods remain the gold standard. These should be correlated with inflammatory markers and airway/tissue remodeling. Considering the complexity of human COPD and species-specific differences in the readouts of the various animal models used, researchers must be aware of the limitations of the models used and their results being of potential clinical benefit. Animal model COPD studies should assess the histopathological patterns and attempt to focus on functional patterns of human COPD such as imaging,

airflow limitation, mucus hypersecretion, chronic cough and exacerbations, and also on pharmacological features such as corticosteroid resistance or diminished β -adrenergic bronchodilator responses.

There are many benefits that can accrue from the development of animal models of disease, the most important of which being the understanding of the fundamentals of immune and inflammatory mechanisms. However, care must be taken in the development of specific drugs for COPD based on these data alone. Recently, animal models of COPD have presented a number of unexpected results, novel ideas, and promising approaches for further research. For example recently we gained evidence for the role of ATP, TLRs and the inflammasome in the pathogenesis of COPD in animal models. These data need to be further confirmed in additional cohorts on COPD patients with relevant disease phenotypes.

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