Targeting Inflammation in Chronic Obstructive Pulmonary Disease (COPD): Hope or Hype

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Chronic Obstructive Pulmonary Disease is a major global burden in terms of health economics, morbidity and mortality. COPD is characterized by marked neutrophilic inflammation which is progressive and poorly reversible. The underlying chronic inflammatory processes results in the complications of COPD viz. obstructive bronchiolitis, mucociliary dysfunction, airway hyper responsiveness and emphysema. Modeling COPD in animals for determining molecular and cellular targets is a complex task because of the associated differences in structural and functional aspects. Till date, corticosteroids and bronchodilators which are the mainstay for the therapy of the disease provide only symptomatic relief. Therefore, there is always a need of exploring novel targets, which can effectively abrogate the progression of the disease. In this context, therapeutic agents with a broad spectrum of anti-inflammatory profile may provide an effective strategy for the treatment of this devastating disease.

Introduction
Chronic obstructive pulmonary disease is defined as, “a disease state characterised by the presence of airflow obstruction due to chronic bronchitis or emphysema; the airflow obstruction is generally progressive, may be accompanied by airway hyper-reactivity, and may be partially reversible.” The World Health Organization estimates that COPD as a single cause of death, shares 4th place with HIV/AIDS (after coronary heart disease, cerebrovascular disease and acute respiratory infection) (www.who.int). COPD is a heterogeneous disorder that encompasses chronic inflammation in small airways and tissue destruction associated with fibrosis, chronic bronchitis and narrowing of small airways (obstructive bronchiolitis) and with lung parenchymal destruction (emphysema) due to the action of various proteases. Mucociliary dysfunction leading to obstructive nature of disease is associated with a decrease in mucus transport due to the damaged cilia, enlargement of the submucosal glands and goblet cell hyperplasia in COPD patients.

The airways of COPD patients experience a marked neutrophilia. COPD is characterized based on the severity of symptoms and progression of the disease. The symptoms include chronic persistent cough, dyspnea, chest tightness and weight loss. Global Obstructive Lung Disease Initiative (GOLD) is an international program on COPD. The objectives of this initiative are mainly to bring the importance of the rising burden of COPD to the attention of the medical community, and the general public and to decrease morbidity and mortality from COPD through implementation and evaluation of effective programs for diagnosis and management. The GOLD classification stratifies COPD patients according to airflow limitation during forced expiration (refer table 1). The risk factors for COPD include predisposing host characteristics such as α-1 antitrypsin deficiency, bronchial hyperresponsiveness or exposure to cigarette smoke and other hazardous chemicals. Amongst these, cigarette smoking is a major cause of COPD in about 90 percent of cases.

COPD - Pathogenesis
The pathologic changes encompassing COPD can be broadly divided into chronic bronchitis (mucus hypersecretion, chronic obstructive bronchiolitis (narrowing of small airways) and emphysema (lung parenchymal destruction) due to the action of various proteinases, such as neutrophil elastase and matrix metalloproteinases (MMPs). Unlike asthma, the airflow limitation in COPD is progressive and is poorly