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New Therapeutic Targets in COPD

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Chronic obstructive pulmonary disease (COPD) is characterized by chronic airway inflammation, mediated by increased expression of inflammatory cytokines such as cytokines, chemokines, adhesion molecules and inflammatory enzymes. Several novel therapeutic approaches for treating inflammation in these diseases have been initiated, such as inhibition of the effects of individual mediators or inhibition of central mechanisms, found in the higher cascade of events. Examples of the latter involve targeting specific transcription factors, such as inhibition of NF-kB or more specific for asthma inhibition of GATA3 function.

Recently, in an animal model for lung emphysema, we have identified a collagen breakdown product (acetyl-proline-glycine-proline; PGP) that can activate and attract neutrophils to the lung and causes lung emphysema via CXCR1 and CXCR2 receptor (Nature Med 2006; 12: 317). PGP levels are increased in COPD patients. A PGP antagonist was able to inhibit all disease symptoms. In another study we showed, that beside IgE mediated mast cell activation, antigen specific immunoglobulin free light chains (FLC), play a role in the pathogenesis of inflammatory diseases by activating the mast cell (Nature Med 2002; 8:694).

In a preclinical model for non-atopic asthma, FLC were found to be of essential importance for the development of clinical symptoms of disease such as airway hyperreactivity, mucosal exudation and local inflammation (PNAS 2005; 102: 1578-1583). FLC concentrations are increased in serum of both allergic and non allergic asthma patients. F991, an FLC antagonist inhibits the clinical symptoms of non-atopic asthma and might be a new agent for the treatment of asthma.