

# Blocking rhinoviral adhesion molecule (ICAM-1): potential to prevent COPD exacerbations

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## Dear editor

Acute exacerbations of COPD (AECOPD) are markers of disease progression and severity, and frequently are used as an outcome variable in interventional studies.<sup>1</sup> AECOPD results in increased severity of symptoms and induces disease progression with accelerated decline in lung function and decreased quality of life. The risk of morbidity and mortality is also significantly increased. Most AECOPD (~85%) have an infectious etiology, induced by bacteria and viruses, often rhinovirus (~50%).<sup>1</sup>

The paper by Johnston et al<sup>2</sup> again emphasized the importance of the common cold and rhinoviruses in AECOPD. They found that cold-like symptoms are a reliable predictor of exacerbations in patients with COPD, occurring in over 80%, although actual viral detection occurred in less than half of these. Notably, the group with virus positivity exhibited more severe symptoms than other groups. They emphasized the need to better understand the relationship between rhinovirus and COPD.

Approximately 60% of human rhinoviruses serotypes adhere to the intercellular adhesion molecule-1 (ICAM-1). Recently, we showed that airway epithelial ICAM-1 expression is upregulated throughout the respiratory tract in smokers, and is further increased in subjects with chronic airflow obstruction (including frank COPD), even when mild. Interestingly, ICAM-1 expression in goblet cells and submucosal glands in the airway wall was also markedly increased. Furthermore, cultured bronchial epithelial cells exposed to cigarette smoke extract exhibited significantly increased levels of ICAM-1, both at mRNA and protein levels.<sup>3</sup> We suggest that such changes in pathogen adhesion sites may explain the increased vulnerability of COPD patients to virally induced exacerbations, which is otherwise essentially unexplained.

The issue of the potential importance of the upregulation of respiratory epithelial adhesion sites as a cause of certain specific bacteria and viruses being able to gain a serendipitous special niche in the airways in COPD needs much more attention, as it may open a potentially new nonantibiotic mode of prevention and treatment.<sup>4</sup> *Haemophilus influenzae* and *Streptococcus pneumoniae* are prominent in respiratory tract infection in smokers/COPD and are also associated with exacerbations. This may well relate to hyper-upregulation of their co-opted major airway epithelial adhesion molecule, the platelet-activating factor receptor. Platelet-activating factor receptor blockers were developed over 20 years ago for the anti-inflammatory treatment of asthma, and proved safe but ineffective; they should now be trialed for this different indication.<sup>5</sup>

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Moreover, the data provided by Johnston et al<sup>2</sup> suggest that an anti-ICAM-1 molecule given at an early stage of a common cold in frequent exacerbations of COPD could potentially have a prophylactic effect against these devastating and expensive events.

## Disclosure

The authors report no conflicts of interest in this communication.

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