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Potential mechanisms of microbial pathogenies in idiopathic interstitial lung diseases (ILD)

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Running head: mechanisms of infections

We read with great interest the review by Dr Natalya Azadeh and colleagues published in *Chest* on the role of infections in idiopathic ILD (1). Mechanisms enhancing infections in chronic respiratory diseases are poorly understood, and wider discussion of new insights into potential mechanisms contributing to bacterial and viral infection vulnerability would be valuable. A fundamental issue is how these pathogens initially adhere to the airway epithelium. We suggest that our recent work on microbial adhesion sites on the airway epithelium in COPD, which might aid the understanding of enhanced infectivity in ILD, and would be an important area of investigation in this context.

We recently published that platelet-activating factor receptor (PAFr) that is potentially an important adhesion site for *Streptococcus pneumoniae* and non-typeable *Haemophilus influenzae* (NTHI) is highly expressed in the airway epithelium of smokers and especially COPD patients and (2, 3). The interaction between these pathogens and the epithelium occurs because these bacteria almost uniquely express ChoP (a molecular mimic of PAF) on their surface (2). Importantly, we also have found that inhaled corticosteroid tends to increase PAFr expression in COPD patients, which might explain why patients on these treatments are at higher risk of pneumococcal infections (2). In a follow up study, we also reported high PAFr expression in the small airway and alveolar epithelium of COPD patients (4). In an *in-vitro* study, we also observed that antagonising PAFr significantly decreased the adherence of both pneumococci and NTHI to pulmonary epithelium (3). We also reported recently that the intracellular adhesion molecule-1 (ICAM-1), an adhesin for most human rhinoviruses, as well as NTHI, is upregulated in COPD airways (5).

Similar to COPD, ILD patients are frequently smokers or ex-smokers, and undergo acute exacerbations in which bacterial and/or viral infections are implicated, but there is little understanding of mechanisms involved. It is again possible that PAFr and ICAM-1 might be up-regulated on respiratory epithelium to provide key adhesion sites, which could explain at least some of this increased susceptibility. However, little if any work has been done on these microbial adhesins in ILD, in spite of a lot of interest in bacterial/viral colonisation. We feel that this deficiency needs to be rectified, as again it could have substantial translational therapeutic implications. Thus, lessons we are beginning to be learned in COPD research that might be applicable to other lung conditions including idiopathic ILDs.

References

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