



# *Rothia mucilaginosa* is an anti-inflammatory bacterium in the respiratory tract of patients with chronic lung disease

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**A commensal bacterium of the lower airways, *Rothia mucilaginosa*, inhibits inflammation by NF- $\kappa$ B pathway inactivation. *R. mucilaginosa* abundance inversely correlates with sputum pro-inflammatory markers in chronic lung disease, indicating a beneficial role.** <https://bit.ly/3INT9th>

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## Abstract

**Background** Chronic airway inflammation is the main driver of pathogenesis in respiratory diseases such as severe asthma, chronic obstructive pulmonary disease, cystic fibrosis (CF) and bronchiectasis. While the role of common pathogens in airway inflammation is widely recognised, the influence of other microbiota members is still poorly understood.

**Methods** We hypothesised that the lung microbiota contains bacteria with immunomodulatory activity which modulate net levels of immune activation by key respiratory pathogens. Therefore, we assessed the immunomodulatory effect of several members of the lung microbiota frequently reported as present in CF lower respiratory tract samples.

**Results** We show that *Rothia mucilaginosa*, a common resident of the oral cavity that is also often detectable in the lower airways in chronic disease, has an inhibitory effect on pathogen- or lipopolysaccharide-induced pro-inflammatory responses, *in vitro* (three-dimensional cell culture model) and *in vivo* (mouse model). Furthermore, in a cohort of adults with bronchiectasis, the abundance of *Rothia* species was negatively correlated with pro-inflammatory markers (interleukin (IL)-8 and IL-1 $\beta$ ) and matrix metalloproteinase (MMP)-1, MMP-8 and MMP-9 in sputum. Mechanistic studies revealed that *R. mucilaginosa* inhibits NF- $\kappa$ B pathway activation by reducing the phosphorylation of I $\kappa$ B $\alpha$  and consequently the expression of NF- $\kappa$ B target genes.

**Conclusions** These findings indicate that the presence of *R. mucilaginosa* in the lower airways potentially mitigates inflammation, which could in turn influence the severity and progression of chronic respiratory disorders.

