Defective bacterial phagocytosis is associated with dysfunctional mitochondria in COPD macrophages

Kylie B.R. Belchamber[1], Richa Singh[1], Craig M. Batista[1], Moira K. Whyte[2], David H. Dockrell[2], Iain Kilty[3], Matthew J. Robinson[4], Jadwiga A. Wedzicha[1], Peter J. Barnes[1] and Louise E. Donnelly[1] on behalf of the COPD-MAP consortium

Affiliations: [1]Airway Disease, National Heart and Lung Institute, Imperial College London, London, UK. [2]MRC Centre for Inflammation Research, University of Edinburgh, Edinburgh, UK. [3]Inflammation and Immunology Research Unit, Pfizer Inc, Cambridge, MA, USA. [4]MedImmune, Cambridge, UK.

Correspondence: Louise E. Donnelly, National Heart and Lung Institute, Guy Scadding Building, Dovehouse Street, London, SW3 6LY, UK. E-mail: l.donnelly@imperial.ac.uk

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ABSTRACT Increased reactive oxygen species (ROS) have been implicated in the pathophysiology of chronic obstructive pulmonary disease (COPD). This study examined the effect of exogenous and endogenous oxidative stress on macrophage phagocytosis in patients with COPD.

Monocyte-derived macrophages (MDMs) were generated from non-smoker, smoker and COPD subjects, differentiated in either granulocyte macrophage-colony stimulating factor (G-Mφ) or macrophage-colony stimulating factor (M-Mφ). Alveolar macrophages were isolated from lung tissue or bronchoalveolar lavage fluid. Macrophages were incubated in ±200 μM H_2O_2 for 24 h, then exposed to fluorescently labelled *Haemophilus influenzae* or *Streptococcus pneumoniae* for 4 h, after which phagocytosis, mitochondrial ROS (mROS) and mitochondrial membrane potential ($\Delta\Psi$m) were measured.

Phagocytosis of bacteria was significantly decreased in both G-Mφ and M-Mφ from COPD patients compared with from non-smoker controls. In non-smokers and smokers, bacterial phagocytosis did not alter mROS or $\Delta\Psi$m; however, in COPD, phagocytosis increased early mROS and decreased $\Delta\Psi$m in both G-Mφ and M-Mφ. Exogenous oxidative stress reduced phagocytosis in non-smoker and COPD alveolar macrophages and non-smoker MDMs, associated with reduced mROS production.

COPD macrophages show defective phagocytosis, which is associated with altered mitochondrial function and an inability to regulate mROS production. Targeting mitochondrial dysfunction may restore the phagocytic defect in COPD.