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Title: Increased susceptibility of M2 monocyte-derived macrophages from COPD patients to oxidative stress

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Body: Chronic obstructive pulmonary disease (COPD) is associated with colonisation of the lower airways with bacteria including Haemophilus influenzae (HI) and Streptococcus pneumoniae (SP), and increased numbers of highly activated lung macrophages (mϕ) with reduced phagocytic ability. Mϕ may exist as M1-like (classically-activated, pro-inflammatory) or M2-like (alternatively-activated, anti-inflammatory) states. In COPD, M1 mϕ may be more prevalent leading to pro-inflammatory conditions in the lung. To test this monocyte-derived mϕ from non-smokers (NS), smokers (S) and COPD patients were cultured in GM-CSF (G-mϕ, M1-like) or M-CSF (M-mϕ, M2-like) for 12 days (n=3-6). Mϕ were exposed to oxidative stress via treatment with 1-200 μM H_2O_2 for 24 h after which phagocytosis of fluorescently labelled inert beads, or heat killed H.influenzae (HI) or S.pneumoniae (SP) was measured fluorimetrically. In all groups, M- mϕ displayed higher phagocytic capacity than G- mϕ ($p<0.05$).

Percentage of phagocytosis of non-treated control (100%). * $p<0.05$

	M2			M1		
	Healthy	Smoker	COPD	Healthy	Smoker	COPD
Beads	98±5	107±8	76±11	93±16	126±28	85±8
HI	109±12	79±12	*65±14	83±3	92±11	82±16
SP	80±21	82±5	74±6	83±13	122±14	98±10

Data are mean±SEM, n=3-6

In M-mϕ from COPD patients, oxidative stress caused a concentration-dependent reduction in phagocytosis of HI ($p<0.05$ at 200μM). This was not seen in smokers and non-smokers. In G-mϕ, oxidative stress had no significant effect. M-mϕ from COPD patients were more susceptible to oxidative stress than G-mϕ which may contribute to their reduced presence in the lung. This abnormality in M-mϕ should be further studied to

elucidate the mechanisms behind this effect. Funded by COPDMAP.