Lack of macrophage plasticity in COPD

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Body: COPD is associated with increased numbers of highly-activated lung macrophages (mφ) with reduced phagocytic ability. Mφ may exist as M1-like (classically-activated) or M2-like (alternatively-activated) states. In COPD, M1-like mφ may persist, and not respond to the environment. 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 12d (n=6-12). Media was switched for 6d and mφ stimulated with LPS. TNFα and IL-10 were measured by ELISA (n=2-3). Beads, H.influenzae (HI) or S.pneumoniae (SP) phagocytosis was measured fluorimetrically (n=10), CD163 and CD16 by FACS (n=3). All G-mφ released similar levels of TNFα and IL-10. Switching to M-CSF, TNFα release decreased in NS and S, but not COPD whereas IL-10 increased in NS but not S and COPD (Table 1). M-mφ from NS and S released less TNFα vs COPD but more IL-10. Switching to GM-CSF, IL-10 decreased in all mφ (Table 1).

LPS-stimulated cytokine release

Bead phagocytosis was similar by all mφ. G-mφ phagocytosed less HI and SP vs M-mφ in all groups (50%, p<0.05). All COPD mφ phagocytosed ~45% less HI and SP vs NS, and expressed less CD163 and CD16. Culturing G-mφ in M-CSF, increased phagocytosis of HI (400%) and SP (200%) in NS vs S and COPD. Culturing M-mφ in GM-CSF, HI and SP phagocytosis was less in all mφ. COPD mφ appear...
“hyper-inflammatory” regardless of environment suggesting lack of plasticity. Altering COPD mϕ plasticity may be a therapeutic target.