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Title: Lectins improve efferocytosis via changes to cytoskeletal remodeling: Relevance to COPD

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Body: We have shown that the defective ability of alveolar macrophages (AM) to phagocytose apoptotic cells (efferocytosis) in COPD could be therapeutically improved using mannose binding lectin (MBL) although the exact mechanisms are unknown. A further lectin, galectin-3, is also known to regulate macrophage phenotype and function, via interaction with its receptor CD98 (an 'M2' mediator). We hypothesized that defective expression of MBL and galectin/CD98 would be associated with defective efferocytosis in COPD via effects on cytoskeletal remodeling and macrophage phenotype. Galectin-3 was measured by ELISA in BAL from controls, smokers and current/ex-smokers with COPD. CD98 was measured on AM using flow cytometry. We assessed the effects of MBL and galectin-3 on efferocytosis, CD98, actin polymerisation, rac activation, and the involvement of PI3K (using β-actin probing and wortmannin inhibition) in vitro using human AM. A significant decrease in galectin-3 was observed in BAL from smokers and COPD subjects vs controls. Galectin 3 and MBL increased efferocytosis via an increase in active GTP bound Rac1. This was confirmed with β-actin probing and the role of PI3k was confirmed using wortmannin inhibition. The increased efferocytosis was associated with increases in available glutathione and expression of CD98. We provide evidence for a role of airway lectins in the failed efferocytosis in COPD, supporting their further investigation as potential macrophage-targeted therapies.