activator Forskolin and the phosphodiesterase 4 (PDE4) inhibitor Roflumilast (all 1μm, 3d) was evaluated. IL-1β (2ng/ml, 24hr) was used for cyclooxygenase 2 (COX-2) induction. β-smooth muscle actin (α-SMA, a myofibroblast marker), COX-2, EP2, EP4 and β2-receptor expression was analysed by Western blotting and immunochemistry, respectively. Adenylyl cyclase mRNA was measured by qPCR and cAMP was measured by radioimmunoassay.

**Results**

F-IPF showed increased α-SMA and collagen expression and repressed COX-2 expression compared to F-NL. PGE2, treatment prevented TGF-β1-induced α-SMA expression and COX-2 repression in F-NL, which was mimicked by β2-agonists and Forskolin. PGE2 also reduced α-SMA expression and increased COX-2 expression in F-IPF despite that it induced significantly less cAMP than in F-NL. This effect on F-IPF was not mimicked by β2-agonists and Forskolin as they induced even less CAMP than PGE2 in these cells. TGF-β1-treated F-NL also produced less CAMP than untreated cells in response to these cAMP stimulants. However, the expression of EP2, EP4, β2-adrenoceptors and adenylyl cyclase isosforms was similar in F-NL and F-IPF. Furthermore, combination of PGE2 with Roflumilast showed greater effect than PGE2 alone on α-SMA reduction and COX-2 expression in F-IPF and F-NL, whereas Roflumilast alone had no effect.

**Conclusions**

CAMP is a key anti-fibrotic regulator of myofibroblast differentiation. However, CAMP production in myofibroblasts is defective, probably due to increased degradation by PDE4.

**Conclusions** Exogenously delivered macrophages are preferentially retained in injured lung and show potential as vehicles to target therapeutic transgenes by localising to damaged areas. Whilst KGF-transduced macrophages induced epithelial proliferation in vitro, any protective effects in vivo may have been negated by the exacerbatory effects of macrophage delivery. Future work will determine whether ex vivo manipulation of macrophage phenotype can confer therapeutic benefit.

**Occupational lung disease**

**S131** **IDENTIFYING OCCUPATIONAL ASTHMA AMONG A COHORT OF CLEANERS IN THE NORTH EAST ENGLAND**

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**Introduction** We have demonstrated a prevalence of asthma of 14% in a survey of 1400 UK hospital and university cleaners, and an estimated incidence of asthma of 3.3/1000 person-years. 26% of cleaners reported work-related symptoms. We have explored the possibility that these cleaners have occupational asthma using serial measurements peak expiratory flow (PEF) and airway responsiveness.

**Objectives** To identify occupational asthma in a cohort of cleaners.

**Methods** A respiratory symptom questionnaire was distributed among 1400 cleaners working in three local hospital trusts and two universities. Airway responsiveness (PD20) was measured in those with asthma symptoms using a methacholine challenge test. Those with measurable airway responsiveness (PD20 <1600ug) were invited to undergo a repeat measurement away from work and to carry out serial PEF measurements. ‘Of these, 56 (33.5%) attended for methacholine challenge testing. 26 (46%) had quantifiable results.

12 subjects underwent serial PD20 measurements at and away from work. Overall, there were no significant changes in airway responsiveness. Geometric mean PD20 at work was 193 ug and away from work was 254 ug (t=0.6; p=0.5). 5 cleaners showed a 3-fold or more increase in PD20 away from work raising the possibility of significant changes in those individuals.

10 subjects completed serial peak expiratory flow measurements. The mean OASYS score was 1.97. One subject had a score of >2.5 suggesting a work related effect.

**Conclusion** Although the prevalence of asthma symptoms in our cohort is consistent with other epidemiological evidence showing a 1.5 to 2.0 fold risk of asthma, we found little evidence of occupational asthma using conventional clinical diagnostic tests in this group. The findings are consistent with the hypothesis that cleaners develop their asthma in an unusual way, possibly though a low dose irritant mechanism.


**S132** **CHRONIC BRONCHITIS, PULMONARY FUNCTION, AND OCCUPATIONAL EXPOSURE IN FRAMINGHAM HEART STUDY**

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**Introduction** Chronic obstructive pulmonary disease (COPD), a common cause of morbidity and mortality, has been linked to occupational hazards. Previous research has suggested that cigarette smoking is an important risk factor for COPD, but little is known about the role of occupational exposures.

**Objectives** To determine if occupational exposure is a risk factor for COPD.

**Methods** The Framingham Heart Study is a prospective cohort study of 5209 male and female subjects who were examined biennially between 1948 and 2007. The participants underwent annual surveys of smoking status, and COPD was diagnosed by the use of standardized smoking and health questionnaires. The study also included repeat surveys of spirometry, and scores for forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were calculated. The occupational cohort was defined as those individuals who reported working in an occupation related to air pollution, dust, or biological agents.

**Results** The occupational cohort had a significantly lower mean FEV1/FVC ratio and a higher prevalence of COPD than the non-occupational cohort. A significant interaction was found between smoking and occupational exposure, with a stronger effect of smoking in the occupational cohort. The OR of COPD for those in the occupational cohort who were currently smoking was 12.9 (95% CI 7.1–23.7), compared to 4.0 (95% CI 3.0–5.2) for those in the non-occupational cohort.

**Conclusion** Occupational exposure is a risk factor for COPD, and the effect of smoking is stronger in those exposed. This finding has important implications for the prevention and control of COPD.