

an allogeneic mixed-lymphocyte reaction (MLR). Lymphocyte proliferation (flow-cytometric measurement of CFSE) and cytokine production (multiplex bead array) were assessed at day 5. The proportion of lymphocytes primed to produce IFN γ was measured at day 7 (intracellular staining).

Results UPM-stimulation increased DC expression of the maturation marker CD83 ($p = 0.0038$) and chemokine receptor CCR7 ($p = 0.0018$). It had no effect on CD40 or MHC Class I expression. UPM-stimulation of DCs also significantly increased CD8 lymphocyte proliferation ($p = 0.020$), and the production of IFN γ , TNF α and IL-13 by CD8 lymphocytes in MLR at day 5 (all $p < 0.05$; Table 1). The proportion of CD8 lymphocytes primed to produce IFN γ was also increased by UPM-stimulation of DCs ($p = 0.034$).

Conclusion No evidence of an impaired Tc1 response was seen with UPM-stimulated DCs, in contrast to our previous findings with CD4 T lymphocytes. This may be because CD8 lymphocytes are more primed to respond and produce cytokines at baseline. However, UPM-treatment of DCs did significantly increase DC expression of CCR7, which directs DCs to lymph nodes, and increased the priming of Tc1 and Tc2 responses in the absence of any other stimulation. Inhalation of UPM may give rise to pathological CD8 responses to otherwise innocuous novel antigens.

S49 TELOMERE ATTRITION IN CIRCULATING WHITE BLOOD CELLS IN COPD RELATES TO LUNG FUNCTION AND OUTCOMES

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Introduction Increasing evidence suggests accelerated ageing as a pathogenic mechanism in COPD.

Methods and results Telomere length in circulating WBC, a marker of biological ageing, was assessed in 200 ex-smoker COPD patients (108 male, age 61.5 ± 6.4 years, FEV₁ $45.6 \pm 17.1\%$ predicted), 50 ex-smokers with normal lung function (27 male, age 59.9 ± 7.3 years, FEV₁ $109.1 \pm 13.4\%$ predicted) and 50 non-smoker healthy subjects (27 male, age 59.3 ± 8.3 years, FEV₁ $113.2 \pm 13.1\%$ predicted). TL was assessed by qPCR and expressed as relative T/S ratio.

TL was shorter in COPD (0.77 ± 0.2 relative T/S ratio) than in both ex-smokers (0.83 ± 0.2 relative T/S ratio) and non-smokers (0.84 ± 0.2 relative T/S ratio) ($p < 0.05$). Furthermore TL correlated negatively with age ($r -0.17$, $p 0.007$), emphysema score ($r -0.217$, $p 0.001$), number of exacerbations in the previous year to inclusion in the study ($r -0.129$, $p 0.04$), number of hospitalisations over 3 years follow-up ($r -0.167$, $p 0.004$) and positively with FEV₁ ($r 0.135$, $p = 0.03$) and arterial oxygen saturation ($r 0.161$, $p 0.01$).

Conclusion COPD patients have evidence of premature ageing (shortened TL) compared to normal subjects irrespective of their smoking history. TL relates to FEV₁, SatO₂, exacerbation rate and hospitalisations.

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S50 AIRWAY SMOOTH MUSCLE INFLAMMATION IS CONTROLLED BY MICRORNA-145 TARGETING OF SMAD3 IN COPD

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Introduction and objectives Airway smooth muscle cells (ASMCs) may contribute to the pathological airway inflammation and remodelling in COPD through the secretion of inflammatory cytokines and increased proliferation. Our previous work demonstrated that ASMCs from patients with COPD release greater amounts of IL-6 and CXCL8 compared to those from healthy subjects and are in a state of hyperproliferation. MicroRNAs (miRNAs) have recently emerged as important homeostatic regulatory molecules in COPD, and we have previously demonstrated the role of these in controlling ASMC proliferation in asthma. We hypothesise that microRNA-145 (miR-145) controls the aberrant phenotype observed in ASMCs from patients with COPD by targeting SMAD3, an important downstream signalling molecule of the TGF- β pathway.

Methods Human primary ASMCs were grown from individuals classified as being healthy non-smokers, healthy smokers, or those with COPD ($n = 9$ per group). Cells were stimulated with TGF- β and foetal calf serum, and miRNA and mRNA expression levels were measured by RT-PCR. IL-6 and CXCL8 release was measured by ELISA. Transfection of miR-145 mimics and inhibitors were used to model the effects of miR-145 over-expression and knock-down, respectively.

Results Low concentrations of TGF- β significantly upregulated SMAD3 expression in ASMCs from patients with COPD. Higher concentrations of TGF- β led to a suppression of SMAD3 expression, with a concomitant increase in miR-145 expression in these cells, to a greater degree than in healthy subjects.

Inhibiting miR-145 in ASMCs from COPD patients reduced the increased IL-6 and CXCL8 release and proliferation back to levels comparable to that of healthy individuals.

Conclusions This is the first time that miR-145 has been demonstrated to be important in controlling the increased inflammatory state of ASM cells from COPD patients. This miRNA may not only act as a novel biomarker for COPD, but may also be a novel target for treatment.

S51 CIRCULATING DESMOSINE RELATES TO CARDIOVASCULAR COMORBIDITY, CORONARY ARTERY CALCIFICATION SCORE (CACS), SYSTEMIC INFLAMMATION AND MORTALITY IN PATIENTS WITH COPD

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