

Conclusions ASM cells express a number of PRMTs at mRNA and protein levels. PRMT1 associates with a number of chemokine and cytokine promoters after TNF- α stimulation. PRMTs may have an important role in regulating chemokine production from ASM cells in asthma, and are a promising target for future investigations in asthma.

P237 LUNG FUNCTION DECLINE IS ASSOCIATED WITH SERUM PERIOSTIN LEVEL BUT NOT FRACTIONAL EXHALED NITRIC OXIDE OR BLOOD EOSINOPHILS IN SEVERE ASTHMA

AH Mansur, V Mitchell, J Sullivan, K O'Shea, L White. *Heart of England NHS Trust, Birmingham, West Midlands*

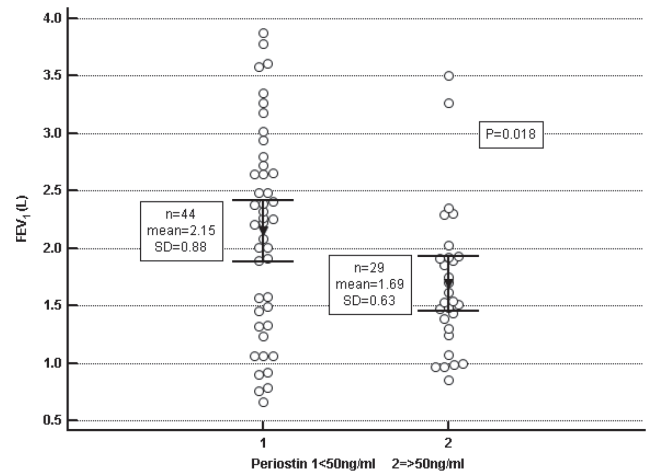
10.1136/thoraxjnl-2016-209333.380

Background In the airways, periostin encoded by the POSTN gene is up-regulated by IL13-IL4-TGF- β axis. It is produced by structural cells such as epithelial cells and fibroblasts and inflammatory cells such as eosinophils and macrophages. Consequently it has been linked to airways remodelling, mucus production and subepithelial fibrosis. However, an association between periostin and lung function impairment in severe asthma has not been confirmed.

Methods Unselected patients attending severe asthma centre were clinically characterised using systematic protocol and undergone lung functions, serum periostin, fraction exhaled nitric oxide (FeNO) and peripheral blood eosinophils (PBE) measurement. Correlation analysis and one way analysis of variance were undertaken to explore the relationships.

Results 127 patients consented to the study (mean age 45.5 yrs [range 17–70], 88 [69%] females), 72/103 (69%) were atopic. The mean FEV1 was 2 L, mean%predicted FEV1 68.1, and mean FEV1/FVC ratio was 71.3. The mean inhaled daily corticosteroids dose was 1.65mg/day and 56.3% were on maintenance oral corticosteroids. Periostin measurement was available in 78 patients who had a mean level of 49.5 ng/L (SD \pm 18.1). Using 50 ng/L as a cut-off point, 30/78 (36%) patients had high periostin and 48/78 (62%) had low periostin. The mean FEV1 in the periostin high group was 1.69 L Compared to 2.15 L in the low group ($p = 0.018$) (see Figure). We also observed significant correlation between serum periostin and% predicted FEV1 ($r = 0.36$, $p = 0.0017$). In contrast the association analysis between FeNO and PBE with FEV1 were both non-significant ($p = 0.8$ and $p = 0.35$ respectively).

Conclusion Raised serum periostin is associated with low lung function in this cohort of severe asthma but not FeNO or BPE. Further research is required to confirm this relation and explore the role of periostin as predictor of decline in lung function and airway remodelling.



Abstract P237 Figure 1 Periostin and FEV1

P238 INVESTIGATING GENOME WIDE DNA METHYLATION IN AIRWAY SMOOTH MUSCLE CELLS FROM ASTHMATIC AND NON-ASTHMATIC DONORS

¹RL Clifford, ¹JK Patel, ¹DE Shaw, ¹AJ Knox, ²MS Kobar. ¹Division of Respiratory Medicine and Nottingham Respiratory Research Unit, University of Nottingham, Nottingham, UK; ²Centre for Molecular Medicine and Therapeutics, Child and Family Research Institute, Vancouver, Canada

10.1136/thoraxjnl-2016-209333.381

Rationale Genetic mechanisms fail to fully explain asthma pathogenesis and environmental factors are considered to play an important role. Environmental factors may lead to permanent changes in epigenetic patterns and contribute to asthma. Epigenetics is the study of heritable changes in gene expression that are not due to changes in DNA sequence. DNA methylation is a reversible modification of DNA structure in which a methyl group is added to cytosine residues. Parental smoking affects the methylation of buccal cell DNA from children and children with early onset wheeze have an altered blood DNA methylation profile to healthy individuals. No studies have compared DNA methylation profiles in the disease relevant cell type of airway smooth muscle (ASM) cells.

Methods DNA was isolated from ASM cells at passage 5 and bisulphite treated to convert epigenetic information into sequence-based information. Site specific, quantitative genome wide methylation was determined using the Illumina 450K Infinium Methylation BeadChip array. Hits were validated by Pyrosequencing. RNA was extracted simultaneously for mRNA expression analysis by real time PCR.

Results There were no independent CpG sites associated with asthmatic status of ASM cells following multiple test correction. Without correction over 13000 CpG sites showed a significant difference in methylation (linear modelling, p value >0.05)

between asthmatic and non-asthmatic cells, and a biologically relevant difference in methylation of greater than 10% (β value >0.1). 10 of these sites were selected as top hits. 7 sites positively validated by pyrosequencing. They were associated with 7 different genes; LGALS3BP, ATP11A, ZNF696, KLF6, TBX1, RUNX3, and SPINT2. Expression of these genes was measured in ASM cells isolated from asthmatic and non-asthmatic donors. LGALS3BP expression was undetectable while ATP11A and ZNF696 displayed no difference in expression between cells from asthmatic and non-asthmatic donors. KLF6 and SPINT2 showed a trend towards increased expression in cells from asthmatic donors while RUNX3 and TBX1 showed a trend towards decreased expression.

Conclusions Differences in CpG methylation exist between ASM isolated from asthmatic and non-asthmatic donors. Future work will focus on identifying differentially methylated regions of DNA and further defining the association to gene and protein expression.

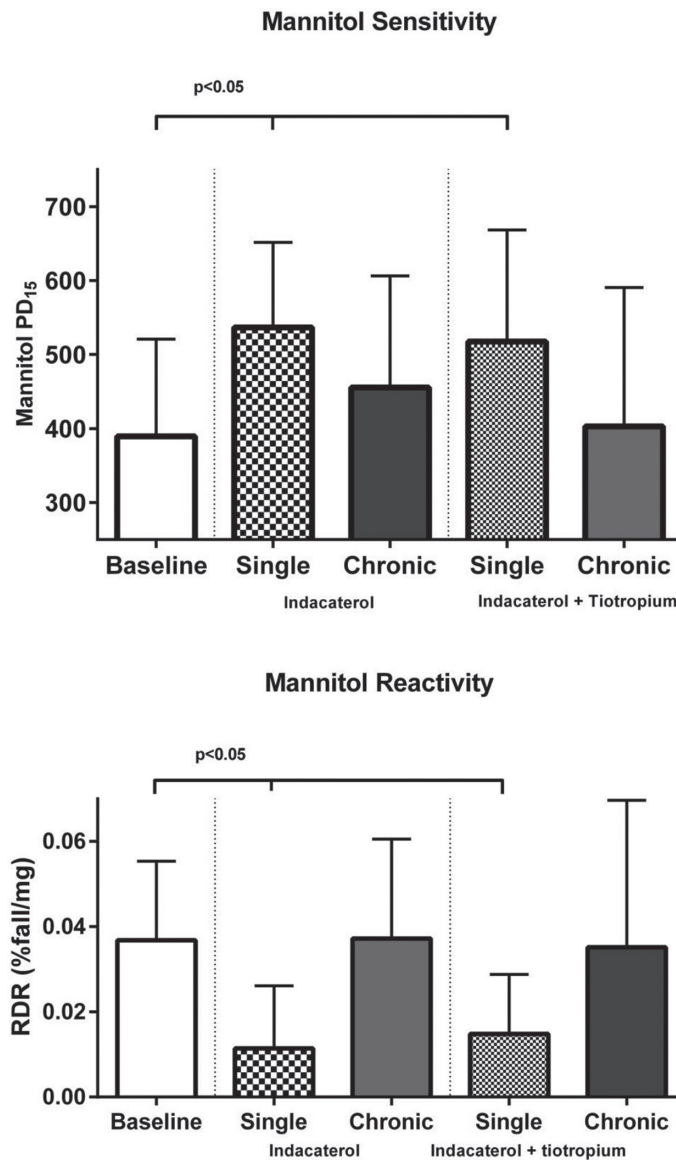
P239 EFFECTS OF TIOTROPIUM ON ASTHMA EXACERBATIONS ARE NOT EXPLAINED BY AIRWAY HYPERRESPONSIVENESS, EXHALED BREATH NITRIC OXIDE OR AIRWAY GEOMETRY

S Jabbal, A Manoharan, BJ Lipworth. *Scottish Centre for Respiratory Research, Dundee, UK*

10.1136/thoraxjnl-2016-209333.382

Background Long acting muscarinic antagonists (LAMA) such as tiotropium (TIO) reduce asthma exacerbations in patients receiving inhaled corticosteroids and long-acting beta-agonists (ICS/LABA). However the mechanism for this protective action of LAMA remains unclear.

Objectives To evaluate the response to indacaterol (IND) either alone in combination with tiotropium (IND/TIO) in addition to ICS on airway hyperresponsiveness (AHR), FeNO and impulse oscillometry (IOS).



Abstract P239 Figure 1 Effects of randomised treatment compared to baseline on mannitol sensitivity and reactivity. Values presented as geometric mean and 95% confidence interval. P value denotes significant difference for randomised treatment compared to baseline. There was also a significant difference between single and chronic dosing for RDR with both treatments.