repeated NTM isolation. Treatment success remains unsatisfactory due to side effects.

This study aimed to explore host factors in patients with NTM isolates and to review treatment completion.

Methods Single region retrospective analysis of patients with NTM isolates from pulmonary source from 2012 to 2017. Comparison was made considering the following factors: age, gender, lung function, autoimmune profile, immunoglobulin levels, immunosuppression, and the presence of cardio-respiratory comorbidities.

Treatment completion was checked through clinic notes. Cases were mapped to explore geographical spread.

Results 90 cases were analysed, 51 females (57%), median age is 72 (IQR 65–78). The commonest co-morbidities were Bronchiectasis (48%), COPD (28%), and Asthma (13%).

The median of forced expiratory volume measured in 1 s (FEV1) was 71% (IQR 48%–87%), 9 patients (10%) had abnormal immunoglobulin levels, 6 (7%) had positive autoimmune screen and only 6 (8%) were immunosuppressed.

At least 13 subspecies were identified. The commonest were Mycobacterium Avium Complex species in 60% cases, then Mycobacterium Chellonae (10%).

4 NTM species were isolated from cases with valvular heart disease. 2 of them had previous aortic valve replacement. One case was of Mycobacterium Chimaera linked to cooler heater units used in aortic valve replacement.

Geographical variation of species and their frequency showed no connection between them.

34 of the NTM cohort (38%) were deemed clinically significant and were started on treatment. Of those, only 9 (26%) completed NTM regime. Further 11 (32%) remained on treatment at time of data analysis while 14 (41%) were intolerant to treatment. At least 19 (56%) of the treated cohort reported side effects.

Conclusion Our data shows that most NTMs were grown from immunocompetent patients with good lung function. Side effects are big barriers to treatment success.

Further work is needed to ascertain treatment success and correlate treatment completion with improvement in lung function and patient-reported measures of quality of life and functional capacity.

Mucosal and microbial drivers of asthma

S27 ADAM33 KNOCKOUT MICE HAVE AN ALTERED METABOLIC TRANSCRIPTIONAL PROFILE IN RESPONSE TO HOUSE DUST MITE WHEN COMPARED TO WILD TYPE MICE

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Rationale *ADAM33* is an asthma susceptibility gene that plays a role in both airway remodelling and susceptibility to allergic airways disease. To study the role of ADAM33 in asthma we have exposed an *Adam33* Knockout (KO) mouse to a house dust mite (HDM) sensitisation and challenge protocol. We have found that these mice exhibit less remodelling, bronchial hyperresponsiveness (BHR) and eosinophilic inflammation than wild type (WT) mice (ER Davies et al., JCI-Insight 2016), however the mechanisms which contribute to this protective phenotype are not well understood.

Methods To study how the response to HDM is altered by loss of *Adam33* we challenged WT and KO mice with HDM or saline and took whole lung RNA samples for next generation RNA sequencing (RNAseq). Gene set enrichment analysis was used to identify pathways and gene ontology terms associated with the differential response to HDM between KO and WT mice.

Results Control WT and KO mice were found to have very similar gene expression profiles at baseline (5 differentially expressed genes, including *Adam33*, FDR $p<0.05$). Differential expression analysis comparing WT saline to HDM treated mice identified the transcriptional profile of the 'normal' response to HDM. The KO response demonstrated a degree of similarity with the WT response (62% of up-regulated genes, 51% of down-regulated gene), including upregulation of hallmark asthma genes *IL13*, *IL5* and *Ccl11*. However, there were also distinct groups of genes modulated only in the WT or the KO in response. Further analysis of the genes identified a predominantly metabolic gene signature, with a particular emphasis on oxidative phosphorylation, where components of the mitochondrial electron transport chain were modulated in opposing directions in the HDM-challenged WT and KO mice.

Discussion The alteration in the pulmonary metabolic gene signature may underpin a shift in immune cell activation and/or modification of smooth muscle energy expenditure during airway contraction. These changes may explain why the KO mouse is protected from both allergic responses and BHR. Further work will aim to identify the source of the different metabolic behaviour at a cellular level and to assess oxidative stress in lungs of normal and Adam33 KO mice.

S28 ADAM33 KNOCK-OUT IS PROTECTIVE AGAINST POST-NATAL AIRWAY HYPERRESPONSIVENESS CAUSED BY MATERNAL ALLERGY

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Background Maternal allergy is a strong risk factor for developing asthma and airway hyperresponsiveness (AHR). *ADAM33* has been identified as an asthma susceptibility gene and is associated with AHR and impaired lung function in early life. Our aim was to investigate the effects of maternal murine allergic airway inflammation on the lungs of offspring before and after birth. We hypothesised that the effects of maternal allergy will be modified in *Adam33* knock out (KO) compared to wild-type (WT) offspring.

Methods Allergic airway inflammation in pregnant heterozygous ($Adam33^{\pm}$) mice was induced by exposure to house dust mite (HDM) through intranasal challenges during pregnancy. Control mice were challenged with saline. WT ($Adam33^{+/+}$)