Conclusions Loss of BMPR-II predisposes to both an abnormal increase in IL-6 and IL-8 after stimulation with LPS and a dysfunctional response to these cytokines in PASMCs and mice. The mechanism for this involves loss of antioxidant function. This abnormal response may underlie the additional lung-specific trigger that promotes the development of PAH in patients with BMPR-II mutations, and may represent a target for future therapeutic interventions.

S102 THE CROSSTALK OF PDE INHIBITOR WITH BMP SIGNALLING PATHWAY IN HUMAN PULMONARY ARTERIAL SMOOTH MUSCLE CELLS

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Rational Sildenafil, a potent PDE inhibitor, is an established treatment for PAH. However, the detailed mechanism of its effects on the proliferation of human pulmonary artery smooth muscle cells (hPASMCs) remains unclear.
Objective Because sidenafil is effective treatments for clinical PAH, we hypothesised that these agents enhance Smad1/Id signalling through cGKI in hPASMCs.
Methods and Results Sildenafil alone has no effect on Smad1 phosphorylation and Id1 gene expression in hPASMCs, However in the presence of BMP4 Sidenafil indeed enhanced BMP-induced phosphorylation of Smad1/5 and Id1 expression in a cGMP/cGKI-dependent manner in hPASMCs. The presumed mechanism is by elevation of intracellular cGKI activity which modulate smad1 phosphorylation and nuclear localisation. Knock down cGKI or use pharmalogical cGMP inhibitor abrogate the effect of Sildenafil on hPASMCs. Furthermore we confirm the rescued pSmad1 signal and elevated proliferation inhibitory effect in hPASMCs from familial pulmonary arterial hypertension patients by Sildenafil.
Conclusions Sildenafil enhance BMP/Smad through cGMP/cGKI pathway to modulate hPASMCs proliferation.

Clinical studies in bronchiectasis

S103 MICROBIAL COMMUNITY COMPOSITION IN THE LUNGS OF PATIENTS WITH CYSTIC FIBROSIS AND NON-CF BRONCHIECTASIS

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Introduction and Aims Persistent bacterial infection is a major cause of morbidity and mortality in patients with both Cystic Fibrosis (CF) and non-CF Bronchiectasis (non-CFBX). Numerous studies have shown that CF and non-CFBX airways are colonised by a complex microbiota. However, many bacteria are difficult, if not impossible, to culture by conventional laboratory techniques. Therefore, molecular detection techniques offer a more comprehensive view of bacterial diversity within clinical specimens. The objective of this study was to characterise and compare bacterial diversity and relative abundance in patients with CF and non-CFBX during exacerbation and when clinically stable.
Methods Sputum samples were collected from CF (n=50 samples) and non-CFBX (n=52 samples) patients at the start and end of treatment for an infective exacerbation and when clinically stable. Pyrosequencing was used to assess the microbial diversity and relative genera (or the closest possibly taxonomic order) abundance within the samples. Each sequence read was defined based on 3% difference.
Results High-throughput pyrosequencing allowed a sensitive and detailed examination of microbial community composition. Rich microbial communities were apparent within both CF (171 species-level phylotypes *per* genus) and non-CFBX airways (144 species-level phylotypes *per* genus). Relative species distribution within those two environments was considerably different; however, relatively few genera formed a core of microorganisms, representing approximately 90% of all sequences, which dominated both environments. Relative abundance based on observed operational taxonomic units demonstrated that the most abundant bacteria in CF were *Pseudomonas* (28%), *Burkholderia* (22%), *Streptococcus* (13%), family *Pseudomonadaceae* (8%) and *Prevotella* (6%). In contrast, the most commonly detected operational taxonomic units in non-CFBX were *Haemophilus* (22%), *Streptococcus* (14%), other (unassigned taxa) (11%), *Pseudomonas* (10%), *Veillonella* (7%) and *Prevotella* (6%).
Conclusions These results suggest that distinctive microbial communities are associated with infection and/or colonisation in patients with both CF and non-CFBX. Although relatively high species richness was observed within the two environments, each was dominated by different core taxa. This suggests that differences in the lung environment of these two diseases may affect adaptability of the relevant bacterial taxa.

S104 THE CULTURE MICROBIOME IN THE LUNGS OF PATIENTS WITH COPD

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Introduction and Aims Previous studies have shown that the lungs of Cystic Fibrosis (CF) and bronchiectasis (BE, not caused by CF) patients are colonised by a range of aerobic and anaerobic bacteria. As bacteria are also implicated in the pathogenesis and progression of chronic obstructive pulmonary disease (COPD), this study aimed to determine the culture microbiome of the COPD airways.
Methods Samples were collected from 13 stable COPD patients during routine bronchoscopy. Bronchial washings were taken at a single location in the right middle lobe by flushing and removing 30 ml of sterile saline. Samples were cultured under strict anaerobic conditions with bacteria detected by plating on both selective and non-selective agar media and quantified by total viable count (TVC). Identification of the cultured bacteria was performed by amplification and subsequent sequencing of the 16sRNA gene.
Results Mean FEV_1 was 1.36 (range 0.84–2.26, mean per cent predicted FEV_1, 54%), and the mean ratio (FEV_1/FVC) was 51%. Bacteria were detected in 12/13 samples (92%) with bacteria from the genera *Streptococcus* [12/13 samples, 92%; mean (range) TVC 9.62×10^5 cfu/ml (1.50×10^3–1.42×10^7)] and *Haemophilus* [4/13 samples, 31%; mean (range) 6.40×10^4 cfu/ml (2.20×10^3–1.60×10^5)] most frequently detected. Anaerobic bacteria primarily from the genera *Prevotella* [8/13 samples, 62%; mean (range) TVC 1.12×10^4 cfu/ml (1.30×10^3–4.20×10^4)] and *Veillonella* [5/13 samples, 38%; mean (range) TVC 1.29×10^5 cfu/ml (4.20×10^3–3.60×10^5)] were also detected. *Pseudomonas* and *Moraxella* were not detected in any samples.
Conclusions Our results show that bacteria from the genera *Streptococcus, Haemophilus, Prevotella and Veillonella* are frequently present the airways of patients suffering from COPD. Taking account of the