serving >400 patients, to establish prevalence and potential risk factors for infection.

Methods Sputum samples were obtained from 100 randomly selected CF outpatients and sent for routine microbiology and *PJ* DNA PCR assay at enrolment, subsequent visits, and pulmonary exacerbations requiring intravenous antibiotics within 4 months. Data were recorded for demographics, co-morbidities symptom score, spirometry, inflammatory markers, and prophylactic or recent therapeutic antibiotic therapy. Univariate comparisons were made between sputum *PJ* positive and negative patients. Chi square tests were used for categorical comparisons and independent sample t-tests for continuous independent variables.

Results Of the 100 patients, 4 of 100 had a positive sputum *PJ* PCR at baseline. 50 patients had a routine follow up sample between 1 and 4 months: 2 were positive for *PJ*. 22 patients had a sputum sample analysed at the onset of a pulmonary exacerbation of which 1 was positive for *PJ*. Hence, a total of 7 of 100 patients had a single positive sample by PCR for *PJ*. No patient has had >1 positive sample. None of the baseline parameters were significantly different between PJ positive and PJ negative patients at the level p

Conclusion These results suggest that *PJ* is not an important infecting pathogen in this UK cohort of CF patients. This may be due to frequent use co-trimoxazole for pulmonary exacerbations and high prevalence of prophylactic macrolide antibiotic therapy at our centre compared to other published studies. These preliminary data were underpowered to accurately compare baseline characteristics between PJ positive and PJ negative patients.

P202 STUDYING THE RELATIONSHIP BETWEEN MATRIX METALLOPROTEINASES AND LUNG TISSUE DAMAGE DURING A CLINICAL EXACERBATION OF CYSTIC FIBROSIS

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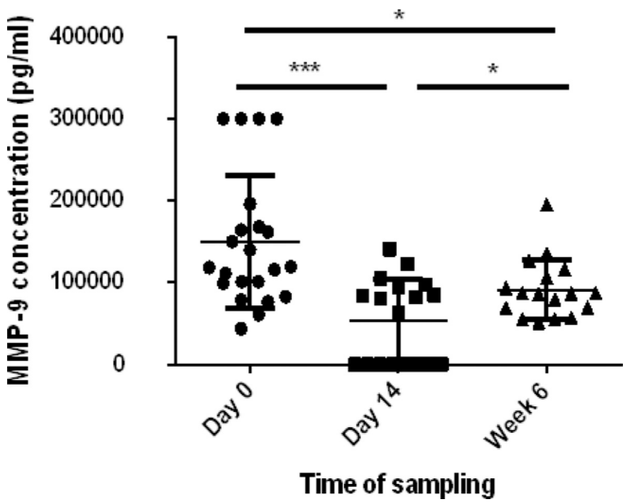
Background Cystic Fibrosis (CF) is the commonest fatal autosomal recessive condition of Caucasians. The lung in CF is characterised by chronic bacterial colonisation, inflammation, and lung tissue destruction. Matrix Metalloproteinases (MMPs) are proteases that are expressed in inflammatory states that degrade lung matrix. Whilst MMPs are known to be raised in many inflammatory lung conditions, their role in CF is poorly understood.

Aims The study aimed to compare lung function and MMP levels throughout an exacerbation.

Methods Sputum samples and clinical information were obtained with written consent from 23 adult subjects with CF. Samples were collected at day 0, day 14 and week 6 of an exacerbation of CF. Samples were frozen, before Luminex bioassay and IL-8 ELISA was performed. The sputum concentration of MMP 1, 2, 3, 7, 8, 9,10,12,13 and IL-8 were measured.

Results A statistically significant increase in IL-8 concentration (pg/ml) occurred between day 14 and week 6 ($p = 0.0387$). The concentration of MMP-9 decreased from day 0 to day 14 ($p = 0.006$), and then rose significantly between day 14 and week 6 ($p = 0.0412$). However, the concentration of MMP-9 at week 6 was significantly less than at day 0 (0.0453). A significant decrease in the concentration of MMP-8 occurred between day 0 and day 14 ($p = 0.0124$); and between day 0 to week 6 ($p = 0.0426$).



Abstract P202 Figure 1 The sputum concentration of MMP-9 (pg/ml) at sample time. Values at 3000 represent values above the level of detection. Significant values are represented with a line and an asterix (*). A significant decrease in MMP-9 concentration was found between Day 0 and Day 14 ($p = 0.006$). An increase in MMP-9 concentration was seen between day 14 and week 6 ($p = 0.0412$). There was a statistically significant decrease in MMP-9 concentration between day 0 and week 6 ($p = 0.0453$)

Conclusions MMPs and other inflammatory markers are raised during exacerbations, and fall with treatment. High proteolytic activity may lead to a worsening lung function and contribute significantly to structural changes within the CF lung. Furthering our understanding of this diverse group of proteases could lead to potential novel therapeutic targets which could help prevent irreversible lung damage.

P203 DEVELOPMENT OF AN OPTIMAL F/HN PSEUDOTYPED SIV VECTOR FOR CF GENE THERAPY

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We are developing lung gene transfer vectors to treat acquired and inherited lung disorders such as cystic fibrosis, and have identified two platforms for efficient respiratory gene delivery: one non-viral system based on CpG-free plasmid DNA combined with cationic lipids (pDNA/GL67A), which has recently completed evaluation in a Phase IIb clinical study; and one novel viral system based on a recombinant simian immunodeficiency virus pseudotyped with the F/HN proteins of Sendai virus (rSIV.F/HN) to promote airway cell uptake. Here we report on the development of a "third generation" rSIV.F/HN vector suitable for use in the clinic. The vector is manufactured by transient transfection of cultured human cells using five producer plasmids, all of which have been engineered to be pharmacopoeia compliant. A variety of vector configurations, including a range of enhancers/promoters and transgenes, were evaluated in a panel of airway models. rSIV.F/HN vectors directed high-level, robust gene expression in fully differentiated human airway cells,