Haemophilus influenzae and Staphylococcus aureus. Opsonisation with ficolin-2 promoted phagocytosis of P. aeruginosa (PA01) by human neutrophils in a MASP-2 but not c1q dependent manner (<p>0.0001) (Abstract T2 figure 1). On multivariable analysis chronic bacterial colonisation (OR=3.5; <p>0.0001) and particularly P. aeruginosa colonisation (OR=2.8; <p>0.0001) were independently associated with ficolin-2 insufficiency. These patients also had more frequent outpatient exacerbations (mean 3.2/yr vs 2.4/yr, <p>0.01) and unscheduled hospital admissions for exacerbations (OR=2.3; <p>0.0001).

Conclusion Single nucleotide polymorphisms in the ficolin-2 gene affecting serum levels and carbohydrate binding are associated with non-CF bronchiectasis and increase susceptibility to colonisation with P. aeruginosa.

Introduction and Objectives Eosinophils are major cellular effectors of allergic inflammation and represent an important therapeutic target in asthma. While much is understood about the generation and activation of eosinophils, little is known about their intravascular kinetics and physiological fate. The purpose of this study was to determine eosinophil kinetics and physiological fate. The purpose of this study was to manipulate eosinophils margination/uptake eosinophils were purified using plasma-Percoll gradients and anti-CD16 immunomagnetic beads, labelled with 111-Indium-tropolonate and re-injected. Blood was sampled 0.75–72 h post-injection. Neutrophils and eosinophils were isolated in parallel, and cell-associated radioactivity was measured. To image sites of eosinophil clearance to baseline by 40 min, with some early accumulation in the liver at 1 and 2 h, and re-appearance in circulating blood, suggesting the liver as a possible site of transient eosinophil sequestration.

Conclusions This work provides the first in vivo measurements of eosinophil kinetics in healthy volunteers. Our data suggest that 111-In-labelled-eosinophils can be used to monitor the organ distribution and fate of eosinophils non-invasively. This technique may have an important role in assessing the therapeutic effects of eosinophil-targeted drugs.

Prize symposium

T4 SAFETY AND EXPRESSION OF A SINGLE DOSE OF LIPOID-MEDIATED CFTR GENE THERAPY TO THE UPPER AND LOWER AIRWAYS OF PATIENTS WITH CYSTIC FIBROSIS

doi:10.1136/thoraxjnl-2011-201054a.4

1G Davies, 2C Davies, 3D R Gill, 4S C Hyde, 5C Boyd, 6A J Innes, 7D J Porteous, 8H Cheng, 9K Scheule, 10H Higgins, 11U Griesenbach, 12E W F W Alton. Imperial College, London, UK; 1University of Oxford, Oxford, UK; 1University of Edinburgh, Edinburgh, UK; 2Genzyme Corporation, Massachusetts, USA; 3Fibrosis Gene Therapy Consortium, UK

Introduction and Objectives We undertook a clinical trial of non-viral CFTR gene therapy assessing safety, dose and transgene expression in preparation for a Multi-dose trial (MDT) designed to assess clinical efficacy.

Methods A single nebulised and/or nasal dose of plasmid CFTR (pGM169)/GL67A was delivered to patients aged ≥16 years with a baseline FEV1 >60% predicted. Clinical and laboratory parameters were measured at intervals until day 28. A cohort of patients also underwent pre- and post-dosing (day 6 or 14) bronchoscopies for functional (airway potential difference (PD)) and molecular (QRT-PCR) evidence of vector-specific CFTR expression. Patients receiving a nasal dose underwent brushing for QRT-PCR and serial nasal PD measurements.

Results 35 patients received a nebulised dose of 20 ml (n=17), 10 ml (n=10) or 5 ml (n=8). A short-lived, dose-related drop in FEV1 was observed over the next 6 h (mean [SD]: 20 ml 25.7 [10.2]%, 10 ml 17.7 [9.9]%, 5 ml 13.0 [4.4]%) of baseline. Subjects also experienced a systemic inflammatory response which was similarly dose-related and generally limited to the first 24–48 h post-dosing. A cohort of 6 patients (4@10 ml; 2@5 ml) received 4 g paracetamol over an 18 h period post-dosing; none of these patients developed a fever. Intriguingly, these subjects also appeared to have reduced systemic inflammatory responses. Molecular (mRNA) evidence of gene transfer was observed in some individuals from upper or lower airway brushings. On lower airway PD measurement, the majority of patients showed an increase towards non-CF values after nebulised gene therapy. 19 patients received a 2 ml nasal dose and 11 (58%) had some response in chloride secretion on nasal PD. In the two most positive individuals, responses were within the normal (non-CF) range and persisted to days 63 and 91, respectively.

Conclusions We consider the side effects after 20 ml nebulised dose excessive for repeated application. Those at 10 and 5 ml were more acceptable. Gene expression was confirmed in some patients, and restoration of CFTR function to the non-CF range has been observed out to 15 weeks following a single nasal dose. These data support progression of this agent to MDT.

Funding UK CF Trust.

T5 THE KCa3.1 K+ CHANNEL MEDIATES WOUND HEALING IN HUMAN MYOFIBROBLASTS

doi:10.1136/thoraxjnl-2011-201054a.5

1K M Roach, 2W Coward, 3C Feghali-Bostwick, 4S M Duffy, 5R Bradling. 1University of Leicester, Leicester, UK; 2University of Nottingham, Nottingham, UK; 3Department of Medicine, Division of Pulmonary, Allergy, and Critical Care Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

Idiopathic pulmonary fibrosis (IPF) is a common progressive interstitial lung disease and current treatments are ineffective. The Ca2+-activated K+ channel KCa3.1 modulates the activity of several structural and inflammatory cells which play important roles in model diseases characterised by tissue remodelling and fibrosis. We hypothesise that KCa3.1-dependent cell processes are a common denominator in IPF. We have therefore examined KCa3.1 expression and function in human myofibroblasts derived from patients with IPF and non-fibrotic controls (NFC). IPF tissue was obtained from diagnostic lung biopsies, and NFC tissue from healthy lung removed...