

elucidated. We hypothesised that Pellino1 would play a critical role in regulating the inflammatory response in the lung airway epithelium. Pellino1 was knocked down in the human bronchial airway epithelial cell line BEAS2B and primary human bronchial epithelial cells (PBECs) using targeted siRNA. Knockdown of Pellino1 at the transcriptional level was measured using qPCR. Pellino1 knockdown cells were stimulated with Toll-like receptor/IL-1R agonists or the natural pathogen rhinovirus 1B (RV1B) and cytokine release was measured using ELISA. Signalling pathways were explored by western blotting. Pellino1 was expressed in BEAS2B and primary bronchial epithelial cells. Pellino1 mRNA transcript level was knocked down by 78% in BEAS2B and 94% in PBECs. Pellino1 knockdown led to reduced IL-8 generation in response to IL-1 $\beta$  and a viral mimic Poly (I:C) stimulation in BEAS2B, however RANTES production was unchanged. In contrast to the BEAS2B, the primary bronchial epithelial cells exhibited preserved IL-1 signalling. However, these cells also showed a reduction in IL-8 production in response to both Poly (I:C) stimulation and RV1B infection. Pellino1 knockdown had no effect on the interferon-stimulated gene RANTES production. Pellino1 knockdown leads to reduced IL-8 production in response to a viral mimic Poly (I:C) in lung airway epithelial cells and RV1B in PBECs. These data indicate that Pellino1 regulates proinflammatory responses in airway epithelium and may be a feasible target to downregulate neutrophilic airway inflammation while retaining antiviral immunity, which would be highly beneficial in the treatment of chronic airway inflammatory disorders such as asthma and COPD. These studies were supported by an MRC/Asthma UK PhD studentship.

## ILD: clinical studies

### S133 THE ASSESSMENT OF HEALTH RELATED QUALITY OF LIFE IN INTERSTITIAL LUNG DISEASE WITH THE KING'S BRIEF INTERSTITIAL LUNG DISEASE QUESTIONNAIRE (K-BILD)

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**Introduction** The King's brief interstitial lung disease questionnaire (K-BILD) is a recently developed and validated 15 item HRQOL questionnaire comprising of 3 health domains (psychological, breathlessness and activities, and chest symptoms) and an overall HRQOL score. We set out to evaluate HRQOL in a large group of

Abstract S133 Table 1 The relationship between the HRQOL assessed with the K-BILD and lung function

	Psychological	Breathlessness and activities	Chest symptoms	Total score
FEV <sub>1</sub> % predicted	r=0.34 p<0.01	r=0.46 p<0.01	r=0.38 p<0.01	r=0.43 p<0.01
FVC % predicted	r=0.32 p<0.01	r=0.45 p<0.01	r=0.38 p<0.01	r=0.42 p<0.01
TLCO % predicted	r=0.41 p<0.01	r=0.48 p<0.01	r=0.35 p<0.01	r=0.46 p<0.01
CPI	r=0.36 p<0.01	r=0.44 p<0.01	r=0.35 p<0.01	r=0.42 p<0.01

Data shown are Spearman's correlation coefficients.  
CPI, Composite physiologic index.

patients with interstitial lung diseases (ILD's) and determine the factors that influence it.

**Methods** 219 patients with ILD (60 idiopathic pulmonary fibrosis (IPF), 81 connective tissue associated ILD, 23 idiopathic non-specific interstitial pneumonitis (NSIP), 21 hypersensitivity pneumonitis, 10 organising pneumonia, 24 other) attending ILD clinics at King's College and Royal Brompton Hospitals completed the K-BILD. The K-BILD Scores range from 0 to 100, with a higher score representing a better HRQOL. Demographic data, immunosuppressant medication, long-term oxygen therapy use, multi-disciplinary team ILD diagnosis and lung function were recorded.

**Results** Patients had a mean (SEM) age of 60 (1) years, 75% of patients were Caucasian, 60% were females, mean (SEM) VC% predicted was 80 (24) % and TLCO % predicted was 47 (18)%. HRQOL was impaired in all domains, mean (SEM) scores: psychological 62 (2), breathlessness and activities 43 (2), chest symptoms 67 (2), total 59 (2). There were no significant associations between overall HRQOL and age ( $r=-0.007$ ) or gender ( $p=0.13$ ). There was a modest correlation between HRQOL and lung function (Abstract S133 table 1). HRQOL was significantly lower in IPF patients compared to other ILD's (total score 51 (3) vs 62 (2);  $p<0.01$ ), those with UIP pattern vs NSIP (total score 51 (3) vs 62 (3);  $p<0.01$ ) and those prescribed long-term oxygen therapy (total score 38 (4) vs 63 (2);  $p<0.01$ ). IPF patients prescribed immunosuppressant medication had significantly worse overall HRQOL (48 (4) vs 74 (8);  $p=0.02$ ). There was no significant difference between CTD-NSIP patients compared with idiopathic NSIP (total score 62 (3) vs 62 (5);  $p=0.91$ ).

**Conclusions** HRQOL is impaired in patients with ILD. The type of ILD, immunosuppressant medication, and lung function all influence HRQOL. This study provides further clinical validation of the K-BILD.

### S134 HIGH PREVALENCE OF ISCHAEMIC HEART DISEASE (IHD) IN PATIENTS MEETING CLINICO-RADIOLOGICAL PROFILE FOR IDIOPATHIC PULMONARY FIBROSIS (IPF)

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**Introduction** IPF and ischaemic cardiac disease may share pathological similarities including aberrant tissue remodelling. Given their recognised heterogeneity, we hypothesised that patterns of IPF (usual interstitial pneumonia, UIP; non-specific interstitial pneumonia, NSIP; indeterminate UIP-NSIP) may inter-relate differently with the prevalence of IHD and associated co-morbidities.

**Methods** Ethical approval was obtained to identify all cases of IPF undergoing high-resolution CT between 2003 and 2010. Details of cardiac disease and its management (risk factors, drug treatment, coronary angiography and revascularisation) were included. Consensus radiological diagnoses were reached by 2 chest physicians and 2 thoracic radiologists. Comparison of multiple variables was undertaken using logistic regression (STATA V.11).

**Results** Of 256 potentially suitable cases, 96 fulfilled ascertainment and were consented: 38 (40%) UIP, 44 (48%) NSIP and 14 (16%) indeterminate (INDET) pattern. An inter-observer k coefficient of 0.56 was calculated for radiological agreement. Regardless of morphological pattern, patients with IPF had a significant cardiovascular risk profile. Where present, IHD predated IPF in the majority of cases, with the highest occurrence (58%) in the UIP subgroup. UIP patients were of comparable age, gender frequency, smoking status and had similar rates of major cardiovascular risk factors as NSIP and INDET subjects. Crucially, they were 2.5 times more likely than NSIP patients to have IHD after adjustment for

Abstract S134 Table 1

	Honeycombed IPF profile		Non-honeycombed IPF profile	
	UIP	NSIP	NSIP	Indeterminate pattern
n	38	44	44	14
Male	29 (76%)	29 (66%)	29 (66%)	9 (64%)
Female	9 (24%)	15 (34%)	15 (34%)	4 (36%)
Age (median)	76 (range 49–90)	74 (54–90)	74 (54–90)	77 (65–91)
FVC % pred. (mean)	83.0% (n=34)	83.3% (n=40)	83.3% (n=40)	82.6% (n=12)
DL <sub>CO</sub> % pred. (mean)	47.6% (n=30)	50.9% (n=35)	50.9% (n=35)	48.8% (n=10)
Smoking status				
Never	11 (29%)	18 (41%)	18 (41%)	6 (43%)
Ex	26 (68%)	25 (57%)	25 (57%)	8 (57%)
Current	1 (3%)	1 (2%)	1 (2%)	0
Body mass index, BMI (median)	26.3 (17.6–45.7)	29.1 (22.3–42.9)	29.1 (22.3–42.9)	26.6 (19.3–34.4)
Ischaemic heart disease (IHD)	22/38 (58%)	18 (41%)	18 (41%)	7 (50%)
IHD diagnosed pre-IPF	18/22 (82%)	12/18 (67%)	12/18 (67%)	6/7 (86%)
IHD diagnosed post-IPF	4/22 (18%)	6/18 (33%)	6/18 (33%)	1/7 (14%)
ST elevation myocardial infarction	8 (21%)	5 (11%)	5 (11%)	1 (7%)
CABG (bypass grafting)	4 (10.5%)	6 (13.6%)	6 (13.6%)	4 (30.8%; n=13)
Cerebrovascular ischaemia (TIA or infarct (CVA))	7 (18%)	2 (4.5%)	2 (4.5%)	0
Statin use at time of IPF diagnosis	20 (53%)	23 (52%)	23 (52%)	8 (57%)
Cardiovascular co-morbidities				
Diabetes mellitus (DM)	9 (24%)	13 (30%)	13 (30%)	3 (23%; n=13)
Hypertension (HTN)	27 (71%)	29 (66%)	29 (66%)	9 (69%)
Hypercholesterolaemia	20 (53%)	24 (55%)	24 (55%)	9 (69%)
Surgical lung biopsy rate	4/38 (11%)	10/44 (23%)	10/44 (23%)	3/14 (21%)

key determinants of smoking, gender, DM, HTN, hypercholesterolaemia and BMI. On univariate analysis, BMI was significantly higher in the NSIP subgroup ( $p=0.025$  vs UIP or INDET). Rates of STEMI and strokes were highest in UIP cases (n/s) whereas that of CABG was highest in the INDET subgroup. These observations were corrected for IPF severity in so far as FVC and DL<sub>CO</sub> were decreased comparably across all three radiological subgroups. Evaluation of co-existing COPD was not undertaken; however, mean FEV<sub>1</sub> did not differ between groups.

**Conclusions** Amongst patients with clinical IPF, UIP morphology correlates with the highest risk of cardiovascular morbidity compared to NSIP. A tendency for ischaemic heart disease to precede IPF in the majority of cases suggests the possibility that broader systemic or cardiac-specific factors may influence the pathogenesis of these pulmonary disorders.

### S135 A RETROSPECTIVE MULTI-CENTRE STUDY OF THE EFFECTS OF ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION ON PULMONARY FUNCTION

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**Introduction** Allogeneic haematopoietic stem cell transplantation (HSCT) is often complicated by serious pulmonary complications including severe infections, drug toxicity and graft vs host disease. However, there is limited data on the prevalence of significant lung function defects in long-term survivors.

**Method** We undertook a UK wide, multi-centre, retrospective study of the effects on pulmonary function in adult patients undergoing HSCT over a 4-year period. Pulmonary function tests (PFT) were evaluated at baseline (pre-transplant) and 12 months post-transplant. Impaired pulmonary function was defined as FEV<sub>1</sub> or FVC less than 80% predicted.

**Results** 532 allogeneic HSCTs were registered in the BSBMT database, having been performed at 6 centres over the 4-year study period. 157 patients underwent PFT pre-HSCT and at least 6 months post-BMT, with 12-month data available for 90 patients (Abstract S135 table 1). The median age was 42 years (range 18–69) and 59% of patients were male. Median FEV<sub>1</sub> and FVC were 98.9% and 101% predicted respectively for patients pre-HSCT, with 25 (15.9%) patients having impaired lung function pre-HSCT. For patients with normal PFT pre-HSCT, 13 (10%) had impaired PFT at 12 months with median reduction in FEV<sub>1</sub> of 1.33 L (33.5%) (range 0.59–2.25) and FVC of 1.29 L (28.9%) (range 0.17–3.33). 38% had obstructive, 46% restrictive and 15% mixed picture spirometry pattern. 69% of patients with newly impaired PFT had acute graft vs host disease, ( $p=0.068$ ). No statistically significant predictive factors were identified for newly impaired PFT: age, sex, total body irradiation, Alemtuzumab treatment, transplant intensity and type of donor. For patients with impaired PFT at baseline, 11 (44%) remained impaired at 12 months with no significant fall in spirometry values (median FEV<sub>1</sub> fell 2% and FVC rose 2%).

Abstract S135 Table 1 PFT data pre and 12 months post-HSCT

PFT	Normal PFT n	Impaired PFT n	Median FEV <sub>1</sub> Litres (% predicted)	Median FVC Litres (% predicted)
Pre-transplant (baseline)	132	25	3.33 (98.9)	4.25 (101)
At 12 months				
Normal	63	3	3.26 (98.9)	4.16 (105.5)
Impaired	13	11	2.36 (67.5)	3.38 (72.3)
Died	3	0	NA	NA
Unknown	53	11	NA	NA

**Conclusion** Although these data represent only a proportion of patients undergoing allogeneic HSCT, we found 10% of patients developed impaired PFT at 12 months with large falls in FEV<sub>1</sub> and FVC. These data suggest there may be as many as 60 to 120 HSCT recipients each year developing major impairment of lung function. Multi-centre prospective studies are required to fully characterise the frequency and risk factors for impaired PFT post-HSCT.

### S136 THE ASSOCIATION BETWEEN COUGH REFLEX SENSITIVITY AND SERUM ACE LEVEL IN PATIENTS WITH SARCOIDOSIS

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**Introduction** Up to 80% of patients with sarcoidosis report a chronic cough. The aim of this study was to investigate whether heightened cough reflex sensitivity (CRS) is an important mechanism and to