vs. high grade dysplasia (HGD- severe dysplasia (SD) and carcinoma-in-situ). A lesion was considered to have progressed/regressed if it crossed between groups (LGD, HGD, invasive cancer).

Results A total of 117 separate lesions that were biopsied on more than one occasion were identified of which 61 were HGD and 56 LGD. Of the low grade lesions 54/56 (96%) regressed or remained static, 1 (2%) progressed to CIS and 1 (2%) to invasive carcinoma both of these lesions progressed from moderate dysplasia. Of the high grade lesions there were 13 SD and 48 CIS, overall 35/61 (57%) of HGD progressed to invasive cancer 9/61 (15%) regressed and 17/61 (28%) remained static. There was a trend toward higher progression to cancer (62% vs 56%) and lower rates of regression (8% vs. 17%) for SD versus CIS in the HGD cohort although the numbers are too small to be statistically significant (see fig. 1). In the HGD group median time to invasion was 9.5 months (range 3–49), static lesions were documented to have remained as such for a median of 17 months (range 4–60).

Conclusions In our cohort we see very few lesions following the traditional stepwise progression and LGD remains relatively indolent. There is a significant proportion of HGD that progresses to invasive cancer and further studies are required to test the role of endobronchial intervention to prevent progression and to determine the most efficacious modality of treatment.

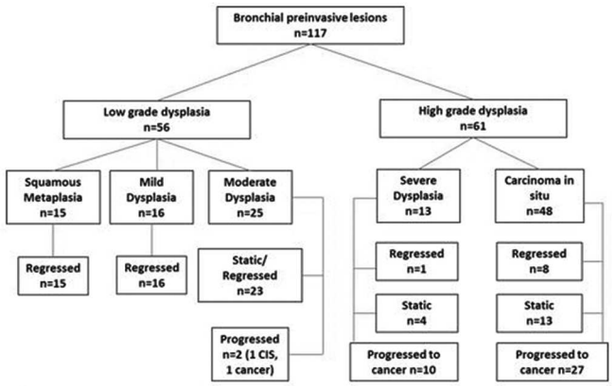

Figure 1. Flow diagram showing progressive vs regressive lesions stratified according to initial histology.

Abstract S129 Figure 1.

S130 ROLE OF CADM1 IN SQUAMOUS CELL CARCINOMA PROGRESSION

S Vallath, EK Sage, VH Teixeira, SM Janes, A Giangreco; *Lungs for Living, Div. of Medicine, UCL, London, UK*

10.1136/thoraxjnl-2013-204457.137

Introduction Lung cancer is the second most common cancer in the UK with about 42,000 people being diagnosed in 2010 alone (Office of National Statistics, 2012). With a tendency to form invasive metastases coupled with its frequent late stage diagnosis, lung cancer attributes to the largest cause of cancer related mortality worldwide. Despite advances in treatment and care, the five-year mortality rate remains at 90%. There is a desperate need to improve patient survival, which can be achieved partly through improved screening techniques and more importantly by expanding our understanding of the molecular changes associated with lung cancer development and progression.

We investigate the role of a tumour suppressor gene, first identified in lung cancer, tumour suppressor in lung cancer 1 (TSLC1) or cell adhesion molecule 1 (Cadm1) in regulating squamous cell carcinoma (SqCC) growth and metastases.

Methods Cadm1 expression levels were examined using q-PCR analysis on human pre-invasive airway and normal lung tissue collected as part of an on-going UCL/CRUK longitudinal-tracking study (Lung-Surveillance and Lung-SEARCH trials). Cadm1 was introduced into an established SqCC cell line (A431) and *in vitro* functional assays performed to investigate its effect on tumour growth, progression and invasion. Pre-clinical mice models were used to study the effect of Cadm1 expression in tumour growth and metastatic potential.

Results q-PCR analyses demonstrated that loss of Cadm1 expression is a frequent early event in pre-invasive human airway compared to normal tissue ($p = 0.001$). Functional assays using A431, with Cadm1 reintroduced, showed Cadm1 expression levels directly associated with a significant decrease in cell proliferation ($p = 0.001$) over 10 days and significant reduction in invasion ($p = 0.001$) over 72 hours compared to control A431 cells without Cadm1. Pre-clinical xenograft tumourigenecity experiments in mice showed that Cadm1 expression significantly inhibited tumour growth ($p = 0.01$) together with a significant reduction in the number of metastases observed ($p = 0.01$) when compared with the control group.

Conclusion These data suggest that restoration of Cadm1 expression in human squamous cell carcinomas play an important role in regulation of tumour growth and metastasis. Understanding the mechanism through which Cadm1 expression is able to modulate cancer progression maybe therapeutically beneficial.

S131 IRON CHELATION REDUCES LUNG CANCER PROLIFERATION IN VITRO

J Kay, G McNab, P Newby, M Bedford, A Turner; *University of Birmingham, Birmingham, United Kingdom*

10.1136/thoraxjnl-2013-204457.138

Introduction There is growing evidence that iron plays an important role within the lung cancer, the leading cause of cancer-related mortality worldwide. As a result of this, iron homeostasis has potential as a new avenue for targeting and treatment of lung cancer. In this study, the effect of iron loading on cellular proliferation and iron homeostasis gene expression was investigated. In addition, the effect of the chelator deferasirox on cellular iron levels and proliferation rates was studied.

Methods Cellular proliferation was assessed by the BrdU assay and cellular iron levels were assessed using the ferrozine assay. Manipulation of *IREB2* gene expression was achieved using short interfering RNA (siRNA) and subsequent expression of this and other iron homeostasis genes was assessed using real time PCR. All experiments were carried out on both the A549 adenocarcinoma and QG56 squamous cell carcinoma cell lines in triplicate. Primary bronchial epithelia cells (PBEC) were used as reference of normal behaviour.

Results A dose of 150uM of iron was seen to cause a significant increase in proliferation in both the A549 (50% increase) and QG56 (40% increase) cell lines ($P = 0.002$ and 0.03 respectively) whilst no change was seen in the PBECs. A corresponding increase in cellular iron was also seen.When the cancer cell lines were treated with deferasirox, cellular iron loading decreased by roughly 25% in each cell line ($P = 0.001$ and 0.01 respectively)

Corrections

S Vallath, EK Sage, VH Teixeira, *et al*. S130: Role of CADM1 in squamous cell carcinoma progression. *Thorax* 2013;63(Supp 3):A67. doi: 10.1136/thoraxjnl-2013-204457.137

The correct author list should read as:

S Vallath, EK Sage, S Lourenco, VH Teixeira, SM Janes, A Giangreco; Lungs for Living, Division of Medicine, UCL, London, UK.

Thorax 2014;**69**:253. doi:10.1136/thoraxjnl-2013-204457.137.corr1