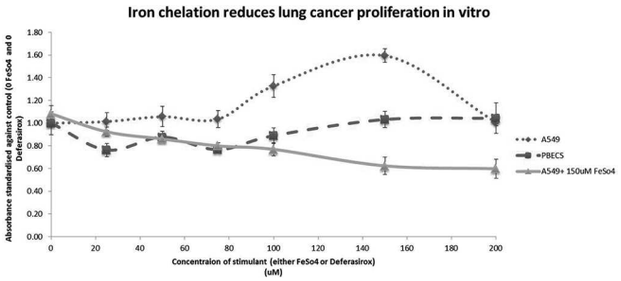
and cellular proliferation decreased below levels seen in unstimulated cells. Deferasirox was also seen to effect unstimulated cancer cells, reducing their proliferation by 50% (P = 0.02 and 0.03 respectively).

Conclusion Iron exposure was shown to have a significant effect on cellular proliferation within lung cancer cell lines, although the underlying mechanism is not yet fully understood. This iron mediated cellular proliferation could be reversed using the chelator deferasirox. Down-regulated expression of *IREB2* may cause the cancer cell lines to exhibit similar behaviour to the PBECs when stimulated with iron. These finding show that iron may provide a potential new target and deferasirox a potential new therapeutic agent for lung cancer.



Abstract S131 Figure 1. The dotted line shows that the increasing concentration of FeSO4 has a statistically significant effect at l00 M (M = 1.33, SD = 0.19 P = 0.04), however, l50 M shows an even more significant increase in proliferation (M = 1.59, SD = 0.12, P = 0.002). A dose of 200 M of FeSO4 shows a return to base line and no significant difference in cellular proliferation. The solid line shows that deferasirox causes a decrease in proliferation when applied to cells after incubation with 150 M of FeSO4. This is statistically significant at 50 (M = 0.86, SD = 0.03, P = 0.04), 150 (M = 0.62, SD = 0.08, P = 0.01) and 200 M (M = 0.60, SD = 0.08, P = 0.0004) of deferasirox and the greater the dose of deferasirox, the greater the decrease in proliferation. The dashed line indicates the effects of FeSO4 incubation on PBECS. There is no statistical significance seen in proliferation rates for any concentration of FeSo4.

S132 LINEAGE TRACING IN HUMANS REVEALS STOCHASTIC HOMEOSTASIS OF AIRWAY EPITHELIUM RESULTING FROM NEUTRAL COMPETITION OF BASAL CELL PROGENITORS

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In recent years, the development of lineage tracing approaches has provided quantitative new insights into tissue homeostasis in mice. However, the relevance of these discoveries to human epithelial homeostasis and alterations in disease is not known. We demonstrate that the statistical analysis of pathologically neutral somatic mitochondrial mutations that are accumulated over time can provide access to clonal fate behaviour at single cell resolution in human, providing a direct means to explore mechanisms of cell fate and tissue maintenance. Employing this approach, we define the progenitor cell population and the cellular hierarchy of the major human airways. By applying a novel quantitative approach to lineage tracing data, we conclude that, in normal homeostasis, the lining of human lung epithelium is maintained by an equipotent progenitor cell population of basal cells, in which the chance loss of cells due to commitment is perfectly compensated by the duplication of neighbouring cells, leading to neutral drift dynamics of the clone population. Further, we show that in airways of smokers, this process is accelerated leading to intensified clonal consolidation and a fertile background for tumorigenesis. This study provides the benchmark for the use of somatic mutations to quantitatively explore patterns of homeostatic growth in human tissues, and a platform to explore factors leading to homeostatic dysregulation and disease.

Outcomes post critical care

S133 OBSERVATIONAL COHORT STUDY OF OUTCOME OF PATIENTS REFERRED TO A REGIONAL WEANING CENTRE

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Introduction Data on outcome of the patients referred to weaning and rehabilitation centres are limited. In this observational cohort study, we report the outcomes of patients referred to a specialist complex home ventilation, weaning and rehabilitation centre.

Methods Data from the LFRU database from February 2005 to February 2011 were analysed. The primary diagnosis causing prolonged mechanical ventilation (MV) were classified into five groups: (1) neuromuscular and chest wall disease (NMD-CWD); (2) chronic obstructive pulmonary disease (COPD); (3) post-surgical patients; (4) obesity related respiratory failure (ORRF); and (5) other causes. The principal outcomes measured were weaning success, hospital mortality, 1-year and 2-year survival following discharge.

Results A total of 369 patients were referred over the 6 year period. Of these, 194 (52.6%) were admitted. The commonest outcome was total liberation from all forms of MV (45%). The remainder were shown to (1) require nocturnal non-invasive ventilation (NIV) (22%); (2) require nocturnal and intermittent daytime NIV (1%); (3) require long-term tracheostomy ventilation (24%); and (4) died in hospital (8%). Post-surgical and COPD patients had the highest rate of total liberation from mechanical ventilation at 60% and 54%, respectively. The median time from admission to tracheostomy decannulation was 18 days (9–33). NMD-CWD patients had the lowest hospital mortality (7%), whereas COPD patients had the highest hospital mortality (29%). The overall survival at 12 and 24 months was 60% and 50%, respectively. 25% of the COPD patients were alive and 59% of the NMD-CWD patients were alive at 24 months (Figure 1).

Conclusions The majority of patients with weaning failure were successfully liberated from mechanical ventilation. The weaning