particle levels (≥0·5 μm diametre) within the breathing zone were measured by laser particle counting. Inhaled cat allergen exposure was measured by nasal air sampling. Time series analysis was used to evaluate changes in particulate exposures with turning.

Results A greater proportion of larger particles than smaller ones were disturbed by turning over ($F=20.6$, $df=5$, $p<0.001$). With the TLA switched off, 9% (95% CI 4 to 18) of total overhead particles >10 μm diametre were accounted for by turning over, compared with 0.2% (95% CI 0.07 to 0.5) of particles >0.5 μm diameter. TLA treatment reduced total particle numbers (size >0.5 μm) by 3010-fold ($p<0.001$) and significantly reduced the turn-associated increase for all particle sizes (Abstract P27 Figure 1, $p<0.015$). Similar turn-associated increases in nasal air sampler cat particle counts were seen. TLA treatment reduced nasal cat allergen exposures by sevenfold ($p=0.043$).

Conclusions Turning over in bed causes a significant increase in breathing zone exposures to particulates which are within the respirable size range. TLA treatment dramatically reduces overhead breathing zone total particulate exposures and also reduces nasal cat allergen exposure. TLA treatment attenuates the increase in particulate exposures caused by turning over. Treatments which result in better sleep quality and a reduced number of bodily turns may result in a reduction in personal breathing zone particulate exposures in bed.

Pulmonary arterial hypertension

P28 INFLAMMATORY PROFILING OF ADVENTITIAL FIBROBLASTS IN PULMONARY HYPERTENSION

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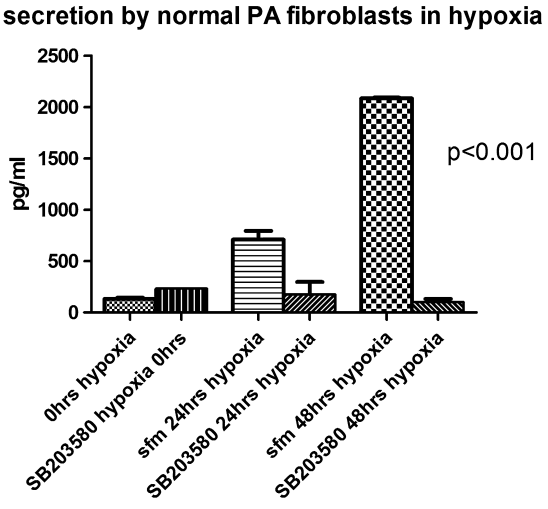
The concept that inflammation is important in the pathogenesis of pulmonary hypertension (PH) is gaining credence. Studies have suggested that Interleukin-6 (IL-6) and -1 are involved in the development of PH and that IL-6 can stimulate smooth muscle cell proliferation. The adventitial fibroblast has been suggested as a potential source of mitogens and inflammatory mediators which contribute to the development of PH.



IL-6 release from pulmonary artery fibroblasts is stimulated in hypoxia and inhibited by p38 MAPK inhibitor

Abstract P28 Figure 1 IL-6 secretion by normal PA fibroblasts in hypoxia. IL-6 release from pulmonary artery fibroblasts is stimulated in hypoxia and inhibited by p38 MAPK inhibitor.

Methods Rat pulmonary artery fibroblasts (RPAF) were isolated from normal Sprague–Dawley rats, rats exposed to 2 weeks of hypobaric hypoxia. Cells were cultured by explant technique. Normal RPAF were quiesced for 24 h in serum free media (SFM) and then exposed to periods of prolonged acute hypoxia or maintained in normoxia. The conditioned media was collected and stored at −70°C. RPAF from the chronic hypoxic and monocrotaline models were exposed to 1% serum or maintained in SFM and conditioned media collected. The effect of p38 MAPK blockade using SB203580 (an alpha-isoform specific inhibitor) was examined. The conditioned media was analysed using cytokine array technology and ELISA.

Results In normoxic conditions after 48 h, conditioned media from normal fibroblasts showed release of TIMP-1 and low levels of VEGF-A. The expression profile changed with 48 h exposure to hypoxia showing increased levels of VEGF-A and immunomodulators such as IL-6 (see Abstract P28 Figure 1), MIP-3α (CXCL20), LIX, CINC-1, sICAM-1. The secretion of these mediators were blocked by the addition of SB203580 suggesting an important role for p38MAPK in the control of these proteins. TNF-α was not released from these cells under the conditions studied. With the chronic hypoxic RPAF after 48 h of 1% serum stimulation in normoxia, the cytokine profile mirrored that of normal RPAF in acute hypoxia. Again this was blocked using SB203580.

Conclusion Pulmonary artery fibroblasts release mediators in response to hypoxia, which have been implicated in both recruitment of inflammatory cells and the proliferation of pulmonary artery smooth muscle cells. We have demonstrated that inhibition of the p38MAPK-alpha isoform can block the secretion of these mediators. This may have therapeutic implications for the treatment of hypoxia related pulmonary hypertension.

P29 ENDOTHELIAL CELL NF-KB ACTIVATION IS INCREASED IN HUMAN IDIOPATHIC PAH

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Background Pulmonary arterial hypertension (PAH) is associated with pulmonary vascular inflammation, and several of the inflammatory genes involved are regulated by nuclear factor-kB (NF-kB). NF-kB is a heterodimer of p65 and p50 subunits which, upon activation, translocate into the nucleus and binds to target gene promoters. NF-kB activation in PAH has not been examined in detail to date. We assessed NF-kB activation by immunohistochemical analysis of nuclear p65.

Methods Samples were obtained from South Paris University from patients with severe idiopathic PAH (IPAH) following lung transplantation (n=10) and from control subjects undergoing lobectomy or pneumonectomy (n=10). Tissue blocks were fixed and paraffin-embedded, 4-mm thick sections underwent immunoperoxidase double staining for macrophage (CD68+)/p65, using mouse anti-human CD68 (Dako; 1:100 dilution) and rabbit anti human p65 (Santa Cruz Biotechnology; 1:50 dilution), before detection with chromogen fast red and counterstaining with haematoxylin. Vessels of interest were defined and quantitative scoring of nuclear p65 immunostaining of ten randomly selected pulmonary arteries per