Introduction The development and use of nanoparticles for medical applications is rapidly increasing. One of the most commonly used nanoparticles is silver, due to its antimicrobial properties. At present the use of silver nanoparticles is unregulated and there is increasing concern regarding their potential adverse health effects, particularly when inhaled. The alveolar region is the primary site of nanoparticle deposition following inhalation, thus it is important to consider the effects they will exert on the alveolar epithelium, including potential toxicity. The alveolar epithelium is covered with a surfactant layer, acting as a barrier to inhaled particulate matter and pathogens, with which nanoparticles will interact before reaching the epithelium. Thus, we hypothesise that the surfactant layer will influence the toxicity and inflammatory response of alveolar epithelial cells to inhaled AgNPs.

Methods Immortalised human alveolar type 1 epithelial (TT1) cells were exposed to increasing concentrations of 20nm or 110nm silver nanoparticles (AgNP) in the presence and absence of porcine surfactant (Curosurf) for 24 hours. Cell viability was measured using the MTS assay and IL-6 and IL-8 release was measured by ELISA. In addition, the effect of the antioxidant glutathione on cytokine release was assessed.

Results Exposure to 20nm and 110nm AgNP did not significantly affect cell viability in the presence or absence of Curosurf (0–50µg/ml). However, IL-6 and IL-8 release was significantly increased (P < 0.0005) for all AgNP at concentrations above 10µg/ml. Furthermore, preincubation of AgNP with Curosurf significantly inhibited this response (P < 0.001). Pre-treatment of cells with glutathione also significantly inhibited IL-6 and IL-8 release following AgNP exposure. When glutathione and Curosurf were combined there was a further inhibition of cytokine release.

Conclusion This study demonstrates that AgNP, whilst not overtly toxic, induce an inflammatory response in human alveolar epithelial cells that is driven by oxidative stress. Furthermore, we have shown that the presence of surfactant significantly attenuates the inflammatory response suggesting a protective effect against inhaled nanoparticles. Thus, this study demonstrates the importance of studying AgNP bioreactivity in the presence of lung secretions to accurately represent the likely effects of inhalation.

P141 DIFFERENTIAL EXPRESSION OF CONVENTIONAL AND INHIBITORY VEGFA ISOFORMS IN NORMAL AND FIBROTIC FIBROBLASTS—A POTENTIAL ROLE IN IPF PATHOGENESIS?

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Introduction Vascular endothelial growth factor (VEGFA) has been implicated in the pathogenesis of Idiopathic Pulmonary Fibrosis (IPF). Two families of endogenous isoforms exist formed by alternative splicing of mRNA transcripts: the conventional potent angiogenic and mitogenic isoforms (VEGF_{xxa} family) and the VEGF_{xxb} family that is thought to have contrasting inhibitory functions.

Hypothesis We hypothesise that differential expression of VEGF_{xxa} and VEGF_{xxb} isoforms by fibroblasts may influence the development of IPF.

Methods Normal (NF) and fibrotic fibroblasts (FF) (from patients with proven UIP) were extracted from lung samples using the explant method. The expression of VEGF_{xxa} and VEGF_{xxb} by NF and FF was analysed at the mRNA level by RT-PCR and quantified by qPCR. Protein expression was determined by western blotting (WB) and ELISA. We sought to establish a potential functional effect of recombinant VEGF_{xxa} and VEGF_{xxb} proteins on fibroblasts by assessing the expression of a) the extracellular matrix (ECM) protein fibronectin and b) α-SMA, a marker of myofibroblast differentiation.

Results Both NF and FF expressed VEGF_{xxa} and VEGF_{xxb} isoforms at the mRNA level as determined by RT-PCR with confirmation by direct sequencing. There was no statistical difference in total VEGF mRNA expression between the two cell types by qPCR (p = 0.9307, NF n = 5, FF n = 6), but FF expressed significantly more VEGF_{xxb} mRNA than NF (p = 0.05, NF n = 5, FF n = 6). Total VEGF protein expression was significantly increased in FF (mean expression