|  |
| --- |
| **Proteomic signatures in BALF from Victorian engineered-stone workers with silicosis** |
| Claudia Sim1, Joel Steele2, Terry Lim2, Simon G Royce1, Paris Papagiannis1, Ryan Hoy3,4, Tracey Leong5, Han-Chung Lee2, Ralf B Schittenhelm2, Jane E Bourke1 |
| *1* Pharmacology, Biomedicine Discovery Institute, Monash University, Clayton, VIC *2* Proteomics and Metabolomics Platform, Biomedicine Discovery Institute, Monash University, Clayton, VIC, Australia 3 School of Public Health, Monash University, Clayton VIC, Australia4 Respiratory Medicine, The Alfred Hospital, Melbourne, VIC; Australia*5* Respiratory and Sleep Medicine, Austin Hospital, Heidelberg, VIC, Australia |
| **Introduction/Aim:** The recent surge in silicosis is associated with high silica-content engineered stone domestic benchtops. This study aimed to determine silica load and proteins as potential biomarker signatures in bronchoalveolar lavage fluid (BALF) from silicosis patients. **Methods:** BALF from Victorian stonemasons (n=22) and control subjects (chronic cough, n=6) was used for total and differential cell counts and silica load quantitation (silica particles/macrophage x %silica-containing macrophages x total cell counts)/mL BALF. BALF supernatant was subjected to untargeted label-free quantitative proteomic analysis. Subsequent pathway over-representation (ORA) and gene set enrichment analysis (GSEA) was conducted using KEGG and Gene Ontology databases on silicosis-unique proteins.Olink® assay was also used to quantitate pre-defined inflammation-associated proteins.**Results:**  Silicosis patients had 2-10-fold higher total BALF cells *cf* control and variable load of 19-3580 silica/mL BALF (n=22). Of the 5097 proteins in silicosis and control BAL, *exclusivity-based analysis* revealed 1784 silicosis-unique proteins, confirming 14 proteins in 10/22 silicosis patients and 1 protein in 21/22 patients. *GSEA* revealed enriched pathways associated with ribosome (p<0.05), spliceosome pathway (p<0.005). ORA cellular component analysis revealed 6 / top 10 enriched pathways localised to the ribosome (p<0.0005) and 2 / top 10 to the spliceosome (p<0.005). Biological process ontology analysis showed 7 / top 10 enriched pathways pertaining to mRNA processing (p<0.0002). *Olink* identified 14 inflammatory cytokines increased in silicosis, with one positively correlated and three inversely correlated with silica load (all p<0.05). **Conclusion:** Our novel metric of silica load did not correlate with spirometry measures. Our untargeted and targeted proteomic strategies showed primary interactions with targets including the spliceosomal complex and identified 4 unique inflammatory cytokines correlated with silica load. Further validation studies will be required to validate highly relevant pathways and determine absolute protein levels to determine a unique silicosis signature.**Grant Support:** Dust Diseases Board Discovery Grant; McDermott and Richards |