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| **Gene expression signatures that are unique to engineered stone dusts** |
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| **Introduction/Aim:** The surge in cases of engineered stone-associated silicosis is an occupational health catastrophe. The severity and progressiveness of the disease associated with exposure to these dusts is striking compared to traditional forms of silicosis which typically develops over decades. The rapid development of symptomatic disease suggests that there is something fundamentally different about the lung response to inhalation of these dusts. The aim of this project was to identify specific pathways that are stimulated in response to engineered stone dusts in alveolar epithelial cells and macrophages.  **Methods:** Alveolar epithelial cells (A549) and macrophages (THP-1) were exposed to 0 or 200 µg/mL of one of two engineered stone dusts (generated under real-world conditions) or a silica standard. Cells were processed for RNAseq analysis (AGRF). Supernatants were collected to assess markers of inflammation (e.g. IL-8) with additional assays conducted to quantify cytotoxicity.  **Results:** Bioinformatics analysis of RNAseq data identified genes (*CYP1A1*, *CYP1B1* and *TIPARP*) related to the aryl-hyrdocarbon receptor (AhR) pathway that were differentially expressed in response to engineered stones. Expression of these genes was positively correlated with IL-8 production in both A549 and THP-1 cells. However, pharmacological inhibition of the AhR pathway had no impact on cell death or the cytokine response.  **Conclusion:** Our data suggest that the AhR pathway may be a useful indicator of the pro-inflammatory potential of engineered stone dusts. However, it is unlikely that AhR plays a critical role in disease pathogenesis. This is consistent with the role of AhR in physiological and pathological processes.    **Grant Support:** Royal Hobart Hospital Research Foundation; MRFF |