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Profiling of the silica-induced pro-inflammatory molecular events in macrophages using the RNA-Seq approach

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INTRODUCTION

Silicosis is a worldwide occupational lung disease problem caused by inhalation of crystalline silica dust (Mishra et al., 2014). The risk group of silicosis in Hong Kong is the workers in construction site (Law et al., 2001). The effect of silica is most likely chronic and the latency period can be up to 10 years. Patients suffered from silicosis would experience a deteriorating lung function due to the extensive fibrosis in lung tissue (Cullinan et al., 2013). Crystalline silica has also been considered as a carcinogen and plays an important role in the pathogenesis of lung cancer. Cohort studies have demonstrated that there is a rigid association of crystalline silica in lung carcinogenesis

(Steenland et al., 2001; Pelucchi et al., 2006; Liu et al., 2013).

Alveolar macrophages are considered as a key component in the development of silicosis. Upon crystalline silica exposure, complex molecular events are triggered inside alveolar macrophage including activation of transcription factors, cytokines and inflammasome, however, the detailed pathogenic mechanisms behind these fibrotic events remains to be elucidated (Leung et al., 2012). In addition, the diagnosis of silicotic disease currently is not sensitive and effective (Leung et al., 2012). For this focus an early prognostic detection using the biomarker approach will be helpful for practitioner to decide a better strategy for silicotic patients to control the disease. By using the RNA-Seq approach we would be able to detect and profile the complete molecular patterns upon different silica polymorphs exposure.

AIMS

1. To delineate and fill the gap of the immediate pro-inflammatory and pathogenic molecular events in respirable silica polymorphs-induced inflammation in macrophages using the RNA-Seq approach.
2. To identify and characterize potential prognostic targets, strategies for future drug target therapies and biomarkers for respirable silica polymorphs-induced fibrotic disease.

Pilot study:

Before starting this project, we have performed a pilot study on lung epithelial cell line with similar methodology as this project. The results of the pilot study were good and inspirable for this project. From the results of the pilot study, it was found that several molecular pathways were significantly highlighted in silica exposed cellular changes. These include known pathways for silicosis such as inflammatory responses and oxidative stress responses. Other mechanisms on transcription factor regulation, aldehyde dehydrogenase and blood vessel development was newly reported to be associated with silicosis (Chan et al., 2017a). Another interesting finding was the association of DNA-binding protein inhibitor (ID) family in the silica exposure to lung cells. The linkage of ID1, ID2 and ID3 to cancer may rationalize themselves to be the markers indicating early response of silicosis (Chan et al., 2017b). The results of this pilot study was shown in the following section of RESULTS. The methodology of this pilot study is valuable and adopted in this project.
