

Grant: AFC820-59

Title: Elucidating the Individual and Combined Toxicity of Coal Mine Dust Constituents and Their Contribution to disease in Modern US Coal Miners

Organization: University of Illinois

Principal Investigators: Leonard Go

Topic: Injury and Disease Exposure and Risk Factors

Priority Area: Respiratory Disease

SYNOPSIS

Problem Statement: Rates of coal workers' pneumoconiosis and progressive massive fibrosis declined dramatically after permissible exposure limits for respirable coal mine and quartz dust were enacted nearly 50 years ago. However, this trend has reversed with a dramatic increase in disease rates. The factors underlying the rise of these preventable lung diseases are not completely understood, but changes in coal mine dust composition and characteristics are likely to be significant contributors. Coal dust and silica dust are known to cause a spectrum of chronic lung diseases, but the contributions of other coal mine dust constituents to pulmonary toxicity, including silicates as well as rock dust products used to mitigate explosion risk, have not been well explored. It is also unknown whether the combination of these constituent dust exposures, as experienced by miners, results in pulmonary toxicity that differs from the effects of the individual exposures. Improved understanding of the relative risks of dust constituents, alone and in combination, will enable both industry and regulatory agencies to focus monitoring and control efforts on the most relevant and hazardous exposures.

Research Approach: In this proposal, we seek to build upon previous and ongoing work to combine a detailed characterization of dust mixtures to which miners are currently exposed and use state-of-the-art approaches to generate toxicologic data, including gene expression signatures of cells implicated in the development of pulmonary fibrosis. These data will be used to inform analysis of mine-level data to generate "mine dust risk profiles" for pulmonary disease. This project will study respirable coal mine dust toxicity, an important determinant of the current resurgence of severe pneumoconiosis, utilizing a multidisciplinary approach. Our team draws from the disciplines of mining engineering, epidemiology and biostatistics, respiratory cell biology, and pulmonary medicine to study this emerging problem. In Specific Aim 1, we will obtain representative source materials for coal mine dust constituents, to encompass coal, silica, silicate, and carbonate rock dust (crushed dolomite or limestone) exposures. Source materials will be used to generate respirable-sized dust for utilization in toxicologic studies. The particle size distribution, mineralogy, and trace element and metal composition for these dusts will be determined. In Specific Aim 2, we will determine the differential development of pulmonary fibrotic responses to instillation of coal mine dust constituents in mice. Monocyte-derived alveolar macrophages, which we have been found to be necessary for disease pathogenesis of pulmonary fibrosis, will be lineage tagged, flow cytometry-sorted and sequenced (RNA-Seq). Gene expression changes linked to different dust exposures and different toxicities will be used to identify possible biomarkers that could be detected in bronchoalveolar lavage fluid or blood from exposed workers. In Specific Aim 3, we will analyze publicly available MSHA data on total respirable coal mine dust, quartz dust, and mine employment and production data to understand factors and mine characteristics that may indicate greater risk of chronic lung disease in miners. Dust toxicology results will be used to generate risk profiles that can be correlated with data on US mines and identify those with mine dust characteristics that may place them at higher risk for disease in their work force.

Impact of the Research: The significant increase in severe forms of pneumoconiosis despite documented reductions in total respirable dust raises the possibility that there has been a significant change in respirable dust toxicity. Improved understanding of relative risks of each type of dust alone, or in combination, will permit industry to focus monitoring and control efforts on the most significant exposures. The methodological advances within this proposal would also provide a framework to facilitate future pulmonary toxicological studies of mine dust exposures and permit more rapid confirmation of high-risk exposures.