



**Research:** Role of Cell Death-Resistant Lung Cells in the Development of Silica-induced Fibrosis

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**Disease/Condition:** Silicosis/Fibrosis

Epidemiological studies indicate that chronic silicosis, the most prevalent form of silicosis, is generally associated with occupational exposure to crystalline silica. It is mostly prevalent in stone dressers, quarry and foundry workers, and miners. Silicosis is a progressive fibrotic lung disease that takes decades to develop; once diagnosed there is no known cure for the disease. With strict limits on silica exposure, occupational silicosis has declined steadily in the U.S.A.; however, silicosis remains a major health concern in developing countries, and 22-32% of career gold miners and 18% of 40 to 49-year-old South African black miners have been diagnosed with silicosis. One of the major hurdles in developing appropriate therapeutics for silicosis is our limited knowledge about the mechanism by which silica inhalation leads to silicosis.

Researchers at LRRRI have developed animal models of silicosis that show strong similarities to the human disease. One of the major findings from this model was that the cells from the fibrotic granulomas (well organized collection of interstitial lung macrophages) show molecular profiles of resistance to cell death, which would allow the diseased cells to grow with impunity. LRRRI researchers are exploring the mechanism that makes these cells resistant to cell death, and are identifying targets for therapeutic interventions. Moreover, in collaboration with scientists from South Africa, we are ascertaining whether lung tissues from silicosis patients have molecular imprints that are similar to lungs of silicotic animals. Once that linkage is established, it would suggest that a successful therapeutics regime in animals has the potential to be effective in human silicosis patients as well.