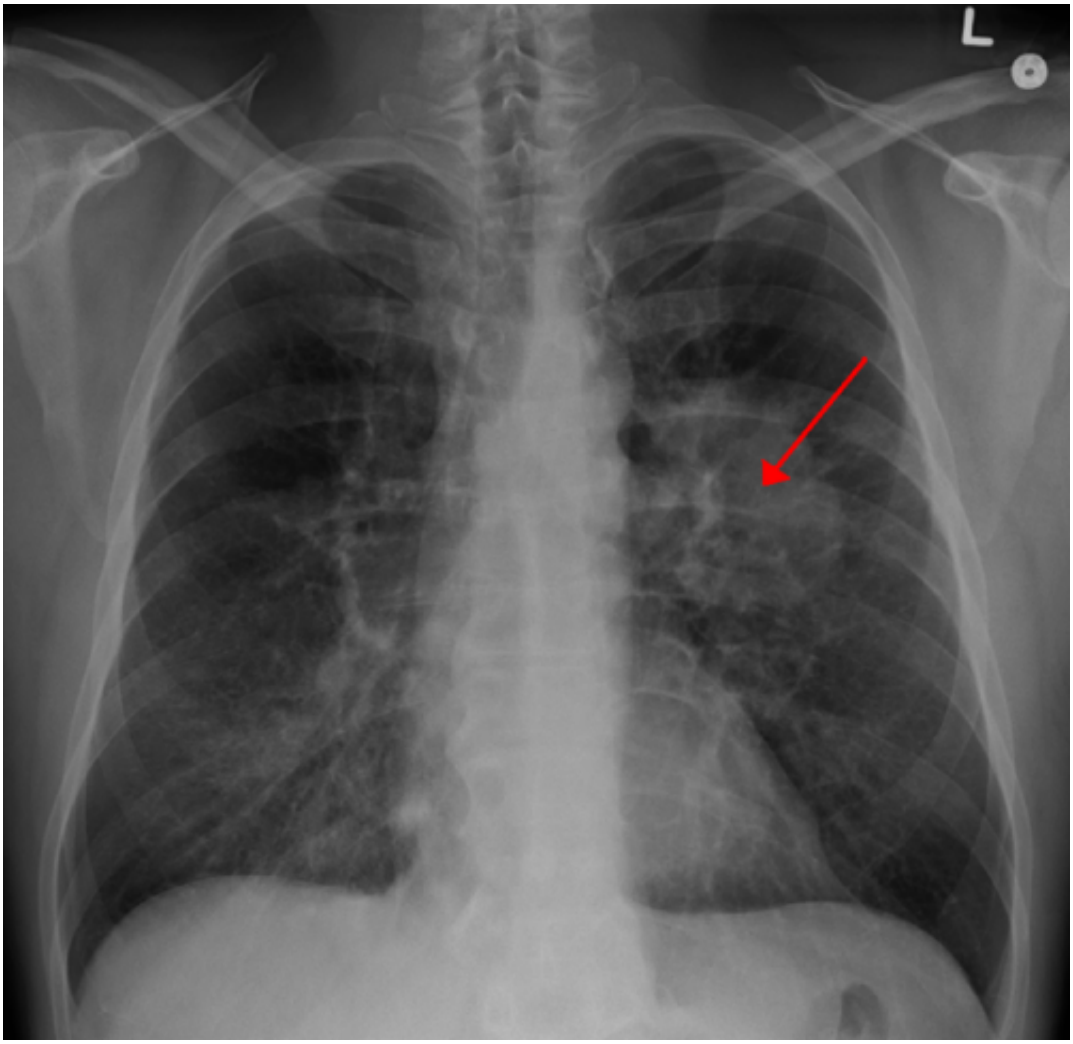
Researchers detail role of silica and lung cancer

April 29 2015



Lung CA seen on CXR. Credit: CC BY-SA 4.0 James Heilman, MD/Wikipedia

Researchers at the University of Louisville have detailed a critical connection associated with a major environmental cause of silicosis and a form of lung cancer. Their study is reported in today's *Nature Communications*.

Haribabu Bodduluri, Ph.D., professor of microbiology and immunology and a researcher in the James Graham Brown Cancer Center, and his team made the crucial connection between exposure to inhaled silica and rapid progression of lung cancers. This study also outlines the critical role of the inflammatory mediator LTB4 and its receptor BLT1 in promoting silica mediated lung tumor growth.

"We believe this is a significant step in our understanding of how environmental exposure alters the way lung cancer progresses," Bodduluri said. "It is our hope that this new information will allow for the more rapid development of treatments for this currently incurable disease."

Exposure to crystalline silica (CS) is common to a variety of industrial operations including mining, quarrying, sandblasting, rock drilling, road construction, pottery making, stone masonry, and tunneling operations. Chronic silica exposure causes severe health complications eventually leading to the irreversible, debilitating disease silicosis.

Approximately 2 million U.S. workers potentially are exposed to breathable crystalline silica. Silicosis in the developing part of the world is of an even higher concern as it is spreading like an epidemic with more than 10 million people affected around the world as a result of rapid industrialization, massive expansion of construction industry and possibly less regulated working environments.

"Silicosis continues to be a growing worldwide health issue. Being from Kentucky, where overall lung cancer is a major health issue, it is exciting

that we may be able to develop treatments that impact people in our backyards, in addition to around the world," Bodduluri said.

Silicosis keeps progressing post-exposure because people are unable to cough up the tiny particles. Macrophages that ingest silica particles end up dying, resulting in persistent sterile inflammation and may eventually lead to lung cancer. Though CS has been designated as a human carcinogen it also has been difficult to discern silicosis associated lung cancer because of a number of confounding factors including the fact that cigarette smoking is a common factor with workers likely to be exposed to silica.

Bodduluri and his colleagues report that in mice that develop spontaneous lung tumors, CS exposure accelerates lung tumor progression. Moreover, this result also was replicated in an implantable lung cancer model.

Their results highlight the importance of silica induced leukotriene B4 mediated inflammation in lung tumor promotion. Leukotrienes are involved in regulating inflammation, especially in the lungs. Mice deficient in leukotriene B4 receptor BLT1 are significantly protected from silica induced tumor promotion, suggesting the possibility for novel treatment strategies for both silicosis and associated lung cancers.

Donald Miller, M.D., Ph.D., director of the James Graham Brown Cancer Center said, "This work reflects the strong commitment of the Brown Cancer Center to better understand the important role of environmental factors in causing lung cancer. Dr. Bodduluri and his team are world leaders in this field and this work may lead to novel therapies for lung cancer."

Provided by University of Louisville