

# Scientists discover mechanism for air pollution-induced liver disease

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A research team led by Kezhong Zhang, Ph.D., at the Wayne State University School of Medicine's Center for Molecular Medicine and Genetics, has discovered that exposure to air pollution has a direct adverse health effect on the liver and causes liver fibrosis, an illness associated with metabolic disease and liver cancer.

Dr. Zhang, assistant professor of Molecular Medicine and Genetics and of Immunology and Microbiology, and his group have been studying the [adverse health effects](#) of air pollution from a unique perspective. While the major research efforts in the field were focused on the effects of air pollution on lung tissues and cardiovascular system, the Zhang lab studied the pathological effects and stress mechanisms of air pollution on the liver, the major organ of detoxification and metabolism. Their work demonstrated that inhalation exposure to high-concentration airborne particulate matter PM<sub>2.5</sub> has direct effects on the liver, triggering liver fibrosis, a pathological condition characterized by accumulation of the extracellular matrix protein collagen that occurs in most types of [chronic liver diseases](#).

PM<sub>2.5</sub> is fine airborne particulate matter with aerodynamic diameter smaller than 2.5 micrometers. It is a complex mixture of particles and gases from gasoline and diesel engines, together with dust from wear of road surfaces, tires and brakes. PM<sub>2.5</sub> is the major and most toxic component of [air pollutants](#) in the real-world air environment of intensive traffic or industrial activity. Recent epidemiological studies confirmed that populations exposed to high-level PM<sub>2.5</sub> are at a higher

risk of developing heart disease and metabolic disease.

Dr. Zhang said that PM2.5 pollution has major impact on the public health for the general population in urban areas, such as Detroit, one of the most PM2.5-polluted cities in the United States, according to annual air quality reports by the American Lung Association.

Dr. Zhang's group, in collaboration with a research group at the Ohio State University College of Public Health led by Qinghua Sun, M.D., Ph.D., professor and assistant dean for Global Public Health, performed both short-time and long-term inhalation exposure of animal models to real-world PM2.5. After a 10-week exposure, the animals developed liver fibrosis. Utilizing molecular, cellular and pathological approaches, the team discovered the stress sensor on the cell membrane that initiates PM2.5-triggered stress signals and the mediators inside the cell that transduces the signaling. The PM2.5-triggered inflammatory stress responses promote collagen deposition—a hallmark of fibrosis—in the liver through activating the transforming growth factor  $\beta$  (TGF $\beta$ ) signaling. This work will soon be published in the *Journal of Hepatology*.

"Our work has a major impact on medical care and health policy-making for the populations under air pollution environment," Dr. Zhang said, "Liver fibrosis is an advanced stage of chronic liver injuries caused by chronic hepatitis viral infection, obesity, alcoholism or autoimmune diseases. Our work defined that air pollution, specifically PM2.5 pollutant, is an independent risk factor of [liver fibrosis](#). This is very significant in terms of identifying new health risk factors and understanding liver diseases. The molecular and cellular mechanisms we revealed in this work have very important implications in clinical disease diagnosis and treatment associated with air pollution."

The liver is an important target organ and a key player in disease development under high-level PM2.5 exposure. Automobile drivers who

experience long-time daily road traffic and car manufacturing employees should pay more attention to the markers or [liver enzymes](#) that indicate liver disease, Dr. Zhang said. "Physicians or health care professionals should monitor liver pathology and consider preventive therapeutic strategies for [liver](#) disease for populations and patients in urban air pollution environments."

**More information:** The ahead of publication edition of the paper is on line at

<http://www.sciencedirect.com/science/article/pii/S0168827815005115>.

Provided by Wayne State University

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