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Real-world airborne particulate matter exposure triggers non-alcoholic hepatic steatosis in an animal model

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Real-world airborne particulate matter exposure triggers non-alcoholic hepatic steatosis in an animal model. Air pollution is a sustained problem to public health for the general population in urban areas, especially for those that live in areas of intensive traffic or industrial activity. Recent studies suggest that exposure to ambient particulate matter with aerodynamic diameters < 2.5 μm(PM2.5) is associated with pulmonary dysfunction, cardiovascular disease, and metabolic syndrome. Here, we delineated the effects of PM2.5 exposure on liver pathogenesis and the mechanisms by which PM2.5 elicits its pathophysiologic effects in the liver. Using the mobile "Air Pollution Exposure System for the Interrogation of Systemic Effects", we performed sub-chronic, whole-body exposure of the mice to environmentally relevant PM2.5. After exposure to concentrated real-world airborne PM2.5 for 10 weeks, animals developed non-alcoholic steatohepatitis (NASH), characterized by hepatic steatosis, inflammation, and fibrosis. As a consequence, the mice after PM2.5 exposure displayed glucose intolerance and insulin resistance. Both in vivo and in vitro studies revealed that inhalation exposure to PM2.5 led to activation of the c-JUN N-terminal kinase (JNK)-mediated inflammation but suppression of the insulin receptor substrate 1 (IRS1)-mediated signaling in hepatic glycogen synthesis. PM2.5 exposure also increased expression of collagens in hepatic stellate cells by stimulating the transforming growth factor β (TGFβ) signaling, thus facilitating hepatic inflammation and fibrosis. Our findings not only confirm that sub-chronic exposure to PM2.5 represents a significant "hit" that triggers NASH, but also provides important novel insights into the cellular and molecular basis by which PM2.5 promotes liver pathogenesis. The related findings are particularly informative to the prevention and treatment of air pollution-induced systemic diseases.

Biography

Kezhong Zhang has completed his Ph.D from Fudan University and postdoctoral training from University of Michigan School of Medicine and Howard Hughes Medical Institute. He has been leading a research team at the Wayne State University, focusing on research in intracellular stress signaling pathways from the ER and mitochondria that modulate cell metabolism and inflammatory responses associated with non-alcoholic fatty liver disease (NAFLD). His research work has led to more than 50 important scientific publications in high-profile journals, including Cell, Nature, Science, Journal of Clinical Investigation, EMBO, and PNAS. He has been serving as editorial board member or associate editor for 6 scientific journals.

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