The role of genes in prenatal responses to air pollution

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Exposure to pollution during pregnancy can have many adverse effects in infants and children that can even extend into adulthood. For example, air pollution exposure is associated with increased risk of low birth weight, preterm birth and risk for developing asthma later in life. Much of this is due to the fast pace of fetal growth and development; however, the exact ways pollutants have these effects and the roles of genes

related to immune function and stress response are not fully understood.

In a study published in the journal *Antioxidants*, researchers from Texas A&M University and the University of Florida worked to clarify how a gene related to oxidant response known as Nrf2 affects fetal development in an experimental model. Natalie Johnson, Ph.D., associate professor at the Texas A&M School of Public Health, along with Carmen Lau, DVM, Jonathan Behlen and others exposed animal models modified to lack the Nrf2 gene and unmodified animal models to particulate pollution like that found in diesel exhaust. They then evaluated the effects on litter size, birth weight and immune markers found in the lung and liver tissue of newborn offspring.

Particulate matter pollution is divided into three categories based on particle size: coarse particles, fine particles and ultrafine particles. Fine particles less than 2.5 microns in diameter and ultrafine particles less than one-tenth of a micron across are of greatest concern. Researchers have found associations between fine particulate pollution and increased odds of respiratory diseases, but less work has been done on ultrafine pollutants, and no health standards currently exist for this smallest category. The tiny size of ultrafine particles means they can work deeper into airways, possibly making them an even bigger health risk than fine particles.

The gene Nrf2 is known to affect immune function and stress response in adults, but research on the effects of this gene in infants and children has been explored less. To better understand the role of Nrf2 during development and clarify how ultrafine particles affect health, researchers exposed both unmodified animal models and those that have had the Nrf2 genes knocked out to fresh, filtered air and air containing ultrafine particles like those found in diesel exhaust, a common pollutant in urban areas. The researchers monitored weight gain in pregnant animal models in all four groups and recorded litter sizes and birth

weights of the offspring.

There were no statistically significant differences in weight gain in the animal models in the four groups during pregnancy. Similarly, there were not notable differences in litter sizes. However, the Nrf2-deficient offspring had lower birth weights than their unmodified counterparts, with the greatest effects in Nrf2-deficient animal models exposed to pollution. Exposure to pollution had no notable effects in unmodified animal models, which may indicate Nrf2 playing some protective role during pregnancy.

The researchers also analyzed lung and liver tissue from the offspring to measure differences in certain immune markers and expression of genes related to oxidative stress response. They found significant differences in immune markers in Nrf2-deficient offspring, indicating a change in immune function in those models. These findings point to the lack of a functioning Nrf2 gene being a main contributor to the differences between the groups.

These results are in line with other studies that have found associations between Nrf2 deficiency and some chronic diseases. For example, previous research found that adult Nrf2-deficient animal models were more likely to develop autoimmune diseases. Although more work lies ahead, this study demonstrates that the absence of a functioning Nrf2 gene affects prenatal growth of animal models, especially when exposed to ultrafine particulate air pollution in utero.

These findings could point to a possible mechanism through which ultrafine particulate matter can affect placental function and prenatal health. This highlights a need for further research into the roles of genes on immune and stress response and how those genes interact with environmental factors. The research also reinforces the importance of establishing health standards for ultrafine particulate matter pollution,

which appear to have serious effects on prenatal and neonatal health and development.

More information: Carmen H. Lau et al, NRF2 Protects against Altered Pulmonary T Cell Differentiation in Neonates Following In Utero Ultrafine Particulate Matter Exposure, *Antioxidants* (2022). DOI: 10.3390/antiox11020202

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