

Study finds changes in DNA patterns are linked to prenatal smoke exposure

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A new study by researchers at the Keck School of Medicine of the University of Southern California (USC) has found that the life-long effects of maternal smoking during pregnancy may occur through specific changes in DNA patterns.

The study found that children exposed in the womb to maternal smoking had differences in DNA methylation, an epigenetic mechanism in which small chemical compounds are added to DNA. The findings provide researchers with valuable insight into a biological process that is not well understood.

The study appears in the September issue of the *American Journal of Respiratory and Critical Care Medicine* and is now available online.

Epigenetics is the study of how chemicals that attach to DNA can switch genes on and off leading to differences in gene expression without changing the fundamental genetic information. While epigenetics has become a robust field in cancer research, little is currently known about how epigenetic changes may be tied to environmental exposures.

"This study provides some of the first evidence that in utero environmental exposures such as tobacco smoke may be associated with epigenetic changes," says one of the lead authors Carrie Breton, Sc.D., assistant professor in the Department of Occupational and Environmental Health at the Keck School of Medicine of USC. "This could open up a new way for researchers to investigate biological



mechanisms that might explain known health effects associated with maternal smoking."

Prenatal exposure to smoke is associated with a number of health problems, including childhood asthma, cardiovascular disease and lower pulmonary function later in life.

"Moms should not be smoking during pregnancy," says Linda Birnbaum, Ph.D., the director of the National Institute of Environmental Health Sciences, a component of the National Institutes of Health that helped fund the USC study. "Maternal smoking during pregnancy is not only detrimental to the health of the mom and the newborn child, but research such as this suggests that it may impact the child into adulthood and possibly even future generations as well."

The study drew upon data from the USC Children's Health Study, a longitudinal study of respiratory health among children in 13 Southern California communities. Researchers looked at a subset of about 300 children from the 5,341 kindergarten and first graders who were enrolled in 2002. Information on maternal smoking exposure was collected using a questionnaire.

The findings showed that prenatal tobacco smoke exposure was associated with detectable changes in DNA methylation patterns for two types of DNA methylation: global methylation and methylation in the promoter region of cancer or developmental related genes. Children exposed to prenatal smoke had a significantly lower level of global methylation, measured using the DNA repetitive element AluYb8. In contrast, children exposed to prenatal smoke had significantly higher methylation levels in the promoters of two genes, AXL and PTPRO. Gene expression of both of these genes has previously been demonstrated to be correlated with DNA methylation levels.



"During pregnancy, there is a natural process of methylation reprogramming where small chemical compounds are removed from the DNA bases and then reattached a short while later, so it's reasonable to think that an environmental exposure could alter DNA methylation during this period," says co-author Hyang-Min Byun.

"This research could be an important first step into understanding how what happens in utero is tied to health outcomes later in life, and how we may be able to intervene in these developments on an epigenetic level," says Breton. "For instance, it's possible that exposure to maternal smoking may cause epigenetic changes that make children more susceptible to developing asthma."

More information: Carrie V. Breton, Hyang-Min Byun, Made Wenten, Fei Pan, Allen Yang, and Frank D. Gilliland. "Prenatal Tobacco Smoke Exposure Affects Global and Gene-Specific <u>DNA Methylation</u>."

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