

Maternal smoking causes changes in fetal DNA

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Children whose mothers or grandmothers smoked during pregnancy are at increased risk of asthma in childhood, but the underlying causes of this are not well understood. Now a new study indicates changes in a process called DNA methylation that occurs before birth may be a root cause.

The study will be presented at the ATS 2011 International Conference.

DNA methylation is a process that can alter a gene's usual function. These altered genes can be passed along from parent to child. In this case, researchers observed DNA methylation-related changes in the AXL gene in children exposed to maternal smoking in utero. The AXL gene plays an important role in many human cancers and in immune response.

"We found that children exposed to maternal smoking in utero had a 2.3 percent increase in DNA methylation in AXL," said Carrie Breton, ScD, assistant professor of preventive medicine at The Keck School of Medicine of the University of Southern California (USC) in Los Angeles.

"These results confirm results from a prior study and present compelling evidence that environmental exposure to tobacco smoke during pregnancy may alter DNA methylation levels."

Using a detailed questionnaire, the researchers targeted the mothers and

[grandmothers](#) of 173 children participating in the Early Asthma Risk Factors Study (EARS), a study within the larger California Children's Health Study, and assessed their smoking habits during pregnancy. [DNA samples](#) collected from cheek cells of mothers and children were evaluated. Dr. Breton and her team found that DNA methylation of AXL was associated with in utero exposure to maternal smoking, and also found that grandmaternal smoking was not significantly associated with AXL methylation in either the mother or the child. The association between DNA methylation of AXL and in utero exposure to smoking was stronger in girls than in boys, she added.

Dr. Breton said the results of the study indicate the need for a greater understanding of the effects environmental factors have on epigenetic changes – that is, changes in gene function or expression that occur as the result of mechanisms other than changes to the underlying DNA sequence – and early development in general.

"Environmental exposures occurring in utero have the potential to affect DNA methylation patterns before birth," she explained. "Imprinted genes appear to be particularly susceptible to these exposures since they come from one parent and only a single copy from one chromosome in DNA is active. Any environmentally-induced epigenetic changes will have greater impact on gene expression and function. In utero and early life exposures are likely to be important, given what we know about timing during development when epigenetic marks are established."

Investigating the effects of environmental exposures on epigenetics is a largely unexplored area of research, and one that holds great promise for understanding biological mechanisms that underlie exposure-disease associations, she added.

"We are interested in further characterizing the pattern of epigenetic marks across this gene and whether there is a widespread response to

both [maternal smoking](#) exposure and air pollution exposure in utero," Dr. Breton said. "We hope to also evaluate timing of effects of exposure during trimester by increasing the number of samples we evaluated in a manner that will let us compare trimester-specific exposures."

Provided by American Thoracic Society

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