Changes in gene may stunt lung development in children

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Mutations in a gene may cause poor lung development in children, making them more vulnerable to diseases such as chronic obstructive pulmonary disease (COPD) later in life, say researchers at the University of Pittsburgh Graduate School of Public Health and the German Research Center for Environmental Health. Their study, published online in *Physiological Genomics*, measured expression levels of the gene and its variants in both mouse lungs and children ages 9 to 11.

Study authors, led by George Leikauf, Ph.D., professor of occupational and environmental health at the University of Pittsburgh Graduate School of Public Health, and Holger Schulz, M.D., professor of medicine at the Institute of Lung Biology and Disease, German Research Center for Environmental Health, Munich, focused on a gene called superoxide dismutase 3 (SOD3), previously shown to protect the lungs from the effects of asbestos and oxidative stress.

"People lose lung function as they age, so it's important to identify possible genetic targets that control healthy development of the lungs during childhood," said Dr. Leikauf.

Drs. Leikauf, Schulz and colleagues compared SOD3 expression levels in strains of mice with poor lung function to one with more efficient airways and lungs two times the size. As with people, the lungs of mice fully form as they mature to adulthood. The better-functioning strain maintained higher levels of SOD3 - levels in these mice were four times higher at the final stage of lung development. They also found the

presence of single nucleotide polymorphisms, or SNPs, variations in DNA sequences, in SOD3 that were linked to lung function in mice.

The researchers went on to assess SOD3 mutations in children ages 9 to 11 by testing for SNPs linked to lung function. After analyzing DNA from 1,555 children in Munich and Dresden who were part of the International Study of Asthma and Allergy in Children, they discovered two common SNPs associated with poorer lung function. One of these SNPs likely alters the expression levels of SOD3. Lung function was tested with spirometry, which measures the amount and speed of exhaled air.

Previously, genetic variants in SOD3 have been associated with loss of lung function in COPD, which is mainly caused by cigarette smoking. "We know SOD3 protects the lung against injury caused by chemicals in cigarette smoke, and it could be a link between childhood exposure to environmental tobacco smoke and poor lung development," said Dr. Leikaf. In the future it might be possible to identify at-risk children and to develop a medication that would foster optimal lung development, he added. The researchers also are exploring sex differences in SOD3 gene expression and lung development, and girls appear to be at greater risk than boys.

COPD is the fourth leading cause of death in the United States, accounting for more than 120,000 deaths annually and costing more than $30 billion per year. It is estimated that more than 16 million Americans have COPD.

More information: physiolgenomics.physiology.org … bstract/90363.2008v1

Source: University of Pittsburgh Schools of the Health Sciences (news : web)