MedicalXpress

Genetic alteration may represent early stage of smoking-induced cardiovascular damage

March 31 2011

A new study uncovers a previously unrecognized link between tobacco smoking and a gene known to influence the cardiovascular system, possibly identifying an early stage of smoking-associated cardiovascular pathology. The research, published by Cell Press in the April issue of The *American Journal of Human Genetics*, may serve to guide future research strategies aimed at identifying and counteracting mechanisms of smoking-induced pathology.

Tobacco smoking is powerfully addictive and damages the pulmonary and cardiovascular systems, leading to malignancy and premature death. "Although the promotion of smoking cessation clearly remains imperative, a better understanding of the pathophysiological processes linking tobacco smoking and its sequelae could yield opportunities to positively influence disease risk in the large population of continuing smokers," explains lead study author Dr. Lutz P. Breitling, from the German Cancer Research Center in Heidelberg, Germany.

One possible mechanism that has the potential for mediating the harmful effects of tobacco smoking is DNA methylation. DNA methylation, the attachment of methyl groups to specific sites within a section of DNA, is recognized as an important mechanism for regulating gene function and may play a significant role in diseases with a complex phenotype. Although previous studies have linked nicotine and smoking with altered methylation of several genes, comparison of methylation status between heavy smokers who do not have cancer and individuals who have never smoked has not been fully examined.

Dr. Breitling and colleagues used a recently developed genetic screening technique to conduct a genome-wide search for differential methylation correlated with tobacco smoking in 177 current, former, and never smokers. The researchers discovered a single section of DNA that exhibited lower methylation in smokers. The site was located within a gene called coagulation factor II receptor-like 3 (F2RL3). F2RL3 has been linked with the process of blood clotting and with other cardiovascular functions. Interestingly, the protein coded by this gene has never been mentioned in the smoking literature.

"Our results show that the gene coding for a potential drug target of cardiovascular importance features altered methylation patterns in smokers," concludes Dr. Breitling. "Intriguing perspectives lie in the possibility that this gene could be causally involved at a very initial stage of smoking-related cardiovascular pathology. A better understanding of its role might open up avenues for preventing the development of associated disease in subjects unable to quit smoking."

Provided by Cell Press