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NIDA Researchers Identify Genetic Variant Linked to Nicotine Addiction and Lung Cancer

Variant also Increases Risk for Cardiovascular Disease

Scientists have identified a genetic variant that not only makes smokers more susceptible to nicotine addiction but also increases their risk of developing two smoking-related diseases, lung cancer and peripheral arterial disease. The research was supported by the National Institute on Drug Abuse (NIDA), part of the National Institutes of Health (NIH).

The study, published in the April 3 issue of the journal *Nature*, “highlights the advances that are being made in genetics research, which can now identify gene variants that increase the risk of complex bio-behavioral disorders,” says NIH Director Dr. Elias Zerhouni. “This finding will help us in our efforts to further reduce the scope and devastating consequences of cigarette smoking.”

“These results suggest for the first time that a single genetic variant not only can predispose to nicotine addiction but may also increase sensitivity to extremely serious smoking-related diseases,” explains NIDA Director Dr. Nora Volkow. “Additionally, it points to potential targets for new smoking-cessation medications that may be more effective at helping smokers to quit.”

The variant is closely linked to two of the known subunits of nicotine receptors, the sites on the surface of many cells in the brain and body that can be bound by nicotine. When nicotine attaches to these receptors in the brain, there are changes in cell activity that results in its addictive effects.

Carriers of this genetic variant are more likely than noncarriers to be heavy smokers, dependent on nicotine, and less likely to quit smoking. “The variant does not increase the likelihood that a person will start smoking, but for people who do smoke it increases the likelihood of addiction,” says Dr. Kári Stefánsson, the study’s principal investigator and

chief executive officer of deCODE Genetics, a biopharmaceutical company based in Reykjavik, Iceland.

The variant was identified through a technique known as genome-wide association, in which DNA samples (from more than 10,000 Icelandic smokers) were analyzed for the presence of more than 300,000 genetic markers. Subsequent investigation showed that carriers of the variant strongly associated with nicotine dependence were also at increased risk for two smoking-related diseases, peripheral arterial disease and lung cancer. The findings were replicated in populations from five European countries and New Zealand. The researchers estimate that the variant explains 18 percent of cases of lung cancer and 10 percent of cases of peripheral arterial disease in smokers.

The same variant was identified as one that increased risk for lung cancer in two other articles appearing in the April 3rd, 2008, issues of *Nature* and *Nature Genetics*, partially funded by two other NIH institutes--the National Cancer Institute and the National Human Genome Research Institute.

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For more information on Smoking/Nicotine:
www.drugabuse.gov/DrugPages/Nicotine.html

The National Institute on Drug Abuse is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports most of the world's research on the health aspects of drug abuse and addiction. The Institute carries out a large variety of programs to inform policy and improve practice. Fact sheets on the health effects of drugs of abuse and information on NIDA research and other activities can be found on the NIDA web site at www.drugabuse.gov.

The National Institutes of Health (NIH)—*The Nation's Medical Research Agency*—includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary Federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.