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NIDA Contacts: Dorie Hightower or
Sara Rosario Wilson
301-443-6245

media@nida.nih.gov

Contacto en Español: 301-594-6145

NIDA Study Identifies Genes That Might Help Some People Abstain From Smoking

Findings Move Science Closer to Targeted, Improved Therapies

Scientists supported by the National Institute on Drug Abuse (NIDA), part of the National Institutes of Health, have for the first time identified genes that might increase a person's ability to abstain from smoking. The breakthrough research was conducted by Dr. George Uhl at NIDA's Intramural Research Program and a team led by Dr. Jed Rose at the Center for Nicotine and Smoking Cessation Research at Duke University Medical Center

The study, published in the journal *BMC Genetics*, available online April 2, brings researchers a step closer toward tailoring individualized drug therapy for addiction based on an individual's unique genetic make-up.

"This research marks the first time we've been able to identify genes involved in the ability to quit smoking," says NIDA Director Dr. Nora D. Volkow. "It marks a movement from identifying the genetics of addiction vulnerability to identifying the genetic basis of successful abstinence. This knowledge could impact the success rate of cessation programs by helping health care providers choose the most appropriate treatment based on individual differences."

Dr. George Uhl and his colleagues performed a genome wide analysis on the DNA of two types of nicotine dependent individuals, one that was able to successfully quit the cigarette smoking behavior and one that was not.

"We identified 221 genes that distinguished successful quitters from those who were unsuccessful," says Dr. Uhl. "We know the functions of about 187 of these genes, but 34 have functions that are unknown at present. We also found that at least 62 of the

genes that we had previously identified as playing roles in dependence to other drugs also contribute to nicotine dependence."

Genes that harbor variants that contribute to both success in quitting smoking and in vulnerability to become dependent on multiple substances include cadherin 13 (a molecule involved in cell adhesion, which governs how cells recognize and connect to their neighbors) and a cyclic G-dependent protein kinase gene (that plays a key role in normal brain development). In addition to genes implicated in intracellular signaling and intercellular interactions, a number of genes involved in other processes have also been identified. While many of the genes identified through this effort make sense because of their role in supporting new neural connections in the brain, more research is now needed to understand the actual mechanisms through which they may increase or reduce the rates of successful quitting.

Dr. Uhl says he and his colleagues have replicated this research in another sample, as he reported at the February 2007 meeting of the Society for Research on Nicotine and Tobacco.

"These findings provide ample justification for continuing the search for even more genetic variants associated with smoking cessation success," says Dr. Volkow. "We soon may be able to make use of this information to match treatments with the smokers most likely to benefit from them."

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