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Clusters of Genetic Variants Linked to Distinct Treatment Responses for Smoking Cessation

Findings May Help to Match Smokers with Treatments Most Likely to Help Them Quit

Scientists have identified distinct clusters of genetic markers associated with the likelihood of success or failure of two smoking cessation treatments, nicotine replacement therapy (NRT) and the medication bupropion (Zyban). This study, supported by the National Institute on Drug Abuse (NIDA) and the National Cancer Institute (NCI), part of the National Institutes of Health (NIH), was published in the June issue of the journal Archives of General Psychiatry.

"We have long known that smoking cessation treatments that help some people fail to help others," says NIDA Director Dr. Nora Volkow. "These findings shed light on the genetic variations that underlie these differences in treatment response, and this knowledge may help make it possible to match smokers with the type or intensity of smoking cessation treatment most likely to benefit them."

Researchers used a technique known as genome-wide association scans to compare DNA extracted from the blood of smokers who were either successful or unsuccessful in quitting using bupropion or various forms of NRT (e.g., nicotine patch or nasal spray). They identified clusters of gene variants that were present more frequently in the successful quitters. Interestingly, the variants were different in those who were successfully treated with bupropion than in those who were helped by NRT. For example, a cluster of genes which regulates the body's ability to process bupropion was associated with success on bupropion therapy - but not NRT. The roles of other genes identified in this study, including several expressed in brain regions important to learning and memory, are not as well understood. These genes may be new targets for future research into smoking cessation medications.

The study was led by Dr. George R. Uhl, chief of NIDA's molecular neurobiology research branch in Baltimore, MD, and coauthored by Caryn Lerman (University of Pennsylvania, Philadelphia, PA), Jed Rose (Duke University, Durham, NC), and from Brown University, Ray Niaura (Butler Hospital, Providence, RI), and Sean David (Memorial Hospital of Rhode Island, Pawtucket, RI)."Our results provide the first genome-wide evidence that the genetics of successful smoking cessation with bupropion are different from the genetics of successful smoking cessation with NRT," says Dr. Uhl. "These findings suggest that we may be able to improve the success rate for smoking cessation by using results of simple DNA tests."

The research is part of NIDA's ongoing commitment to using genome wide association studies to help develop more targeted prevention and treatment strategies for addiction. For example, in another study, also published in the Archives of General Psychiatry in March, Uhl's team identified for the first time clusters of genetic variants associated with vulnerability to methamphetamine dependence, showing that many of the same genetic variants underlie addiction to multiple drugs of abuse. The findings suggested that addictions share common underlying genetic vulnerabilities, providing new insights into the nature of addiction and suggesting novel approaches to the treatment of addiction and the prevention of relapse.

For more information go to: http://www.drugabuse.gov/DrugPages/Nicotine.html

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