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Genetic Variant May Impact Smoking Cessation

(Philadelphia, PA) Smokers with a specific genetic variant may be more vulnerable to cigarette cravings and relapse when trying to quit smoking, a study by researchers from **the Tobacco Use Research Center of the University of Pennsylvania School of Medicine** indicates. This study also shows that the anti-depressant drug bupropion – better known by its brand name, Zyban[®] – may lessen these effects, especially among females. The study, titled “Pharmacogenetic Investigation of Smoking Cessation Treatment,” appears in the November issue of *Pharmacogenetics*.

While previous research has shown that bupropion is an effective smoking cessation aid, smokers experience variability in response to this drug and only 30-45 percent remain abstinent. By identifying the genetic factors that influence response to bupropion, researchers hope to aid in the development of more effective treatment strategies that are tailored to individual smokers.

Lead author **Caryn Lerman, Ph.D.**, Associate Director for Cancer Control and Population Science at the **Abramson Cancer Center of the University of Pennsylvania** and Professor in Penn’s **School of Medicine** and the **Annenberg Public Policy Center**, led a research team that examined 426 smokers enrolled in a randomized clinical trial of bupropion for smoking cessation. Participants all provided blood samples and received bupropion or placebo plus seven sessions of behavioral group counseling. Smoking status, abstinence symptoms and side effects were recorded weekly, and smoking status was verified at the end of treatment and again at a six-month follow-up appointment.

The researchers found that participants with a decreased activity variant of the *CYP2B6* gene reported greater increases in cravings for cigarettes following the quit date and were about one and a half times more likely to relapse during the treatment phase.

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“This study provides an important first step toward utilizing genotype to identify smokers who are more vulnerable to relapse and who may benefit most from more intensive smoking cessation treatment,” said Lerman.

In previous research, the CYP2B6 enzyme (the product of this gene) has been found to affect both nicotine metabolism and bupropion metabolism. Lerman and her colleagues speculate that the effect of the genetic variant on cessation may be due to inherited differences in nicotine metabolism. “Brain concentrations of human CYP2B6 may alter local metabolism of nicotine. Such effects could contribute to neuroadaptations that alter the subjective effects of abstinence from smoking, thereby promoting relapse,” said Lerman. The present data do not suggest that the *CYP2B6* genetic effect on smoking cessation is attributable to individual differences in bupropion metabolism; however, further research in this area is needed.

The study also provides preliminary evidence that bupropion may help smokers, especially females, overcome the effects of genetic predisposition on relapse rates. Among women with the *CYP2B6* polymorphism, 54 percent of those who were treated with bupropion were abstinent at the end of treatment, compared with 19 percent of those who received placebo. The researchers believe that this difference might be due to bupropion’s effect on abstinence-induced negative moods that are more common among women.

This research was funded by the National Cancer Institute and the National Institute on Drug Abuse and was conducted by the University of Pennsylvania/Georgetown University Transdisciplinary Tobacco Use Research Center.

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