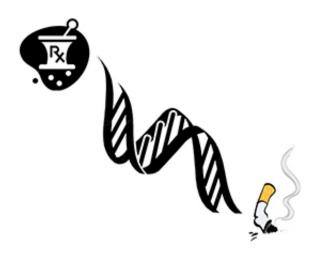


## Gene influences success of nicotine replacement therapy in smokers

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People with a gene variation that helps them process nicotine quickly are more likely to respond to nicotine replacement therapy when they try to quit smoking compared to people who don't have the variation. Credit: LI-SHIUN CHEN, MD

(Medical Xpress)—A gene that controls how quickly smokers process nicotine also predicts whether people who try to kick the habit are likely to respond to nicotine replacement therapy, a new study shows.

Researchers at Washington University School of Medicine in St. Louis, the University of Wisconsin School of Medicine and the University of Minnesota also have found that the gene has very little impact on the success of treatment with the drug buproprion—commercially known as Zyban—an antidepressant that is used to help people stop smoking by



reducing their cravings and other withdrawal effects.

The study is available online in the journal *Addiction*.

"Smokers often struggle with cravings and withdrawal when stopping smoking." said senior investigator Laura Jean Bierut, MD, professor of psychiatry. "This study gives us insights into who may respond to different types of smoking cessation medications so that we can improve the odds of quiting."

About seven in 10 former smokers begin smoking again within three months of quitting. By one year, the number is close to nine in 10, even with the help of medication. The study is a step toward improving those odds by gaining a better understanding of the contributions of a person's genetic makeup to nicotine dependence.

"Clinically, we often observe that responses to medication vary from one patient to another," said first author Li-Shiun Chen, MD, assistant professor of psychiatry. "To understand those differences, we studied a gene called CYP2A6, which controls nicotine metabolism in our bodies. It turns out that most of us metabolize nicotine rapidly, but others can metabolize it much more slowly."

Earlier research has shown that roughly 70 percent of individuals have a variation of the CYP2A6 gene that helps them metabolize nicotine quickly, while 30 percent metabolize nicotine more slowly.

"Nicotine levels drop more quickly in fast metabolizers after they quit smoking," she said. "In slow metabolizers, nicotine stays in the body longer. We have found that fast metabolizers of nicotine are more likely to relapse when they try to quit because when their nicotine levels drop rapidly, they can fall victim to cravings, but they're also more likely to be helped by nicotine replacement therapy, which can increase nicotine



levels and help control those cravings."

Chen and her colleagues studied more than 700 smokers who took part in a study, conducted at the University of Wisconsin Transdisciplinary Tobacco Use Research Center. All subjects were at least 18 years old, smoked 10 or more cigarettes per day, were of European ancestry and wanted to quit smoking.

During eight weeks of smoking cessation therapy, study subjects received six 10-minute counseling sessions to help them quit. Some also received buproprion or nicotine replacement therapy with nicotine patches and/or lozenges. Another group received both buproprion and nicotine replacement, and the rest were given inactive placebos.

The researchers found that one in three fast metabolizers responded to nicotine replacement therapy. Among slow metabolizers, the response rate was only one in 1,000.

In addition, the investigators discovered that the CYP2A6 gene could not predict whether a smoker would respond to treatment with the drug buproprion.

Previous research from the same group had demonstrated that a different nicotine gene called CHRNA5 also influences the success of smokers who try to quit, as well as the likelihood that a person will respond to nicotine replacement therapy. Chen expects that a next step in this research will involve looking closely at the interplay between the CHRNA5 and CYP2A6 genes and their overall effect on quitting smoking and treatment with nicotine replacement therapy or buproprion.

She also is planning to study how genes influence the effectiveness of other drugs frequently prescribed to help people quit smoking.



"Individual genetic analysis is becoming more and more common, and the cost is getting lower all the time," Chen said. "I think eventually we will be able to locate these gene variants quickly and inexpensively so that we can tailor treatments to individuals so they can avoid therapies that probably won't help them very much."

**More information:** Chen, L. et al. Pharmacotherapy effects on smoking cessation vary with nicotine metabolism gene (CYP2A6), *Addiction*, Advance Online Publication, Sept. 2013. doi: 10.111/add.12353

Provided by Washington University School of Medicine in St. Louis

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