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# New Vaccine for Nicotine Addiction

ScienceDaily (June 27, 2012) — Researchers at Weill Cornell Medical College have developed and successfully tested in mice an innovative vaccine to treat nicotine addiction.

In the journal *Science Translational Medicine*, the scientists describe how a single dose of their novel vaccine protects mice, over their lifetime, against nicotine addiction. The vaccine is designed to use the animal's liver as a factory to continuously produce antibodies that gobble up nicotine the moment it enters the bloodstream, preventing the chemical from reaching the brain and even the heart.

"As far as we can see, the best way to treat chronic nicotine addiction from smoking is to have these Pacman-like antibodies on patrol, clearing the blood as needed before nicotine can have any biological effect," says the study's lead investigator, Dr. Ronald G. Crystal, chairman and professor of Genetic Medicine at Weill Cornell Medical College.

"Our vaccine allows the body to make its own monoclonal antibodies against nicotine, and in that way, develop a workable immunity," Dr. Crystal says.

Previously tested nicotine vaccines have failed in clinical trials because they all directly deliver nicotine antibodies, which only last a few weeks and require repeated, expensive injections, Dr. Crystal says. Plus, this kind of impractical, passive vaccine has had inconsistent results, perhaps because the dose needed may be different for each person, especially if they start smoking again, he adds.

"While we have only tested mice to date, we are very hopeful that this kind of vaccine strategy can finally help the millions of smokers who have tried to stop, exhausting all the methods on the market today, but find their nicotine addiction to be strong enough to overcome these current approaches," he says. Studies show that between 70 and 80 percent of smokers who try to quit light up again within six months, Dr. Crystal adds.

About 20 percent of adult Americans smoke, and while it is the 4,000 chemicals within the burning cigarette that causes the health problems associated with smoking -- diseases that lead to one out of every five deaths in the U.S. -- it is the nicotine within the tobacco that keeps the smoker hooked.

**A New Kind of Vaccine**

There are, in general, two kinds of vaccines. One is an active vaccine, like those used to protect humans against polio, the mumps, and so on. This kind of vaccine presents a bit of the foreign substance (a piece of virus, for example) to the immune system, which "sees" it and activates a lifetime immune response against the intruder. Since nicotine is a small molecule, it is not recognized by the immune system and cannot be built into an active vaccine.

The second type of vaccine is a passive vaccine, which delivers readymade antibodies to elicit an immune response. For example, the delivery of monoclonal (identically produced) antibodies that bind on to growth factor proteins on breast cancer cells shut down their activity.

The Weill Cornell research team developed a new, third kind -- a genetic vaccine -- that they initially tested in mice to treat certain eye diseases and tumor types. The team's new nicotine vaccine is based on this model.

The researchers took the genetic sequence of an engineered nicotine antibody, created by co-author Dr. Jim D. Janda, of The Scripps Research Institute, and put it into an adeno-associated virus (AAV), a virus engineered to not be harmful. They also included information that directed the vaccine to go to hepatocytes, which are liver cells. The antibody's genetic sequence then inserts itself into the nucleus of hepatocytes, and these cells start to churn out a steady stream of the antibodies, along with all the other molecules they make.

In mice studies, the vaccine produced high levels of the antibody continuously, which the researchers measured in the blood. They also discovered that little of the nicotine they administered to these mice reached the brain. Researchers tested activity of the experimental mice, treated with both a vaccine and nicotine, and saw that it was not altered; infrared beams in the animals' cages showed they were just as active as before the vaccine was delivered. In contrast, mice that received nicotine and not treated with the vaccine basically "chilled out" -- they relaxed and their blood pressure and heart activity were lowered -- signs that the nicotine had reached the brain and cardiovascular system.

The researchers are preparing to test the novel nicotine vaccine in rats and then in primates -- steps needed before it can be tested ultimately in humans.

Dr. Crystal says that, if successful, such a vaccine would best be used in smokers who are committed to quitting. "They will know if they start smoking again, they will receive no pleasure from it due to the nicotine vaccine, and that can help them kick the habit," he says.

He adds that it might be possible, given the complete safety of the vaccine, to use it to preempt nicotine addiction in individuals who have never smoked, in the same way that vaccines are used now to prevent a number of disease-producing infections. "Just as parents decide to give their children an HPV vaccine, they might decide to use a nicotine vaccine. But that is only theoretically an option at this point," Dr. Crystal says. "We would of course have to weight benefit versus risk, and it would take years of studies to establish such a threshold."

"Smoking affects a huge number of people worldwide, and there are many people who would like to quit, but need effective help," he says. "This novel vaccine may offer a much-needed solution."

The study was funded by the National Institutes of Health, the National Foundation for Cancer Research, and the Malcolm Hewitt Wiener Foundation.

The Cornell Center for Technology Enterprise and Commercialization, on behalf of Cornell University, has filed patent applications on the work described in this study.

Other study co-authors are Dr. Martin J. Hicks, Dr. Jonathan B. Rosenberg, Dr. Bishnu P. De, Dr. Odelya Pagovich, Dr. Jian-ping Qiu, Dr. Stephen M. Kaminsky, Dr. Neil R. Hackett, and Dr. Stefan Worgall from Weill Cornell Medical College, and Dr. Colin N. Young and Dr. Robin L. Davisson from Cornell University.

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