

## Vaccines move forward against a range of addictions

Illicit drug use has reached a near-decade high in the US, so it's perhaps not surprising that public health officials harbor strong hopes for vaccines to treat various addictions. But whereas some experimental vaccines of this sort have shown promise in animal studies and early clinical trials, it seems that some of these shots against addiction—such as immunizations against nicotine—are better positioned to reach the market than others.

Last month, a team led by Ronald Crystal, a pulmonologist at Weill Cornell Medical College in New York, reported that mice immunized with a cocaine vaccine made from parts of a disabled cold virus attached to an inactive cocaine analog developed large numbers of antibodies against the drug. When subsequently injected with cocaine, vaccinated mice acted far less hyper compared with controls (*Mol. Ther.* doi:10.1038/mt.2010.280, 2011).

The vaccine approach triggers the immune system to detect and sequester cocaine or other drugs before they reach the brain. Crystal's group is now tweaking the anticocaine shot to further boost immune responses. "We need a lot of very-high-affinity antibodies," says Crystal, adding that his lab also has encouraging, unpublished data in rats and that they plan to test the vaccine in monkeys within the next two months.

Other experimental substance abuse-fighting vaccines are already in human trials. Two years ago, for instance, a team led by Thomas Kosten, an addiction researcher at Baylor College of Medicine in Houston, tested a vaccine—made of cocaine-like molecules coupled to an inactivated cholera toxin protein that stimulates the immune system—in 115 addicts from a methadone-treatment program in Connecticut. About 40% of vaccinated individuals built high antibody titers, and this group was more likely to stay off cocaine compared to those who received placebo injections or had lower antibody counts (*Arch. Gen. Psychiatry* 66, 1116–1123, 2009).

However, starting eight weeks after the final vaccine booster, some addicts in the study began taking more cocaine to overcome the vaccine's effects, suggesting that an integrated intervention and improved vaccines are necessary. Kosten's team is now recruiting drug users for a 300-person phase 2 trial of the same vaccine.

### Smacking down

Concurrently, Kosten and his colleagues have also developed new vaccines for



**Life line:** Researchers hope to tackle drug abuse with addiction-curbing vaccines.

combating methamphetamine and morphine dependence with promising, as-yet-unpublished results in mice. "They look at least as good as the cocaine vaccine does, at least in animals," Kosten says. In collaboration with two Beijing-based pharmaceutical companies, Kosten is now planning follow-up work in humans to further develop these vaccines.

Meanwhile, a team led by medicinal chemist Kim Janda at the Scripps Research Institute in La Jolla, California is working on a new heroin vaccine that relies on some new twists in the design of heroin-like molecules. "It's the best vaccine we've ever made," Janda says of his unpublished results from animal studies. In addition, researchers at the University of Chile in Santiago, in collaboration with the Chilean biotech company Recalcine, announced plans last month to develop a vaccine against alcoholism, by targeting the enzyme aldehyde dehydrogenase, whose absence makes people nauseated when they drink.

The majority of researchers, however, agree that the most likely anti-substance abuse vaccine to first gain market approval will be a nicotine vaccine aimed at helping people quit smoking. The most advanced product is being tested by Maryland-based Nabi Biopharmaceuticals, which is conducting two phase 3 trials of its shot NicVax. This vaccine involves a nicotine-

like molecule attached to a surface protein from the bacterium *Pseudomonas aeruginosa* that has been rendered non-toxic but still stimulates an immune response. Results of these trials are expected by early next year, and the company plans to draft its biologic license application shortly thereafter. "The results we have had from the proof-of-concept studies support the concept that the higher the antibody [titer], the more likely people will quit," says Nabi chief executive Raafat Fahim. "The other vaccines have not been able to show that."

In 2009, Nabi announced a licensing agreement with the UK pharmaceutical giant GlaxoSmithKline for NicVax. But Kosten notes that few drug makers are willing to take on vaccines for substance abuse, partly because the market might not be sufficient to support the cost to develop these products. "We could hand them all the data on a silver platter, but it just doesn't seem to the powers that be in these companies that there's enough of a profit in it," he says.

At the very least, smokers themselves seem to be ready for a nicotine vaccine. Last year, researchers at the University of Pennsylvania in Philadelphia surveyed more than 400 adult smokers and found that more than half the respondents would be willing to try a nicotine vaccine if one became available (*Nicotine Tob. Res.* 12, 390–397, 2010).

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