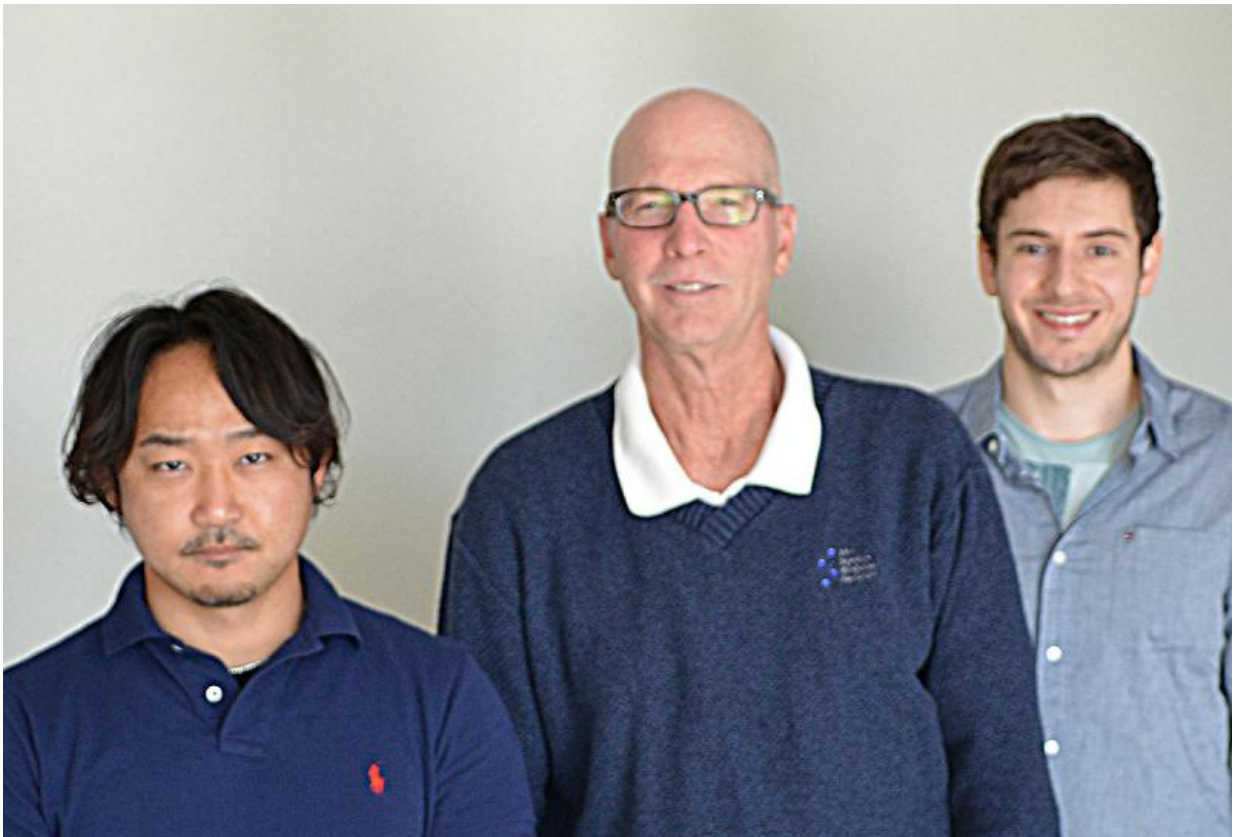


Scientists create vaccine against dangerous designer opioids

February 16 2016



Key authors of the new study from The Scripps Research Institute were (left to right) Research Associate Atsushi Kimishima, Professor Kim Janda and Graduate Student Paul Bremer. Credit: Photo courtesy of The Scripps Research Institute.

With use of synthetic opioid "designer drugs" on the rise, scientists from The Scripps Research Institute (TSRI) have a new strategy to curb addiction and even prevent fatal overdoses.

In a new study, published today in the journal *Angewandte Chemie*, the scientists report successful preclinical tests of a [vaccine](#) that prevents the synthetic opioid fentanyl—which some [drug](#) dealers now use as a mix-in or substitute for heroin—from reaching the brain.

"We want to stay one step ahead of these clandestine laboratories making illegal opioids for black market demand," said Kim Janda, the Ely R. Callaway Jr. Professor of Chemistry and member of the Skaggs Institute for Chemical Biology at TSRI. "The importance of this new vaccine is that it can block the toxic effects of this drug, a first in the field."

The Need for Treatments

The new vaccine targets an opioid called fentanyl, a painkiller 50 to 500 times more potent than morphine. Over the years—to skirt U.S. Drug Enforcement Administration detection—many illicit laboratories have tweaked fentanyl's molecular structure, selling fentanyl variants under names such as "China white" and acetyl fentanyl, the latter of which was responsible for a cluster of deaths recently in Rhode Island and Pennsylvania.

With so many variants on the market, users have no way of knowing the strength of the drugs they are using, which can lead to fatal overdoses. The U.S. Centers for Disease Control and Prevention reported a 200-percent increase in overdose deaths involving opioids from 2000 to 2014, citing the availability of fentanyl and fentanyl variants as a major contributor.

While there are treatments such as naloxone for opioid overdose or methadone for addiction, Janda noted that many people still relapse. "These treatments are working for some people, but there is clearly a gap that needs attention," he said.

A Potential Vaccine

The new vaccine takes advantage of the body's own [immune system](#). The vaccine cocktail contains a molecule that mimics fentanyl's core structure. When given the vaccine, the immune system is "trained" to produce antibodies to neutralize it.

The idea is that when a person then tries to get high from fentanyl or its variants, their antibodies bind to the drug and keep it from reaching the brain. In theory, blocking the ability to feel a high could stop drug-seeking and drug-taking behavior.

Janda and his colleagues tested the vaccine in mouse models of fentanyl addiction and overdose. Mice were given three vaccinations, each two weeks apart—like a series of booster shots. By studying antibodies in the blood, the researchers saw that the immune system was successfully neutralizing fentanyl for months after the last injection. In further tests, the researchers observed that vaccinated mice given fentanyl did not demonstrate "high" behavior (such as ignoring discomfort).

In fact, a 30-fold greater-than-normal dose of fentanyl was necessary for the drug to activate neural circuits in vaccinated mice. Remarkably, antibodies generated by the vaccine protected against overdose, neutralizing lethal levels of fentanyl.

"To the best of our knowledge, our active vaccine is the first to ablate lethal doses of any drug of abuse," said TSRI Research Associate Atsushi Kimishima, co-first author of the new study with TSRI graduate

student Paul Bremer.

"This surprised us the most," added Bremer.

Importantly, the potential vaccine protects against virtually all fentanyl derivatives and does not cross-react with other drug classes, such as oxycodone. This means those vaccinated would still have painkiller options in medical situations.

The researchers said the next step in this research is to design an even more potent vaccine, perhaps a combined anti-fentanyl and heroin vaccine. "Since heroin is often cut with [fentanyl](#) derivatives, a [combination vaccine](#) targeting both opioids would be worth investigating," said Bremer.

More information: Paul T. Bremer et al. Combatting Synthetic Designer Opioids: A Conjugate Vaccine Ablates Lethal Doses of Fentanyl Class Drugs, *Angewandte Chemie International Edition* (2016). DOI: [10.1002/anie.201511654](https://doi.org/10.1002/anie.201511654)

Provided by The Scripps Research Institute

Citation: Scientists create vaccine against dangerous designer opioids (2016, February 16) retrieved 27 April 2024 from <https://phys.org/news/2016-02-scientists-vaccine-dangerous-opioids.html>

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