

Arkansas scientists' invention would block PCP addiction

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LITTLE ROCK -- A company run by University of Arkansas medical researchers has received a \$3 million grant to conduct the first clinical trials of antibodies to basically neutralize the effects of the illicit drug known as angel dust.

The four people who started Inflexion Therapeutics LLC and developed it in the University of Arkansas for Medical Sciences' biomedical incubator, announced the grant Thursday. The award comes from the National Institutes of Health's National Institute on Drug Addiction.

The money will help researchers develop a vaccine they believe will be able to negate addiction to angel dust, the popular street name for phencyclidine, or PCP.

They also are developing a similar addiction-busting injection for methamphetamine, the recreational, home-cooked drug that has gripped rural America, but that process is more complicated and is two years behind the PCP blocker.

NIDA says more than 400,000 meth and PCP addicts are currently seeking help.

In 1981, clinical pharmacologist Michael Owens began developing a powerful protein coding that can single out molecules of PCP and other drugs and block them from flowing from the bloodstream into the brain.

In 2000, funding from Arkansas' share of the nationwide settlement in a tobacco lawsuit helped Owens connect with anesthesiologist Dr. Brooks Gentry, pharmaceutical expert Barry Holtz and biologist Ralph Henry to develop a production and commercialization plan.

Years of research on rats indicate that even if a PCP addict continued to snort angel dust after receiving the antibody, the drug would have no impact because it wouldn't be able to infiltrate the brain.

The NIDA grant forecasts clinical trials within 18 months, likely in the Hartford-New Haven, Conn., area, where PCP abuse is most concentrated, Gentry said.

Inflexion's therapy is unique because, unlike methadone for morphine addiction, the vaccine is not a substitute drug to wean people off an illegal one.

There have been previous attempts to use active antibody vaccines against nicotine and cocaine addiction, but they are still in the review stages, Holtz told The Associated Press in a telephone interview from a World Health Organization conference in Geneva, Switzerland.

But possibly the most striking aspect of Inflexion's approach is that Henry, a biology professor at the University of Arkansas at Fayetteville, developed a way to cultivate the antibodies in plants. Gentry said that method is far cheaper than creating strains in a laboratory and likely helped convince the NIH's National Institute on Drug Abuse to back the project.

Monoclonal antibodies like those used in the vaccine have been produced to treat certain cancers, autoimmune diseases like lupus and rheumatoid arthritis and for transplant rejection, but they never before have been developed in plants, Owens said.

The university's Fayetteville campus is located in the heart of meth-afflicted northwest Arkansas, where studies have shown that 5.6 percent of all 18-25 year olds are routine meth users and 24 percent of burn victims suffer their injuries in meth laboratory fires. So, with Henry taking the lead, Fayetteville has provided greenhouses to grow massive quantities of plants that can support the antibodies.

The plants can store and grow proteins that are later extracted and purified for use in the vaccine. The resulting monoclonal antibodies can identify and bind to targeted toxins through a process called "affinity chromatography."

In addition to blocking the effects of future drug use in recipients of the injection, the antibodies can also treat an overdosing user by essentially sucking the drug out of the brain and back into the bloodstream. Owens said the antibodies have several thousand times higher affinity for the targeted drug than anything else in the bloodstream and 50-100 times greater affinity than any binding site in the brain.

When Owens was a postdoctoral fellow 25 years ago, nobody thought that monoclonal antibodies could be developed to counteract PCP or meth, but he has steadily championed the idea since.

"Monoclonal antibodies were not a new invention, but what they could do was still not known," Owens said. "So, when I started at Little Rock on the faculty, I immediately started writing grants to make monoclonal antibodies rather than specific vaccines."

A traditional vaccine can only stimulate the body to form a general immune response, which can take three to six weeks. Monoclonal antibodies, however, can act against extremely high doses of specific toxins right at the point of impact.

"The advantage is, if you try to stop using the drug today, but next week you might not be in that mood, we want the medicine to be able to work immediately and be long-lasting, and we think this will last as long as a month," Owens said.

Holtz said NIDA, particularly recently, has been eager to support alternative treatments for illicit drug addiction because larger pharmaceuticals could be scared away by "the perceived reimbursement issues" of eventually having to sell a treatment largely to Medicaid recipients.

"Why we formed Inflexion is we realized the big drug companies are not going to take the risk that we can as a small organization," Gentry said. "We realized we couldn't wait around and twiddle our thumbs for others to make it happen."

Even after the physiological addiction is controlled, drug users will still need to rehabilitate their psychological habits. Theoretically, the vaccine could be used after a high to prevent the debilitating effects of addiction, and a user could simply wait for the vaccine to wear off and get high again. But Gentry said that was unlikely because the therapy would only be available for those admitted to the hospital or drug-treatment programs.