Long-acting anti-meth treatment demonstrates protective benefits for meth addiction

November 4 2014

A recently developed Adeno-Associated Virus (AAV)-based medication has the potential to offer substantial protective effects for patients attempting to cease methamphetamine use. This research is being presented at the 2014 American Association of Pharmaceutical Scientists (AAPS) Annual Meeting and Exposition, the world's largest pharmaceutical sciences meeting, in San Diego, Nov. 2-6.

Methamphetamine, commonly referred to as meth, is an addictive substance that can cause brain damage, organ failure, stroke, open sores, rotting teeth, mania, paranoia, obsessive compulsive behaviors, psychosis, and death. Meth increases the amount of the neurotransmitter dopamine, and chronic use has been found to be coupled with chemical and molecular changes in the brain. According to the latest National Survey on Drug Use and Health, more than 12 million people nationwide aged 12 or older have used meth in their lifetime. Currently, there are no FDA-approved therapies that specifically treat meth abuse.

Dr. Eric Peterson and colleagues at the University of Arkansas for Medical Sciences used AAV particles to deliver genes that produce high-affinity anti-meth antibody fragments in mice. The animals were injected with either the AAV-based medications (AAV-scFv6H4 or AAV-scFv7F9) or saline as a negative control. To test the extended functionality of the AAV medications, one milligram per kilogram of meth was administered 50 days after the initial dose. Serum samples

were then taken 30, 60, 120, and 180 minutes after meth dosing and analyzed for sustained serum concentrations of meth. Mice injected with AAV-scFv6H4 exhibited a significantly higher concentration of meth at 60, 120, and 180 minute time points, suggesting that meth was sequestered in the serum by the circulating AAV-scFv6H4 and AAV-scFv7F9 molecules.

"The goals of this project are to integrate antibody engineering and gene therapy technology to generate a long-acting (months to years) antibody-based medicine that will both protect patients from relapse to meth use and minimize treatment failures associated with long-term patient compliance," said Peterson.

Medications designed to diminish the psychologically rewarding effects of meth abuse could offer substantial protective effects for patients wanting to stop drug use, especially if they have the ability to reduce medical setbacks caused by relapses. Anti-meth antibody-based therapies that tightly bind and sequester meth away from its sites of action in the brain are showing promise as a viable treatment option. In addition, they are non-addicting and suitable for use in combination with existing behavioral therapies.

Extensive characterization of this therapy is the next step for Peterson and his team. Future experiments will include testing different high affinity antibody fragments (with extended half-life versions of these fragments), efficacy studies in animal models of drug abuse, dose-response studies, and assessment of safety and immunogenicity. The group recently received a four-year National Institutes of Health/National Institute on Drug Abuse grant to support this research.

Provided by American Association of Pharmaceutical Scientists