

Long Lasting Protection Against G-Type Nerve Agents

The Army seeks a partner interested in commercializing this technology.

Status

Patent Applications

US Provisional
62/475,502 filed 23
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PCT/US2018/023746
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Title

Recombinant adeno-associated virus-
paraoxonase 1-I-F11
particles and the
methods of making
and using thereof

Inventors

Chilukuri,
Nageswararao

Betapudi, Venkaiah

Laboratory

U.S. Army Medical
Research Institute
of Chemical
Defense (RICD)

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Gene delivery of
Paraoxonase 1
variant provides
long term protection
against G-type
Nerve Agents.

The Market Need

Nerve agents are colorless, tasteless, and odorless organophosphate compounds used as invisible chemical weapons. They are known to inhibit acetylcholinesterase (AChE) and disrupt the normal functioning of the central nervous system inducing seizures and causing rapid death by respiratory paralysis. There are a few inorganic chemical therapies/antidotes available for protection against nerve agents. However, the potential antidotes of G series nerve agents cannot prevent brain damage due to their inability to cross the blood-brain barrier and often come with undesired side-effects such as difficulty breathing and behavior abnormalities. Pesticides, which also contain organophosphate compounds, are less toxic than nerve agents but are believed to be responsible for nearly 250,000 deaths in developing countries each year. Therefore, identification of new therapeutic approaches with safe and broad-spectrum efficacy is essential to offer complete protection against organophosphate nerve agents.

The Technology

RICD inventors developed an adeno-virus 8 (AAV8)-mediated paraoxonase 1 variant gene therapy that has increased catalytic efficiency against G-series nerve agents. This therapy provides safe, long-term protection against nerve agents. Based on the results obtained from a mouse model system, just one intramuscular shot of a therapeutic formulation given to a subject three days before going to the battlefield will offer complete protection against G-type nerve agents from 6 months to potentially the life-span of the animal.



Applications

The technology provides evidence that gene therapy using an AAV8 vector containing a paraoxonase 1 variant has the potential to protect soldiers and medical personnel against G-type nerve agents and threats during medical and military operations. The technology will also provide protection from organophosphate compound toxicity to agricultural workers without the side effects of inorganic chemical therapies.

Highlighted Benefits

- Technology is a viable option for the abundant expression of recombinant paraoxonase 1 variant, a promising catalytic bioscavenger that hydrolyzes G-type nerve agents in the blood stream
- In a mouse model, one intramuscular administration provides protection for 6 months to potentially the entire life span of the animal with no signs of toxicity

Stage of Development

A single injection of liver-specific AAV8 viral particles loaded with paraoxonase 1 variant gene in mice resulted in expression and secretion of recombinant protein in milligram quantities which has the ability to break down G-type agents into biologically inactive products. Mice containing milligram concentrations of recombinant paraoxonase 1 variant in their blood displayed no clinical signs of toxicity based on blood and serum chemistry profiles. The circulating recombinant protein may be able to protect humans against G-type nerve agents for several weeks to months with a single administration, a significant improvement over existing, post exposure therapies.

Contact: Dave Humphrey, 301-619-6975, david.h.humphrey7.civ@mail.mil

