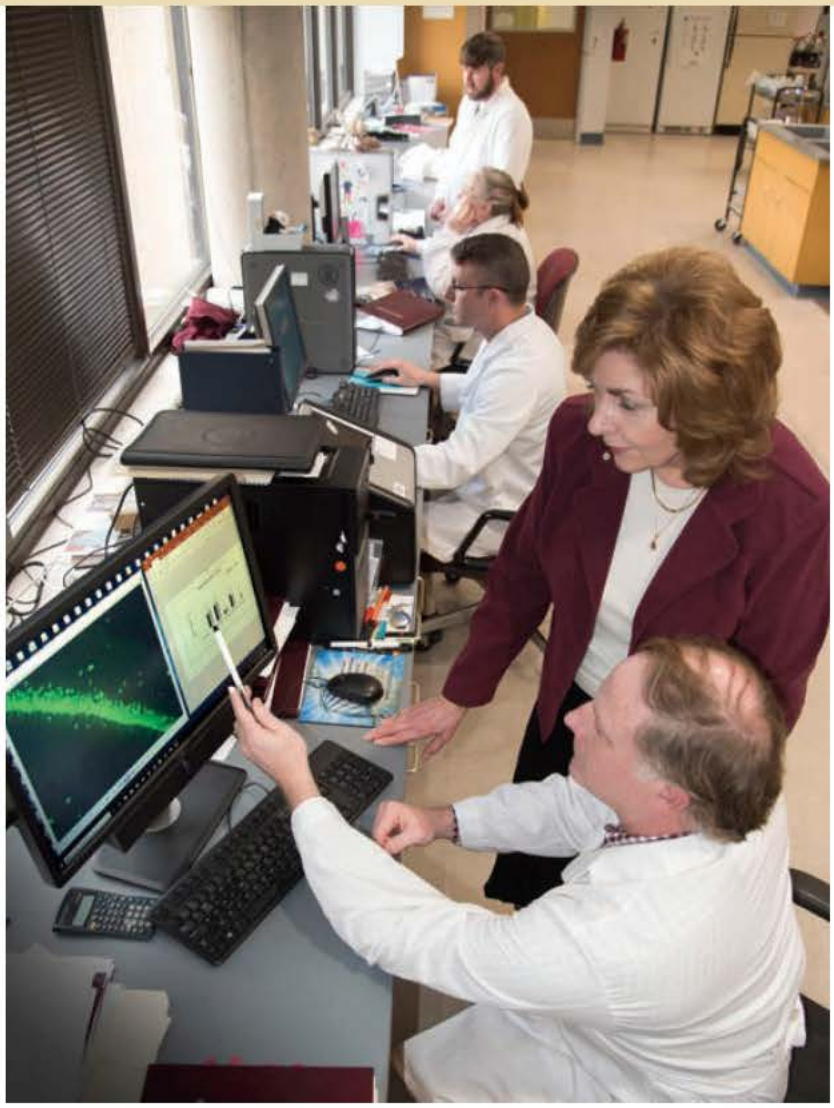
CEHS TO FURTHER DEVELOP NOVEL ANTIDOTES



The MSU CVM Center for Environmental Health Sciences (CEHS) recently received two NIH Countermeasures Against Chemical Threats (CounterACT) awards for further development of the Center's novel antidotes to nerve agent and organophosphate insecticide poisoning with an anti-terrorist perspective.

CounterACT is focused on research aimed at the identification of better therapeutic medical countermeasures against chemical threats.

According to CVM CEHS Director and Toxicologist Dr. Janice Chambers, a major concern for survivors of a chemical attack is the potential for permanent brain damage caused by seizures. Since the brain cannot repair such damage easily, there is critical need for an antidote that can enter the brain and reverse any early biochemical effects before long-term effects set in.

For the past eight years, Chambers and her team have been developing antidotes that improve survival rates after nerve agent exposure.

"We're trying to develop antidotes that might replace or be used in conjunction with the currently approved antidote. The goal is to get an antidote into the brain and reduce some of the toxic action to prevent, or at least attenuate, the brain damage," said Dr. Chambers.

Current antidotes, which protect the heart, lungs, and other vital organs, used for such instances do not work because they are unable to cross the blood-brain barrier, which is a layer of cells between the blood and the brain. This prevents many chemicals, and some drugs, from moving from the blood into the brain.

"If approved, these antidotes would give more confidence to both warfighters and civilians that not only could their lives be saved, but also their brain function could be preserved," Dr. Chambers said.

Each of the two CEHS projects is predicated on continuing development of the patented and licensed antidotes that display the ability to penetrate the blood-brain barrier and can attenuate some of the brain damage.

The larger of the two projects is an NIH U01, a three-year award with a total cost of $1,297,133, and titled "Identification of Novel Brain-Penetrating Phenoxyalkyl Pyridinium Oxime Countermeasures." Dr. Chambers will lead this project and will accumulate the data sets that are needed to down-select to a lead compound and an alternate compound to present for FDA approval.

Along with Dr. Chambers, co-investigators on the project are CVM Toxicology and Pharmacology Professor Dr. Matt Ross and Interim Basic Sciences Department Head Dr. Bob Wills.

The smaller project is an NIH R21, a two-year award with a total cost of $394,764, and titled "Identification of Novel Brain-Penetrating Antidotes for Phorate Toxicity." R21 awards are high-risk, high-payoff projects. This one will search the antidote library for efficacious compounds that can remediate poisoning from phorate, a very toxic organophosphate insecticide that elicits unusual delays and violent signs of poisoning. Dr. Chambers will lead this project, with Dr. Matt Ross and MSU chemistry professor Dr. Steve Gwaltney as co-investigators.

"Either alone, or in combination with 2-PAM, the only FDA-approved reactivator drug in the U.S., these novel oximes could contribute to survival," said Dr. Chambers. "Uniquely, they could reduce or prevent the brain damage caused by the prolonged seizures induced by organophosphate insecticides."

According to Dr. Chambers, the idea is that those in combat could carry the antidote with them in the event they are likely to enter an area where nerve agents have been released. From a civilian standpoint, the antidote would be available in the strategic stockpile of countermeasures maintained in the event of terrorist attacks or accidents.

Right now, though, Chambers and team must move forward in determining if the antidote is even safe to administer in humans, how much of it can be tolerated if so, and how long it will be effective in the body.

"Our perspective is not just to save the life, but to save the brain, too, to allow the person who is exposed to this type of chemical the hope of a normal life after that event," she said.

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>
> – DR. JANICE CHAMBERS