(October 14, 2010 Stillwater, OK) – A team of toxicologists at Oklahoma State University's Center for Veterinary Health Sciences recently received a 2-year National Institutes of Health grant funded through the Countermeasures Against Chemical Terrorism (CounterACT) program to study persistent neurological complications following organophosphate intoxication.

Carey Pope, Ph.D., is the Principal Investigator, with Jing Liu Pope, Ph.D., as co-Principal Investigator, and Linnzi Wright, Ph.D., Post Doctoral Fellow, as co-investigator. All three work in the Department of Physiological Sciences at the veterinary center. The OSU team is working in collaboration with Ben Cravatt, Ph.D., at The Scripps Research Institute in La Jolla, California.

"The $500,000 grant is supported through multiple Institutes with the National Institute of Neurological Disorders and Stroke as lead institute," explains Dr. Carey Pope. "This project will allow us to more fully characterize a neurobehavioral model of depression following acute organophosphate intoxication. The goal is to develop novel therapeutic approaches to protect against these long-term neurological changes."

Pope uses an example of a person being exposed to an organophosphorus nerve agent, such as the one in the Tokyo subway attack in the 1990's.

“The medical emergency is initially an acute problem. With sufficiently high exposures, there is a risk of death primarily from respiratory depression relatively soon after exposure,” he says. “As organophosphorus pesticides elicit toxicity by the same mechanism, similar responses can happen with overexposure to these types of chemicals. If a person is exposed to a toxic but sub-lethal level of nerve agent or organophosphorus insecticide, however, long-term, persistent, neurological/neuropsychological problems can be elicited long after the acute poisoning incident.”

According to Pope, one persistent neurological problem is clinical depression. Neuropsychological problems have been shown both in epidemiological studies in humans and in experimental studies in animal models.

Pope’s team recently published a paper in the journal Neurotoxicology and Teratology showing long-term depressive-like neurobehavioral changes in rats following acute exposure to the organophosphorus toxicant, diisopropylfluorophosphate or DFP.

“While the animals show signs of acute neurotoxicity within the first few days after exposure, those signs subside. However, neurobehavioral signs of depression were noted after recovery from the acute toxicity,” says Pope. “Interestingly, if you give drugs that block the inactivation of endocannabinoids—endogenous neuromodulating molecules in the nervous system—immediately after DFP, the induction of both acute toxicity and persistent behavioral changes are blocked.”

The toxicologists will be looking at neurobehavioral endpoints to evaluate persistence of the changes as well as determining how the endocannabinoid-active drugs are modulating expression of acute and persistent changes following organophosphate intoxication. While this project studies neurological complications following acute toxicity and their modulation by endocannabinoids, mechanistic information gained in these studies could be useful in therapeutic strategies for treating other neurological conditions.

Dr. Carey Pope is the head of the Department of Physiological Sciences at OSU's veterinary center, a Regents Professor, and the Sitlington Chair in Toxicology.

The Oklahoma State University Center for Veterinary Health Sciences is one of 28 veterinary colleges in the United States and is fully accredited by the Council on Education of the American Veterinary Medical Association. The center's Boren Veterinary Medical Teaching Hospital is open to the public and provides routine and specialized care for small and large animals. It also offers 24-hour emergency care and is certified by the American Animal Hospital Association. For more information, visit www.cvhs.okstate.edu or call (405) 744-7000.

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