Protecting our Defense

UNMC researcher studies enzyme that neutralizes chemical warfare agent

For nearly 30 years, Oksana Lockridge, Ph.D., has been focused on one enzyme: butyrylcholinesterase.

But, never in that time has the world's interest in the enzyme – which effectively neutralizes any pesticide or chemical warfare agent – been as great as it is now.

UNMC researchers have received a four-year, $1.7 million grant from the U.S. Department of Defense to develop an efficient way to protect humans against the toxic effects of nerve agents used in chemical warfare. Nerve agents are chemicals related to the organophosphorus group of pesticides, which interfere with the functioning of the nervous system.

"The goal of the study is to find a way to treat people who have been exposed to chemical warfare nerve agents, which can be fatal or cause extensive health damage," said Dr. Lockridge, principal investigator of the grant. "The Army is very interested in developing protection against chemical warfare agents, because the agents are so easy to make."

Gene and Protein Therapy

Dr. Lockridge is an associate professor in both the UNMC Eppley Institute for Research in Cancer and Allied Diseases and the department of biochemistry and molecular biology.

The study will use gene and protein therapy, the treatment of disease by replacing, altering or supplementing a gene or protein responsible for the disease, to better protect against effects of nerve agents. A technique being tested through Dr. Lockridge's research is administration of a protein applied through a skin patch.

"We know the identity of a human enzyme, butyrylcholinesterase, that will neutralize any pesticide or chemical warfare agent very effectively without being toxic to a person or an animal," Dr. Lockridge said. "With this protection, you won't even know you got hit with something."

Butyrylcholinesterase is found in blood, the liver, and other tissues; however, its function is not specifically known.

Dr. Lockridge's research already has intrigued a San Diego company, interested in using the application in the treatment of cocaine overdose toxicity, and a Montreal company, interested in creating transgenic goats that produce butyrylcholinesterase in their milk.

Breathing 10 milligrams – the weight of a grain of rice – of the deadliest nerve agent, called VX, can kill in 15 minutes. Symptoms of nerve agent exposure include reduced vision, diarrhea, vomiting, paralysis and respiratory failure. Ultimately, individuals experience convulsions and go into a coma. An antidote kit called the Mark 1, distributed to U.S. troops during the Gulf War, is currently available for protection against death by nerve agent exposure. Dr. Lockridge's study is looking for a better alternative.

Chemical warfare was used in the 1995 Tokyo subway terrorist attacks, when members of a cult placed sarin gas on the trains, killing 12 and injuring more than 5,500. Agents such as sarin, VX and tabun are inexpensive and easy to manufacture and have been used as weapons of terrorism and defense mechanisms for Third World countries.

"A method must be developed that shields humans from the effects of chemical warfare agents and provides medical treatment for those who become exposed," said Dr. Lockridge, who joined the UNMC faculty in 1990.

Her study also is relevant to Nebraska farmers because of the similarity in makeup of chemical warfare agents and pesticides. About 80,000 cases of pesticide poisoning are reported annually in the United States. Common pesticides such as roach and ant killers are in the same class of chemicals as the chemical nerve agents.

With the system of gene and protein therapy currently developed in Dr. Lockridge's lab, the cost of protecting one person is at least $1 million. Researchers are looking for ways to lower the cost so it would be a realistic option to protect the general public.

Co-investigators of the study are Steven Hinrichs, M.D., associate professor of pathology and microbiology and director of the Nebraska Public Health Laboratory; and Angie Rizzino, Ph.D., professor in the Eppley Institute and department of biochemistry and molecular biology.