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Researchers developing new drug class to combat Alzheimer's

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The University of Illinois at Chicago College of Pharmacy has received a four-year, $1.87 million grant from the National Institutes of Health to continue research into discovering a new drug class that will treat Alzheimer's disease.

Gregory Thatcher, professor of medicinal chemistry and pharmacognosy and the grant's principal investigator, and his former colleagues at Queen's University in Kingston, Ontario, proposed a dozen years ago that delivering nitric oxide to the brain would be beneficial in combating neurodegenerative diseases, since nitric oxide is a messenger molecule essential for learning and memory.

"But this wasn't a popular notion, because nitric oxide is a free radical gas and toxic at higher concentrations," Thatcher said. "But then again, so is oxygen, and it's also rather important for life. It's a question of understanding the chemistry and engineering the molecule to deliver nitric oxide bioactivity, but also additional activity to restore and protect brain function."

Alzheimer's disease is a devastating illness affecting one out of three people over the age of 80, and is the sixth leading cause of death in the United States, according to the Alzheimer's Association. There are currently no drugs to slow the rate of progression of the disease. "Even new drugs that effectively treat the symptoms would be of enormous benefit to patients and caregivers," Thatcher said.

Along with working on the new NIH grant, Thatcher and Pavel Petukhov, assistant professor of medicinal chemistry and pharmacognosy, are assisting Dr. Ottavio Arancio of Columbia University in studying how the inhibition of the enzyme calpain can be a therapeutic target for Alzheimer's. Arancio received a four-year, $2.1 million grant from the NIH for the study.

Arancio, who in turn is assisting Thatcher on his new research project, recently showed the importance of controlling nitric oxide signaling in restoring normal brain function in animal models of Alzheimer's.

Thatcher is also the beneficiary of a new five-year, $1.6 million NIH grant to study nitric oxide chimera drugs in colon cancer chemoprevention.

"It might seem strange that nitric oxide delivery could benefit both the brain and colon," Thatcher said. But nitric oxide bound to aspirin -- or nitro-aspirin -- was in clinical trials for colon cancer chemoprevention before the trial was stopped for safety concerns, he said.

"Our brain-targeted nitric oxide chimera drugs were the first to be studied in humans, and although we did not pioneer the nitric oxide related drugs for colon cancer, we believe that they hold promise."

Dr. Richard Benya and Dr. Robert Carroll in the department of medicine at UIC are assisting Thatcher in the colon cancer research project.

"There have been no significant advances in the survival of patients with colon cancer since President Richard Nixon declared the war on cancer in 1971," Benya said. "We desperately need new drugs, not only to treat this type of tumor, but to prevent it as well."

Source: University of Illinois at Chicago