Cool Research Project Spotlight

$1.5M Grant Helps Turn Chemical Weapon into Medical Marvel

By Rebecca E. Phillips

PULLMAN, Wash. – A middle-aged man is stricken by a heart attack and crumples to the floor. But when paramedics arrive, they skip the oxygen and instead administer a bit of toxic gas that puts the patient into a protective state of "hibernation." Later, fully recovered in the hospital, the man's heart shows little sign of damage.

Though futuristic, such treatment is nearly within reach thanks to chemical tools created by Ming Xian, an associate professor of chemistry at Washington State University.

Xian runs the world's leading laboratory for development and production of bioactive hydrogen sulfide donors and sensors – a new class of chemical compounds aimed at some of medicine's worst enemies: heart disease, traumatic shock and blood loss, complications of diabetes and possibly even Parkinson's and Alzheimer's disease.

He has just been awarded $1.5 million from the National Institutes of Health to investigate hydrogen sulfide releasing agents for tissue damage that occurs during heart attacks and other conditions.

Controllable compound patented

Previous studies have shown that hydrogen sulfide (H2S) gas – once used as a deadly chemical agent in WWI – can reduce the body's need for oxygen by temporarily slowing down metabolism. That could be a boon for medicine, especially for critical care workers treating trauma patients.

Unfortunately, H2S is not only toxic but is also extremely short-lived and difficult to study, blocking prior attempts to recruit it for health care.

In 2009, Xian began developing a controllable source of hydrogen sulfide gas for use in biomedical research. Today, his team has patented the first controllable hydrogen sulfide donors and one of the first sensors.

Xian's donors and sensors are novel organic chemical compounds that allow H2S to be studied in living tissue with reliability and precision.

Donors are engineered to release H2S when they contact specific molecules in the body and may one day be used to deliver medical treatments. Sensors – fluorescent probes – glow when they discover H2S within cells and tissues, helping unlock the mysteries of the gas's protective effects on the body.

Dr. Xian and grad student Tyler Biggs.

70 percent less heart attack injury

For ages, hydrogen sulfide has had a bad rap, says Xian. Although sulfur is the third most abundant mineral in the body, important for protein and enzyme systems, its rotten egg smell has made it something of a joke. Most people know H2S as the warning odor in natural gas leaks.

But by 2008, researchers had clearly established that the body itself produces H2S and uses it as a signaling molecule to help regulate physiological processes in the brain, heart and other organs.

For example, hydrogen sulfide maintains heart health through a number of actions, including dilating vessels to help control blood pressure.

"During a heart attack, blood flow to cardiac tissue is blocked, resulting in a lack of oxygen," says Xian. "In response, cell metabolism starts to slow down to protect the heart from injury."

The worst damage occurs when blood pours back into the heart carrying normal levels of oxygen. The sudden influx triggers the release of oxidizing molecules that can destroy heart tissue.

Because H2S also acts as an antioxidant, Xian says that quickly treating a patient with hydrogen sulfide at this point could block oxidizing molecules and protect the heart from further harm.

"Experiments prove it works, but it hasn't been used in humans," he says.

In a 2010 TED talk, Mark Roth, a cell biologist at the Fred Hutchinson Cancer Research Center in Seattle, described how animals treated with H2S showed 70 percent less injury in heart attacks than animals receiving the usual human standard of care.

Injury, disease treatment possibilities

Hydrogen sulfide is also being eyed for use when the entire body is deprived of oxygen by blood loss or shock. Early treatment with H2S could allow tissues to survive on lower concentrations of oxygen, potentially buying a patient enough time to secure proper treatment.

Studies on Parkinson's and Alzheimer's disease have found severely reduced levels of hydrogen sulfide in brain tissue where it should be abundant. This has led to speculation that supplemental H2S might also benefit these conditions.

"So, hydrogen sulfide could have lots of applications, from helping soldiers injured in battle, to treating heart attacks, to healing inflammatory conditions such as skin lesions in diabetics," says Xian.

References

Phillips, Rebecca E. (2014, March 19). *$1.5M grant helps turn chemical weapon into medical marvel.* Retrieved March 19, 2014, with permission from Washington State University. Photos courtesy of Rebecca E. Phillips and WSU University Communications.

If you want to share a "cool" project idea, please email Danielle Anthony at danthony@wsu.edu

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Professor Ming Xian *received his B.S. in chemistry from Nankai University China. He then joined Professor Jin-Pei Cheng's group at Nankai for his early graduate study. In 1999, he moved to the Wayne State University to continue his research under Professor Peng George Wang. After received his Ph.D. in organic chemistry in 2003, he did postdoctoral research with Professor Amos B. Smith, III as a DOD postdoctoral fellow at the University of Pennsylvania. In August 2006, he joined the faculty at the Washington State University in the Department of Chemistry.*

The core of Dr. Xian's research interests comprises the desire to combine organic synthesis with bioorganic chemistry to examine, understand, and solve problems of biological and medicinal significance. We are interested in the areas of (1) synthetic methodology development; (2) natural product synthesis; (3) bioorthogonal reactions for protein identification; and (4) the development of bio-based new materials.

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