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Cooperative State Research, Education, and Extension Service

National Research Initiative (NRI)

Research on Insects Leads to New Treatments for High Blood Pressure

by Stacy Kish, CSREES

Research into the hormone that controls the growth of insects has led to a new approach to treating human disorders, including hypertension. >>

The insect juvenile hormone controls the different stages of development. With funding from USDA's Cooperative State Research, Education, and Extension Service's (CSREES), a team of scientists in California developed insect growth regulators that mimic juvenile hormone as a form of biologically-based insect control, which in turn led to the unexpected discovery of a new approach to treat high blood pressure and other disorders in humans.

Bruce Hammock and colleagues at the University of California, Davis set out to understand the key enzymes involved in the metabolism of insect juvenile hormone. They identified and characterized epoxide hydrolase, an important enzyme in the metabolism of this hormone.

The researchers determined that by preventing the juvenile hormone from breaking down, they could stop caterpillar metamorphosis into moths

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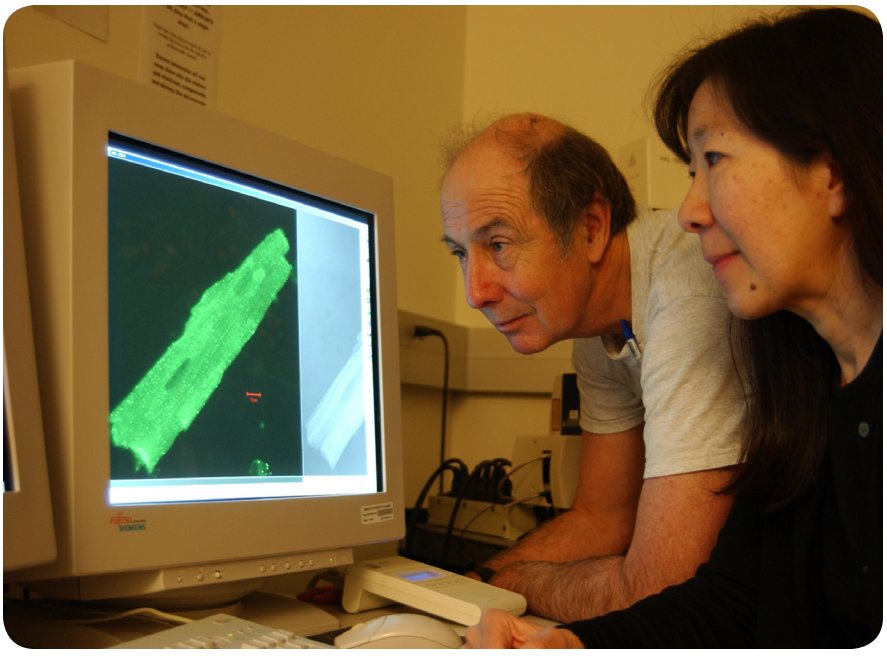

Right: University of California, Davis research physician Nipavan Chiamvimonvat (right) and entomologist Bruce Hammock look at confocal photomicrographs showing distribution of the enzyme soluble epoxide hydrolase in a mouse heart muscle cell. The Chiamvimonvat laboratory has found that inhibition of the enzyme in the heart prevents heart failure.

Credit: Kathy Keatley Garvey

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or butterflies. This work may lead to a new strategy for insect pest control.

"This work [has led to the] training [of] a number of wonderful students," Hammock said. "It also shows how basic curiosity-driven research has yielded valuable methods to control insect pests and unexpectedly led to a new class of drugs for a number of serious human diseases."

To the researchers' surprise, the enzyme important in insect juvenile hormone can break down polyunsaturated fatty acid in humans. This particular fatty acid is known as arachidonic acid, which are involved in many biological processes such as how the body responds to pain, high blood pressure, or childbirth.

Previous research on arachidonate metabolites focused on the pathways inhibited by aspirin, indomethacin, Celebrex, and related compounds. The enzyme was involved in a critical, but little studied, pathway in the breakdown of anti-inflammatory arachidonate metabolites called EETs or epoxyeicosatrienoic acids. The researchers found that by inhibiting the break down of EETs, the blood pressure in rodent was reduced.

Further work led to the development of an orally active form of the chemical. The oral agent was easily absorbed and distributed in mammals, resulting in more potent anti-inflammatory drugs than the commonly used non-steroidal anti-inflammatory drugs.

The orally active form of the chemical reduced the most common type of high blood pressure in middle-aged humans. The newly discovered chemical also reduced vascular inflammation and organ damage, the long-term effects of high blood pressure

The oral compound developed in this study is in Phase I human clinical trials and being developed as a pharmaceutical to treat high blood pressure, inflammation, diabetes, pain and other disorders.

This work illustrates how fundamental research on agriculturally important insects can lead to a novel and environmentally friendly pest control strategy as well as the first new method to control high blood pressure in humans in over 20 years.

CSREES funded this research project through the National Research Initiative (NRI) Suborganismal Biology of Arthropods and Nematodes program. Through federal funding and leadership for research, education and extension programs, CSREES focuses on investing in science and solving critical issues impacting people's daily lives and the nation's future. For more information, visit www.csrees.usda.gov.■

NRI awards grants for research, education, and extension activities that address key problems of national and regional importance in biological, environmental, physical, and social sciences relevant to agriculture, food, the environment, and communities on a peer-reviewed, competitive basis. For more information, visit:

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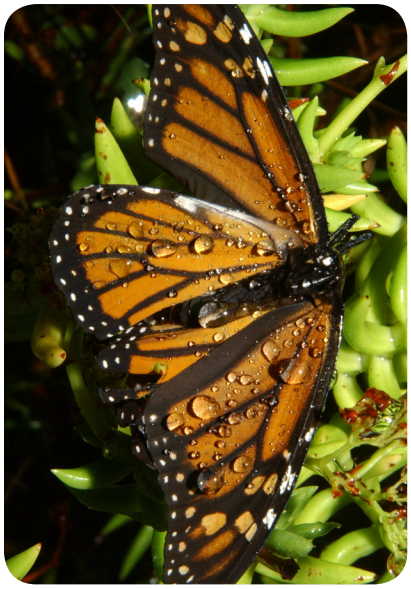

Above: A monarch butterfly.
Credit: Kathy Keatley Garvey

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Chiamvimonvat, N., C.-M. Ho, H.-J. Tsai and B.D. Hammock. 2007. The soluble epoxide hydrolase as a pharmaceutical target for hypertension. J. Carviovasc. Pharm. 50:225-237.