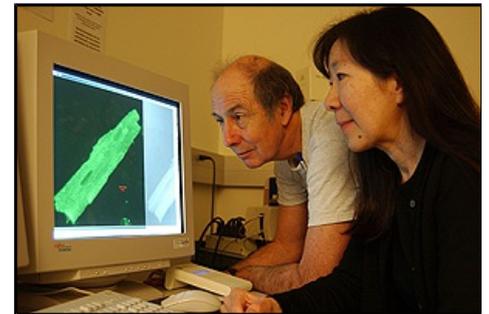


Potential new therapy for stopping cardiac fibrosis

By Carol Kelly

A unique therapy for preventing or reducing harmful cardiac scar tissue, a common development in people following a heart attack, may result from a new finding by NIEHS-supported researchers at the University of California, Davis (UC Davis). Their [study](http://www.ncbi.nlm.nih.gov/pubmed/23493561?dopt=Abstract) (<http://www.ncbi.nlm.nih.gov/pubmed/23493561?dopt=Abstract>) shows that blocking an enzyme that promotes inflammation can prevent cardiac fibrosis, scar tissue damage that often leads to heart failure.

"Cardiac fibrosis is a common final pathway for many cardiac diseases and heart failure that has been difficult to treat in the clinic," said [Javier Lopez, M.D.](http://www.ucdmc.ucdavis.edu/publish/facultybio/internalmedicine/1519), (<http://www.ucdmc.ucdavis.edu/publish/facultybio/internalmedicine/1519>) a professor at UC Davis specializing in cardiovascular medicine and part of the research team. "This study shines some light onto this pathway and offers perhaps a new therapeutic target that may expand available treatments for these patients in the future."



Chiamvimonvat, right, and Hammock look over the distribution of an enzyme in a rodent heart muscle cell. (Photo courtesy of UC Regents)

Inhibiting the enzyme soluble epoxide hydrolase

An 11-scientist team determined the molecular mechanisms underlying the beneficial effects of inhibiting the enzyme soluble epoxide hydrolase (sEH) after a heart attack. The scientists were led by [Bruce Hammock, Ph.D.](http://www.biopestlab.ucdavis.edu/), (<http://www.biopestlab.ucdavis.edu/>) who directs the UC Davis Superfund Research Program, and [Nipavan Chiamvimonvat, M.D.](http://www.ucdmc.ucdavis.edu/publish/facultybio/internalmedicine/682), (<http://www.ucdmc.ucdavis.edu/publish/facultybio/internalmedicine/682>) a professor of cardiovascular medicine at UC Davis.

In the study, mice receiving sEH inhibitors showed significant decreases in adverse cardiac muscle remodeling, or enlargement, following a heart attack. Their overall cardiac function also improved. Additional tests performed in Hammock's lab indicated significantly reduced levels of inflammatory factors in the mice. The research team hopes to next test the compound on another animal model, as a precursor to human clinical trials.

The enzyme sEH typically plays a lead role in tissue healing following an injury. However, this role can become counterproductive after a cardiac event.

Chiamvimonvat explained that sEH exacerbates inflammatory conditions. It also causes the cells that typically link together to provide the foundation for heart tissue to overwork. The outcome is cardiac fibrosis, which results in an abnormal relaxation of the heart after each beat. Undamaged heart muscle is remodeled as it performs double duty, eventually leading to a decline in the heart's pumping action.

Potentially impacting a major public health issue

Heart failure, a condition where the heart cannot pump enough blood to support other organs, affects 5.7 million people in the United States, and costs the nation \$34.4 billion in health care services, medications, and lost productivity, according to the [Centers for Disease Control and Prevention](http://www.cdc.gov/dhdspl/data_statistics/fact_sheets/fs_heart_failure.htm). (http://www.cdc.gov/dhdspl/data_statistics/fact_sheets/fs_heart_failure.htm) About half of the people who have heart failure die within five years of diagnosis.

"This study is the result of a long-term, exciting collaboration between the College of Agricultural and Environmental Sciences and the UC Davis School of Medicine, which has been very productive," said Hammock. "The translational value of our research is significant."

Linked Video

[Watch a video about translation of Hammock's findings to help alleviate a hoof disease in horses \(02:02\).](#)

This finding is also the latest in a long line of success in Hammock's [research](http://www.biopestlab.ucdavis.edu/) (<http://www.biopestlab.ucdavis.edu/>) related to sEH inhibitors. Forty years ago, Hammock discovered sEH inhibitors while studying insect development. His previous work with sEH inhibitors led to beneficial discoveries related to controlling blood pressure and treating neuropathic pain associated with diabetes.

Citation: Sirish P, Li N, Liu JY, Lee KS, Hwang SH, Qiu H, Zhao C, Ma SM, Lopez JE, Hammock BD, Chiamvimonvat N. (<http://www.ncbi.nlm.nih.gov/pubmed/23493561>) 2013. Unique mechanistic insights into the beneficial effects of soluble epoxide hydrolase inhibitors in the prevention of cardiac fibrosis. *Proc Natl Acad Sci U S A*; doi:10.1073/pnas.1221972110 [Online 14 March 2013].

(Carol Kelly is a health communication specialist with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

The Environmental Factor is produced monthly by the [National Institute of Environmental Health Sciences \(NIEHS\)](http://www.niehs.nih.gov/) (<http://www.niehs.nih.gov/>), Office of Communications and Public Liaison. The content is not copyrighted, and it can be reprinted without permission. If you use parts of Environmental Factor in your publication, we ask that you provide us with a copy for our records. We welcome your [comments and suggestions](#). (bruskec@niehs.nih.gov)

This page URL: http://www.niehs.nih.gov/assets//Sites/NIEHS_eFactor/2013/4/
NIEHS website: <http://www.niehs.nih.gov/>
Email the Web Manager at webmanager@niehs.nih.gov