National Institute of Environmental Health Sciences

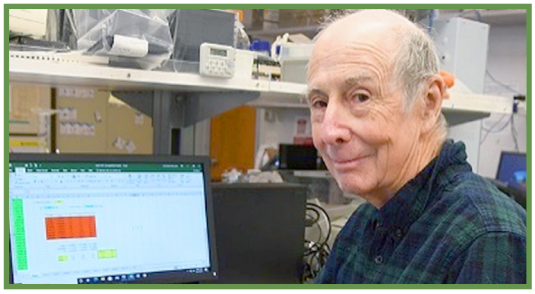
Uncovering Targets to Treat Pain and Chronic Diseases

From insect hormones to human health, NIEHS-funded research decodes the biology behind environmental risk, pain, and organ damage — and how to intervene.

With funding from the National Institute of Environmental Health Sciences (NIEHS) for nearly five decades, Bruce Hammock, Ph.D., has followed a scientific thread that began in insects and now spans human health, environmental monitoring, and drug development. Hammock, a researcher at the University of California (UC), Davis, is renowned for the discovery of soluble epoxide hydrolase (sEH), an enzyme that regulates beneficial fatty acid molecules that help control inflammation. When sEH breaks down the fatty acids too quickly, it can trigger pathways that worsen chronic pain, organ damage, and neurological disease.

This discovery led Hammock to develop treatments that inhibit sEH to preserve these anti-inflammatory fatty acids. These compounds are now being tested in humans, offering a potential nonaddictive alternative for chronic pain and other inflammation-linked disorders.

Hammock's work has illuminated the connections between environmental exposures, diet, inflammation, and disease. By targeting the sEH pathway, his lab is revealing how environmental exposures and other stressors in the body drive illness. They are also building new tools to prevent and treat chronic diseases, transforming decades of basic research into real-world impact.



NIEHS first funded Hammock's research in 1975, and the same grant continues to be funded.

"Support from NIEHS has empowered us to follow bold scientific questions. This long-term funding has been instrumental in our discovery of soluble epoxide hydrolase and its role in inflammation and pain, ultimately leading to therapies now advancing through clinical trials," Hammock said. "It's a testament to how foundational science, supported consistently, can evolve into real-world medical innovation."

Impacts of Uncovering Targets to Treat Pain and Chronic Diseases

Targeting Inflammation:

- Discovery of soluble epoxide hydrolase (sEH) laid the foundation for decades of research teasing apart how regulating sEH can reduce inflammation and protect against disease.

Advancing Drug Development:

- Developed a range of stable sEH inhibitors, enabling long-lasting therapeutic treatments for a growing list of diseases.
- Launched the clinical startup EicOsis and developed EC5026, a non-addictive pain medication currently in clinical trials.

Treating Chronic Diseases and Pain:

- Demonstrated that sEH inhibitors alleviate nerve-related pain from diabetes, trauma, and multiple sclerosis.
- Found that sEH inhibitors play a role in treating depression, Parkinson's, Alzheimer's, and vision loss.

Protecting Vital Organs:

- Revealed that inhibiting sEH can prevent damage to the heart, kidneys, lungs, and liver, reducing tissue scarring, preserving function, and improving health outcomes.

Understanding Diet and Gut Health:

- Identified links between sEH, high-sugar diets, and obesity-related gut injury.
- Targeting sEH offers a new strategy for treating inflammation-driven gut damage and metabolic diseases.

Then and Now

- **Then:** Ultra processed diets contribute to chronic inflammation, but the mechanism behind health outcomes was poorly understood.
- **Now:** Hammock revealed a link between linoleic acid, a fatty acid elevated by processed diets, and inflammation. Controlling the levels of linoleic acid led to improved health outcomes, including reduced headaches, better pain management, and decreased risk of gut diseases.[1,2]
- **Then:** Analyzing toxic substances in the environment was costly, time-consuming, and often lacked the sensitivity needed to assess human exposure.
- **Now:** Hammock pioneered immunoassay technologies that use antibodies to quickly and affordably detect hazardous chemicals, providing more sensitive and accessible tools for environmental monitoring and public health protection.

Research Timeline

Fundamental Questions | Application and Synthesis | Implementation and Adjustment | Policy and Practice | Impact

1980

Fundamental Questions

Discovered the sEH enzyme in mammalian tissues. sEH, previously only studied in insects, is an enzyme that breaks down fatty acids and plays a key role in insect metamorphosis.[3]

1999

Application and Synthesis

Developed highly potent and stable compounds to inhibit sEH, a significant advance over earlier unstable, short-acting inhibitors.[4,5]

2002-2010

Fundamental Questions

Showed that sEH inhibition protects against high blood pressure and atherosclerosis.[6,7]

2006-Present

Fundamental Questions

Demonstrated that sEH inhibitors can treat chronic pain from nerve damage from trauma, diabetes, shingles, multiple sclerosis, and side effects of chemotherapy drugs.[8,9,10,11,12]

2011

Fundamental Questions

Demonstrated that blocking sEH preserves beneficial fatty acid epoxides, such as from omega-3 and omega-6, enhancing anti-inflammatory effects.[13]

2011

Policy and Practice

Founded EicOsis, a clinical startup to develop develop non-opioid treatments for chronic pain and inflammation.

2013

Application and Synthesis

Developed an sEH inhibitor that prevents cardiac fibrosis, a heart condition resulting from the formation of scar tissue after heart attacks, which can lead to heart failure.[14]

2014-2023

Fundamental Questions

Found that sEH inhibitors reduce kidney damage associated with obesity and diabetes[15] and revealed potential therapeutic agents to treat kidney failure.[16]

2014-2015

Fundamental Questions

Revealed that blocking sEH reduces inflammation and airway hyperresponsiveness, and decreases oxidative stress related to asthma.[17,18]

2016

Fundamental Questions

Reported elevated sEH expression in the brains of chronically stressed mice and discovered that TPPU, an sEH inhibitor, has rapid antidepressant effects.[19]

2016

Fundamental Questions

Found that TTPU treatment lessened the harmful effects of carbon tetrachloride, a chemical previously used in pesticides, on the liver.[20]

2017-2023

Fundamental Questions

Found that sEH inhibitors protect against lipopolysaccharide-induced acute lung injury. Lipopolysaccharide is a toxic component of bacteria such as E. coli and salmonella and has been linked to a variety of adverse health effects.[21,22,23]

2018

Application and Synthesis

Linked sEH to endoplasmic reticulum stress pathways that regulate inflammation and cell death; reported that inhibition of sEH can resolve inflammation across many disease types.[24]

2018

Fundamental Questions

Found that sEH inhibition may prevent vision loss in mice affected by macular degeneration and diabetic retinopathy.[25,26]

2020

Fundamental Questions

Reported a link between sEH and obesity-related leaky gut, a type of intestinal damage that allows toxins to leak into the bloodstream.[27]

2021-Present

Implementation and Adjustment

Developed EC5026, a nonaddictive anti-inflammatory drug to target sEH that is advancing through clinical trials.[28,29]

2021-2024

Application and Synthesis

Identified sEH-related anti-inflammatory therapies to improve outcomes from SARS-CoV-2 infection.[31,32]

2022

Application and Synthesis

Demonstrated that combining sEH inhibitors with kurarinone, a plant-derived compound, reduces neuroinflammation in a Parkinson's disease mouse model.[33]

2023-2024

Application and Synthesis

Synthesized PROTACs, a type of molecule that target sEH to reduce inflammation in cells, with applications for diabetes, metabolic disease, and chemical exposures.[34,35]

2024

Application and Synthesis

Identified an sEH inhibitor that can alleviate gut injury resulting from high sugar consumption, offering a potential treatment for diet-related health issues.[36]

2024

Application and Synthesis

Demonstrated that sEH inhibition protects against lung injury from air pollution and effectively treats inflammatory pain.[37,38]

2025

Application and Synthesis

Found that sEH inhibitors can protect against neurodegeneration associated with Alzheimer's disease.[39]

NIH National Institute of Environmental Health Sciences

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EicOsis: A New Chapter in the Fight Against Pain and Inflammation

Chronic inflammation can disrupt the body's natural balance, contributing to a wide range of debilitating conditions. Driven by a lifelong commitment to finding safer, more effective ways to treat pain and chronic disease, Hammock co-founded EicOsis in 2011. The company emerged from decades of research on the sEH enzyme and a lifelong mission to find a better way to treat pain, without relying on opioids or bringing dangerous side effects.

Hammock co-founded EicOsis alongside UC Davis alumna and pharmacologist-toxicologist Cindy McReynolds, Ph.D.

Before joining UC Davis, Hammock served as a medical officer at the U.S. Army Academy of Health Sciences, where he witnessed firsthand the devastating effects of acute and chronic pain.

"Chronic pain is an enormous emotional and economic burden for more than 100 million people in the United States alone," Hammock said. "The extreme and poorly treated pain that I observed as a medical officer is a major driver for me to translate laboratory research to help patients with severe pain."

EicOsis derives its name from eicosanoids, the lipid signaling molecules involved in the body's inflammatory response, and epoxide, a key chemical group targeted by sEH inhibitors.

With funding from NIEHS, EicOsis developed and successfully advanced its lead compound, EC5026, through Phase I human clinical trials with no drug-related adverse events. EC5026 is a first-in-class inhibitor of sEH that enhances the body's natural protective pathways, showing promise for treating conditions like neuropathic pain, arthritis, and potentially even neurodegenerative diseases.

"The company's work is rooted in basic research but focused on improving people's lives," Hammock said. "Our goal is to help people suffering from pain feel like themselves again."

Research Challenges and Solutions

Challenge:
Early inhibitors of sEH were chemically unstable and short-acting, limiting their utility for long-term therapeutic applications.

Solution:
Hammock's team synthesized potent and stable inhibitors that had long-lasting activity, making them suitable for drug development.

Challenge:
Translating lab discoveries into real-world treatments is a long and uncertain process.

Solution:
Hammock co-founded EicOsis to translate basic science into clinical impact. Strategic partnerships and support from the NIEHS Small Business Innovation Research program helped bring sEH inhibitors into clinical trials.

Immunoassays: Precision Tools for Exposure Detection

Hammock's lab pioneered more than 40 immunoassays for analyzing pesticides and other contaminants in both human and environmental samples. Immunoassays use antibodies to bind to a chemical of interest. Once bound, a detectable label — like a color change or fluorescent signal — indicates the presence and concentration of the chemical.

To improve sensitivity and efficiency, the team has integrated luminescent nanoparticles into their immunoassays. These nanoparticles can carry multiple labels to amplify the signal, making it possible to detect trace amounts of chemicals. By tagging different nanoparticles with specific antibodies or labels, the tests can screen for multiple contaminants simultaneously. The use of microfluidic "lab-on-a-chip" platforms enables portable, on-site testing outside the lab.[40,41]

Following studies that linked triclosan to liver tumors in mice[42] and showed triclocarban can be absorbed through the skin and metabolized into reactive compounds associated with allergic reactions,[43,44] Hammock's lab developed immunoassays to track human and environmental exposure. These assays detect triclosan and triclocarban in water and biological samples, such as urine and serum, providing essential tools for exposure assessment.[45,46] This work contributed to the body of evidence that informed the U.S. Food and Drug Administration's decision to ban both chemicals from over-the-counter antibacterial hand and body washes in 2017.[47]

Beyond antibacterials, Hammock's immunoassays have been applied to:

- Measuring a variety of pesticides — even at trace amounts — in urine, blood, foods, soil, sediment, and water.[48,49,50,51]
- Detecting foodborne pathogenic bacteria.[52]
- Measuring dioxins in sediments and soil.[53]
- Monitoring flame retardants in water.[54]

Through these innovations, Hammock's work continues to provide essential tools for environmental monitoring and public health protection.