NIH AWARDS $38 MILLION GRANT RENEWAL TO UC SAN DIEGO FOR LIPID MAPPING PROJECT

October 13, 2008 |

The University of California, San Diego School of Medicine has been awarded nearly $38 million by the National Institute of General Medical Sciences (NIGMS), part of the National Institutes of Health, to continue leading "LIPID MAPS," a national consortium studying the structure and function of lipids – cellular fats and oils that serve as building blocks for cells or as energy sources for the body. Lipids are implicated in a wide range of disorders, including heart disease, stroke, arthritis, cancer, diabetes and Alzheimer's disease.

The five-year competitive renewal grant will enable the continuation of this ambitious national effort that brings together the work of dozens of researchers at 16 universities, medical research institutes and companies across the United States. This $38 million builds upon $35.6 million awarded to UC San Diego in 2003 to establish and fund the consortium, designed to lead to breakthroughs in the understanding of lipid metabolism and the treatment of lipid-based diseases.

Genes and proteins are often the focus of biomedical research, but lipids have a more direct impact on disease, according to the consortium's principal investigator, Edward Dennis, Ph.D., distinguished professor of pharmacology and chemistry and biochemistry at UC San Diego, who also serves as the editor-in-chief of the *Journal of Lipid Research.* Just as the past decade marked the era of the human genome, Dennis and many other scientists regard lipids as the next revolution in medical research.

"Lipids are key to the regulation of both normal cellular function and to disease pathology," said Dennis. "Lipid imbalances play a role in most serious illnesses. If we hope to find cures and treatments, we must understand the metabolism of the many diverse types of lipids."

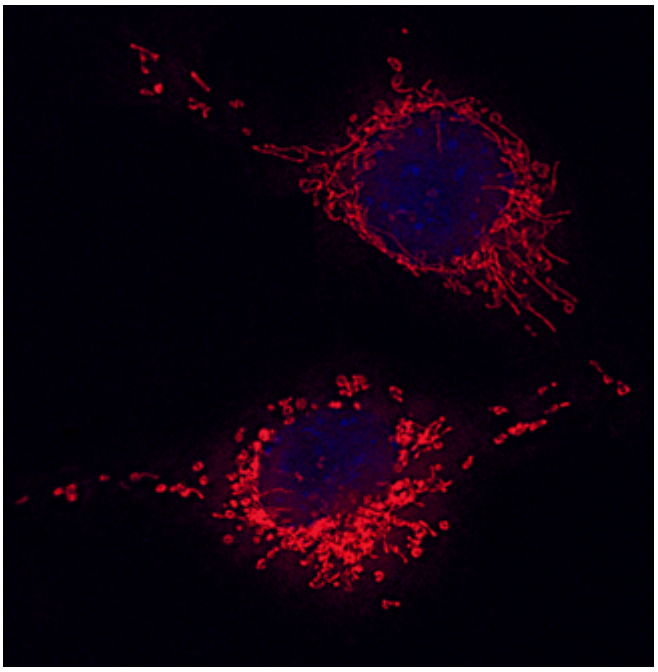
Lipids are vital components of cell membranes, and are involved in communication and signaling within and between cells. Lipids are numerous and diverse. For example, one class of lipids, the sterols, includes estrogen and testosterone – hormones that direct not only the reproductive system, but some types of brain functions as well. Prostaglandins are lipids that are implicated in pain and inflammation. Production of these hormone lipids are blocked by aspirin and other non-steroidal anti-inflammatory drugs (NSAIDS). With tens of thousands of other kinds of lipids, the

consortium is tackling a major challenge in analyzing the array of lipid molecular species, then quantifying their changes in response to cellular stimulation or stress.

Dennis explains: "The research has been organized into major lipid categories, with each category headed by a lipidomics core director at one of the participating institutions. In order to be able take the data gathered by each lab and put them together, it was essential to develop new technologies and methods and to standardize them so that they could be applied in the same way at each research site."

The Bioinformatics Core, under the direction of Shankar Subramaniam, Ph.D. – professor of chemistry, chair of the department of bioengineering at UC San Diego's Jacobs School of Engineering, and senior fellow at the San Diego Supercomputer Center – integrates and analyzes the huge amount of resulting data gathered by participating researchers.

This approach has provided a "lipidome," or complete picture of all the lipids contained in one particular type of cell, the macrophage. The macrophage is a cell best known for its role in immune reactions and was chosen by the consortium researchers to begin its study of biological systems. By determining the macrophage lipidome, the researchers are gaining an understanding of how the lipid molecules change when subjected to infection or inflammation. This will enable scientists to look beyond the genome and proteome, with the hopes of discovering new biomarkers of disease.



macrophage cells with nucleus stained blue and mitochondria stained pink

"For example, our preliminary studies demonstrated a large impact of a Western high fat diet on the lipid composition of the macrophage and lipid gene message levels," said Christopher K. Glass, M.D., Ph.D., professor of medicine and cellular and molecular medicine at UC San Diego and director of LIPID MAPS' Macrophage Biology Core. "Many of these changes were unexpected and can't currently be explained, but this will stimulate future studies on the nutritional effects of lipids."

"We are in a strong position to begin determining the impact of specific therapeutic interventions, such as statins and their effects on the lipidome," says Dennis. "Importantly, we are also determining the identity of the oxidized lipids in oxidized LDL, a type of lipid that plays a critical role in making LDL atherogenic," added Joseph Witztum, M.D., professor of medicine at UC San Diego and Director of the Oxidized Lipid Bridge. Atherosclerosis is a chronic inflammatory response in the arteries, due to the accumulation of plaques on the artery walls. Commonly known as "hardening of the arteries," the disease can lead to a heart attack or blood clot.

The grant renewal brings total funding to date for LIPID MAPS to more than $73 million, one of the largest grants ever awarded to an investigator at UC San Diego.

In addition to UC San Diego, participants in the consortium include Duke University, Georgia Institute of Technology, Indiana University, Pennsylvania State University, University of Colorado at Denver, University of Texas Southwestern Medical School, and Vanderbilt University, as well as one company, Avanti Polar Lipids, Inc.

Additional participating investigators include scientists from Boston University, Case Western Reserve University, Cayman Chemical Company, Inc., Harvard, Massachusetts Institute of Technology, Medical College of Georgia, National Jewish Medical and Research Center, Scripps Research Institute, University of Utah, and Virginia Commonwealth University.

A distinguished international Advisory Committee that includes Nobel Prize laureate Bengt I. Samuelsson of the Karolinska Institute, Stockholm, advises Dennis and the LIPID MAPS Steering Committee.

Take a tour of the LIPIDS MAPS web site.

More about LIPID MAPS

LIPID MAPS (Lipid Metabolites And Pathways Strategy) uses a systems biology approach. Six "Lipidomics Cores" – each handling a major lipid category – employ mass spectrometry to analyze the numerous lipid molecular species.

In its first five years, LIPID MAPS made major strides, in addition to building a complete map of the macrophage: establishing mass spectrometry facilities, synthesizing the chemical standards

necessary to identify and quantitate multiple lipids, developing specialized cell biology protocols, and building a laboratory information system to handle the raw data as well as web-based tools to analyze and present the large data sets. LIPID MAPS investigators were instrumental in creating the first internationally accepted lipid classification, nomenclature and structural representation system.

A key function of LIPID MAPS has been ensuring that its findings, methodologies and tools are widely accessible to investigators in broader medical and scientific community via its website publications, and presentations. To date, consortium members have had more than 100 peer-reviewed papers published in scientific journals. The usefulness of the LIPID MAPS initiative to the international research community is highlighted by the impact of the Lipid Classification scheme. Since its publication, there have been more 30,000 visits to the paper at the *Journal of Lipid Research* website, including some 15,000 downloads.

* The LIPID MAPS Cores and Bridges:

Core/Bridge	**Institution**	**Director**
Fatty Aclys	UC San Diego	Edward A. Dennis
Glycerolipids	University of Colorado, Denver	Robert C. Murphy
Glycerophospholipids	Vanderbilt University	H. Alex Brown
Sphingolipids	Georgia Institute of Technology	Alfred H. Merrill, Jr.
Sterol Lipids	UT Southwestern Medical Center	David w. Russell
Prenol and Other Lipids	Duke University	Christian R. H. Raetz
Bioinformatics	UC San Diego	Shankar Subramaniam
Macrophage Biology	UC San Diego	Christopher K. Glass
Lipid Synthesis	Avanti Ploar Lipids, Inc./Indiana Univeristy	Walter A. Shaw/Michale S. VanNieuwenhze
LIPID MAPS Networks	UC San Diego	Shankar Subramaniam
Transcriptional Regulation	UC San Diego	Christopher K. Glass
Lipid Imaging	University of Colorado, Denver/Pennsylvania State University	Robert C. Murphy/Nicholas Winograd
Oxidized Lipids	UC San Diego	Joseph L. Witztum

# # #

Media Contact: Debra Kain, 619-543-6163, ddkain@ucsd.edu

Share This Article

Related News

UC San Diego Health Begins Treating Multiple Myeloma with CAR T-cell Therapy
6/3/2021

Social Justice as Part of the Remedy for What Ails Us
6/3/2021

Diet Plays Critical Role in NASH Progressing to Liver Cancer in Mouse Model
6/1/2021

Noted Researcher and Scientific Leader Jack E. Dixon Retires
5/27/2021

View All News >

Follow Us

Follow @ucsdhealth