Lipidomics: taking it one lipid at a time

With initiatives and consortia around the world garnering significant grant money for lipidomics research, the field as a whole is poised to make an important contribution to the ever-increasing pool of knowledge about the role of lipids in human disease and metabolism.

Chelsey D. Hillyer

Lipidomics is a branch of metabolomics that has undergone an important growth spurt in terms of technological advancements and research. Lipidomics is specifically concerned with the study of non-water-soluble metabolites (lipids) by researching how a cell functions in terms of its lipid content. This includes knowledge of the enzymes in lipid metabolism and transport, as well as knowledge of the biophysics of lipid-lipid and lipid-protein interactions.

Nowadays, a quick search for “lipidomics” on any internet search engine will point you in the direction of a significant number of lipidomics-focused projects and databases, but in 2003 few laboratories defined their focus as “lipidomics.” That year, however, the U.S. National Institute of General Medical Sciences approved $35 million in funding for the Lipid Metabolites Pathways Strategy (Lipid MAPS) Consortium. Since then, researchers from all over the world have worked together to increase the lipidomics knowledge pool.

Three of the largest programs in the world have contributed to some of the most important strides in lipidomics in recent history, both independently and in collaboration. These are the LipidBank for Web in Japan, the Lipid MAPS consortium based in the United States, and the European Lipidomics Initiative (ELife). Together, the groups have developed a new lipid classification system, and individually they are responsible for important new developments in research methods and data dissemination. With so much new information available to lipidomics researchers, the field of lipidomics is poised to make a major contribution to the understanding of the mammalian cell.

LipidBank for Web in Japan

Japan’s LipidBank for Web has the distinction of being the oldest of the three lipidomics resources listed above. In December of 1996, a joint research project between the International Medical Center of Japan and the Japan Science and Technology Corporation organized an initiative to collect information on 27 lipid classes for a searchable internet database. Since then, researchers from all over the world have worked together to increase the lipidomics knowledge pool.

From that initiative, more than 6,000 records were collected by September of 1999. The database is composed of three main parts:

- Factual data including the name of the lipid, chemical and physical properties, information on biological activities, metabolism, genetic information, etc.
- Graphic data, including structural formula, chromatographic data, UV data, IR data, NMR data, Mass spectra, etc.
- Related food reference data.

Since its initial release to the public in October of 1999, members of the Japanese Conference on the Biochemistry of Lipids (JCBL) have shared responsibility for maintaining and revising posted information, and the database has been supported by a Grant-in-Aid for Science Research from the Japan Society for the Promotion of Science.

“[This database] gets a lot of access from all over the world,” said Yousuke Seyama, who acted as President of the JCBL from 1998 to 2003 and still acts as chairman of the database construction committee. “Scientists at universities, research institutions, and company personnel all use it.”

Seyama reported that people from over 60 countries, including developing countries, access the database, and that sections including information on fatty acids, glycolipids, and the bile acids are the most viewed.
Lipid MAPS Consortium

The earlier work in the Japanese database helped to provide a framework when Edward Dennis of the United States assembled the largest research team ever to study lipids at the cellular level in 2003. The consortium is comprised of six core groups dedicated to lipidomics, four core groups dedicated to administrative and analytical areas and five ‘bridge’ groups. With $35 million from the U.S. National Institute of General Medical Sciences, the consortium set out to analyze the structure and function of lipids within the mouse microphage.

The group’s goals are threefold:

- To separate and detect all of the lipids in the mouse macrophage and to discover and characterize any novel lipids.
- To quantify each of the lipid metabolites, as well as the changes in their levels and location during cellular function.
- To define the biochemical pathways for each lipid and develop Lipid MAPS that define the interaction networks.

Thus far, the consortium has made several notable accomplishments, including the development of over 160 quantitative standards for mass spectrometry technology. According to the LC/Mass Spectrometry Core leader Robert Murphy of the University of Colorado in Aurora, these changes allow scientists to “seriously approach questions as to the global changes in lipids during normal and abnormal cell biochemistry.”

Novel research strategies, new relationships between lipid classes, and revealing pathways not previously considered in other research are some of the more specific goals of the consortium.

European Lipidomics Initiative

With major research groups assembling all over the world, Gerd Schmitz of Regensburg, Germany, began to assemble the European Lipidomics Initiative (ELIfe). Together, the group wrote to the European Commission, expressing the opinion that novel technology could be used in boosting lipid research. The group cited the startling increase in obesity worldwide as one piece of evidence of the need for lipid research. With a kickoff meeting held in February 2005, ELIfe set a progressive schedule of meetings and goals for the next two years in order to organize the field for future endeavors.

“It is a challenge to bring the essential actors together at the European level to devise strategies on how to develop the field of lipidomics,” says an explanation of the ELIfe goals on its website. “To mobilize and network the European basic and medical researchers and industry, a series of dedicated workshops and a concluding conference will be organized on technology development, scientific challenges, and medical applications of lipidomics.”

The three main goals of ELIfe are:

- To create a European technology platform bringing together technological know-how and industry.
- To shape the way lipidomics research is organized in Europe.
- To define the most suitable ways new technologies can be applied in the clinical setting to assess, cure, and prevent membrane lipid disorders.

Already, ELIfe has succeeded in creating an online platform for scientists to share information by launching the Lipidomics Expertise Platform (LEP) in November 2005. The LEP is maintained by the participation and input of its members, and ELIfe encourages lipid scientists to register to the platform and post lipidomics-related information on methods and lipid standards.

Collaborative efforts

Though the LEP was launched as an ELIfe effort, ELIfe hopes to use it as a platform for the standardization of lipidome-related nomenclatures and to harmonize lipid metabolic pathways and tools on a global scale. Already, their collaboration with Lipid MAPS and the LipidBank for Web in Japan has resulted in significant progress in lipid classification.

Seyama of the JCBL — which maintains the LipidBank for Web — stated, “Since 2004, three groups — Lipid MAPS, European Lipidomics Initiative, and ours — collaborated to systemize a nomenclature of lipids, and published the results.”

The collaborative paper was published in the May 2005 issue of the Journal of Lipid Research (see sidebar for full citation), and detailed the comprehensive classification, nomenclature, and chemical representation system for lipids. In the paper, the international group of authors explains the need for this system: “To facilitate international communication about lipids, a comprehensive classification of lipids with a common platform that is compatible with informatics requirements has been developed to deal with the massive amounts of data that will be generated by our lipid community.”

The new classification system involves dividing lipids into eight categories (Fatty Acyls, Glycerolipids, Glycerosphospholipids, Sphingolipids, Sterol Lipids, Prenol Lipids, Saccharolipids, and Polyketides) containing distinct classes and subclasses of molecules. The authors then devised a common manner of representing the chemical structures of individual lipids and their derivatives and provide a 12-digit identifier for each unique lipid molecule.

“The classification scheme was designed to be a broad-based scheme covering eukaryotic and prokaryotic sources, to include new classes of lipids which have been discovered in recent years to be extensible to accommodate future novel classes and to be compatible with modern-day informatics requirements,” Eoin Fahy, one author of the paper and Bioinformatics Project Coordinator for Lipid MAPS out of San Diego, California, USA, explained in an interview in June 2005.

In addition to this collaboration, lipidomics leaders Dennis and Seyama met with, Fritz Spener of Germany at the International Conference on the Bioscience of Lipids (ICBL) in France during September 2005. There, the lipid scientists discussed the future collaboration and sharing of roles among these three groups. As the lipidomics field makes more discoveries, entities worldwide see the importance in cooperation.

Because a cell’s metabolome is such an enormous entity, characterizing it can only be accomplished in sections. For
this reason, collaboration and the sharing of information is important to the furtherance of the field of lipidomics as a whole.

The future of lipidomics

As sequencing of the human genome opened the way for scientists to build a comprehensive picture of the mammalian cell, lipidomics follows genomics and proteomics in filling in the missing information about how the cell’s metabolome ties into genomic and proteomic maps.

“Lipidomics is one window into the universe of cellular function and dysfunction,” says Lipid MAPS core leader Shankar Subramaniam. “The more windows you can peek through, the more integrated a picture you get.”

While many of the initiatives are currently in the early stages of large-scale experiments regarding lipidomics, the researchers are certain that lipidomics provides key information in understanding health and disease.

“This is a central area to the biological and life sciences underlying health and human disease,” said Dennis. “Hopefully, [lipidomics] will take its place alongside genomics and proteomics as a key approach to following human disease and metabolism.”

Learn more about lipidomics

- The websites for each of the three lipidomics entities mentioned in the article provide a vast array of information and resources for lipid researchers and those interested in lipidomics:
  - Japan’s LipidBANK for Web at netlink: http://lipidbank.jp
  - Lipid MAPS at netlink: www.lipidmaps.com
  - European Lipidomics Initiative at netlink: www.lipidomics.net

- Attend lipidomics-related presentations at the 97th AOCS Annual Meeting & Expo in St. Louis, Missouri, USA from April 30 to May 3, 2006. Lipidomics-related topics include:
  - Discovery of Genes for Synthesis of Plant Surface Lipids: Transcriptomic, Bioinformatic, and Reverse Genetic Approaches. F. Beisson, Michigan State University, USA.
  - Lipidomic Analysis of Physiological Responses in Arabidopsis. R. Welti, Kansas State University, USA.
  - Integrating Lipidomics and Proteomics to Study Lipid Metabolism and Cellular Regulation. X. Wang1,2, X. Pan1,2, M. Li1,3, and R. Welti3, 1University of Missouri, USA, 2Danforth Planet Science Center, USA, 3Kansas State University.

- Keep an eye out for future inform articles updating other lipidomics initiatives in the United States.

- Citation for “A comprehensive classification system for lipids” mentioned in the article:

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