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SCIENCE POLICY BRIEFING • June 2008 31

Structural Medicine II: The Importance of Lipidomics for Health and Disease[1]

Contents

Foreword

The time has come for generating broad insights into the role of lipids in physiology and pathology. Given that thousands of different lipids are present within a single cell and that many of these lipids are involved in modulating the processes of life in an area that is upcoming, lipidomics describes and quantitatively analyses the full complement of lipids, in the human body for example body fluids, cells and tissues. Lipidomics integrates these data with knowledge of their protein targets, i.e. the metabolic enzymes and transporters, and of the relevant genes and the regulatory aspects of these physiological systems. Above all, an understanding of cell membranes is only possible with a comprehensive understanding of their lipid constituents.

Lipids are commonly known as high-energy fuel and storage molecules for cellular maintenance. In addition, lipids are the building blocks of cell membranes, providing these membranes with their physical characteristics. It is now understood that membranes are not the fluid, homogeneous two-dimensional liquid as proposed in the famous Singer and Nicholson fluid mosaic bilayer model (1972), but that the various lipids display transverse and lateral heterogeneities that are dynamic and governed by specific chemical and physical mechanisms that include lipid metabolism. The realisation that cell membranes can subcompartmentalise to form dynamic liquid-ordered platforms (sphingolipid-cholesterol rafts) has given lipid research a new emphasis. In addition, a host of dedicated lipids, but also many intermediates of lipid metabolism serve a second function as primary or secondary messengers. Their synthesis and clearance is under strict regulatory control. Finally, a variety of lipids serves to anchor proteins and glycans to membrane surfaces, thereby affecting and regulating their functions.

Most important is the fact that many of the widespread diseases that plague humankind involve lipids. Prime examples are cardiovascular disease, obesity-related type-2 diabetes, and stroke. Other major diseases such as cancer and Alzheimer's disease also have a lipid involvement. In addition to these disorders of epidemic proportions, there are many other diseases that are directly caused by inherited defects in lipid metabolic enzymes and transporters, such as defects in cholesterol synthesis and lipid storage diseases. Lipids also play major roles in autoimmune diseases and act as (co-)receptors for bacteria, viruses and toxins. An increase in our knowledge of disease-related changes in lipid patterns and its integration into proteomic and genomic data will provide new basic biomedical insights; thus, far-reaching possibilities for diagnostic application (prognostic assessment, diagnosis and monitoring) as well as for the development of prevention and new therapeutic approaches can be expected.

The European Medical Research Councils (EMRC) at the European Science Foundation (ESF) established a task force comprised of leading European scientists in the field of lipid science with the goal to develop a science policy briefing (SPB) addressed to national and European research funding and performing organisations.The scientific experts were nominated through the European Lipidomics Initiative, a specific support action of the European Commission 2005-2007, and by broad consultation within the European scientific community. The task force met on several occasions to address scientific issues and to formulate recommendations for this policy briefing. The draft SPB was presented to the EMRC Standing Committee which reviewed the recommendations in the wider context of medical research priorities.

Coordination and integration of interdisciplinary research efforts have been recognised by the EMRC at ESF as an essential ingredient to promote Structural Medicine as a discipline in Europe. The recommendations put forward in this policy document will be an important step towards the goal of joint efforts by European research funding organisations and the research community devoted to Structural Medicine.

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[1] The present policy document was preceded by Part I, the ESF Science Policy Briefing 27 (July 2006) entitled *Structural Medicine: The Importance of Glycomics for Health and Disease.*

Introduction

Health research touches us all. Both basic and applied biomedical research are crucial for a better understanding of life processes. Biomedical research that is focused on furthering the fundamental knowledge of structures of molecules and their interactions is referred to as Structural Medicine. It will aid in developing improved diagnostic tools and appropriate medical treatment.

Lipidology and Lipidomics

While lipidology is the general science of lipids, the term 'lipidomics' has a different connotation. Lipidomics covers everything connected with the study of the lipidome, the total complement of lipids. Thus, lipidomics covers quantitatively the spatial and temporal determination of all lipids. In addition, lipidomics includes the study of the lipid-metabolising enzymes and lipid transporters, both of which determine the local concentration of a lipid, and of their genes and regulation. Finally, lipidomics concerns lipid function, which cannot be understood without a thorough understanding of the physical basis of lipid behaviour, especially of lipid-lipid and lipid-protein interactions. Lipidomics is part of metabolomics, which is the systematic study of the unique chemical fingerprints linked to all cellular processes.

Lipids have long been neglected. Why? Because tools to analyse lipid diversity have not been available until recently. Through the development of mass spectrometric methods we can now for the first time quantitatively analyse the different lipid molecular species in biological samples. This remarkable breakthrough will make it possible to better understand the membrane machineries that are responsible for producing and storing energy in cells, for the transport across and between cell membranes, and for the signalling in and out of cells, only to name a few examples. The research on these important topics has so far concentrated on the proteins involved and has largely left the lipids out of the mechanistic dissection. Cells commit large amounts of chemical energy to synthesise thousands of different lipid molecules and it is now imperative to learn how these chemical constituents contribute to body function in health and disease. At the level of the whole human organism there is a complex machinery for the selective uptake of lipids from the food and for transporting lipids between tissues through blood and lymph. This transport concerns dietary lipids as well as cell-derived lipids including a large repertoire of messenger lipids that transmit signals within and between cells and tissues. Here, the analysis of lipids should offer direct ways of diagnosing disease states with the implicit potential for prognosis. Such prognosis extends to monitoring the effect of nutritional and therapeutic regimens. To counter deficiencies of information on this functionally important class of biomolecules, Europe needs a multidisciplinary research initiative focusing on lipidology and lipidomics.

Europe has had a long tradition in lipid research, but interest declined towards the end of the 20th century due to lack of technology to study lipids. With the recent retirement of many active lipidologists that started their careers in the 1960s, currently the number of qualified researchers in this field is low. On the other hand, in the USA and Japan lipidomics consortia have been created and funded by national grants of tens of millions of dollars, and they have now been working at full speed for years. The EU Framework Programme 7, launched in 2006, is trying to catch up and has, so far, awarded one major research grant for lipidomics research. However, there are many more research groups all over Europe that are ready to take on the lipidomics challenge. The new mass spectrometric methodology for lipid analysis has largely been developed in Europe. Major insights into the organisation of cell membranes and into the role of specific lipid molecules in cell signalling come from European laboratories. Thus the European lipidomics community is ready to tackle both the basic and the applied research that will be required to unravel how lipids contribute to cellular and body function and to take on the challenge of combating the involvement of lipids in disease pathogenesis. It is recommended that Europe creates a structure for lipidomics research for the next decades. With this goal in mind Europe should fund initiatives to further develop holistic, high-throughput and high-content lipid analysis, and to devise standard operating protocols for applying these techniques in the clinic. Europe should take a leading role in integrating the information in connected databases containing the subsets of data in lipid structure, lipid metabolomics, proteomics, and genomics; this includes the responsibility for the maintenance of such infrastructure.

Considering the potential of quantitative measurements offered by the new technologies, a true systems biological approach to lipidomics becomes possible. It will be necessary to attract more chemists and physicists into this field because the biological and medical relevance of lipids is a result of their chemical and physical properties. This will require training of researchers with a background in the areas of kinetics and thermodynamics who simultaneously have an interest in biology and medicine.

Major Diseases of Mankind Involve Lipids

In the European community, metabolic and vascular diseases are the leading cause of disability and death with a major impact on health care costs. Metabolic overload is a paramount problem for people in industrial countries in which the caloric intake exceeds the dietary needs, because of associated risks of secondary disorders including atherosclerosis, hypertension, diabetes and the metabolic syndrome. It has been established that more than 30% of the population in developed countries can be regarded as obese according to WHO standards (Body Mass Index≥30). Moreover, obesity is the entry gate for type-2 diabetes. Thus, the pandemics of obesity will be soon followed by an epidemic of diabetes. By 2020 it is estimated that 130 million people will be afflicted by type-2 diabetes with an estimated cost of 75 billion Euros for health care worldwide. Even though diet, exercise, hypolipidemic drugs and changes in attitude seem most efficient in reducing such health threats, we have a poor understanding of the mechanisms involved in regulating the number of fat cells and their size and metabolism. Here, the lipidomics field will play an increasingly important role in unravelling the mechanisms responsible for obesity and in finding ways to prevent people from overeating.

Dietary habits may account for 25-40% of the preventable causes of all cancers. Among food components, lipids are the main determinants of the lipid composition of tissues, i.e. fatty acids, and it is the fatty acid profile of stored lipids that has been used to elaborate a biomarker for the modifiable part of the risk of breast cancer in healthy women (Figs.1 and 2). Furthermore, a pilot phase 2 clinical trial in metastatic breast cancer patients has provided the proof of concept that dietary enrichment of mammary tumours in polyunsaturated fatty acids (mainly DHA) leads to reversal of the tumour chemoresistance. None of these advances have incorporated the new tools of mass spectrometry. Nowadays these will allow high-throughput analysis suitable for mass screening, and exploration of lipidomes as novel system markers in wide-range populations.

One other alarming example of a common disease caused or strongly influenced by lipids is Alzheimer's disease. It has been established only very recently that cholesterol is a major risk factor for Alzheimer's; the most dangerous aspect is that the pathological molecular events leading to this degenerative brain disease are part of the regulation of lipid metabolism under normal physiological conditions. This shows once again that frequent and costly diseases can be caused by the malfunctioning of complex lipid regulatory cycles. Still, a first simple approach showed preliminary potential: in two clinical trials well-established drugs that

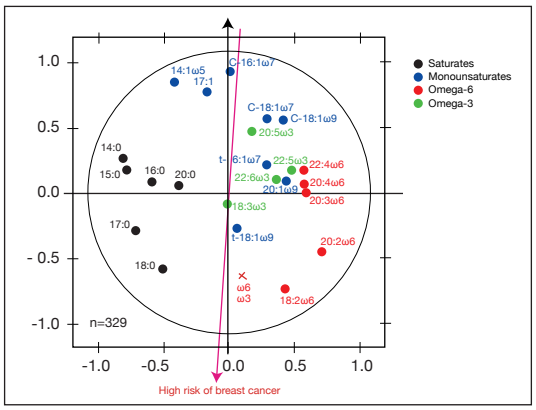

Figure 1: The lipidome in connection with breast cancer risk. In this principal component analysis of adipose tissue fatty acids, the red arrow indicates an increased risk of breast cancer (Bougnoux, P., Giraudeau, B., and Couet, C. 2006. Diet, cancer, and the lipidome. Cancer Epidemiol. Biomarkers Prev. 15:416-421).

Figure 2: Fatty acid level array in patients with malignant (cases) or benign (controls) breast tumors. Each lane represents a patient and each line one fatty acid, ordered according to their correlation with the second principal component in Figure 1. Fatty acid values: green (low) to red (elevated). The n-6/n-3 ratio of the polyunsaturated fatty acids appears as a main distinctive feature of malignancy versus control (Bougnoux et al., idem).

lower cholesterol reduced disease progression in mild and moderate Alzheimer's disease patients. Several epidemiological studies suggest that the same drugs reduced the prevalence of the disease in a preventive pharmacological approach. Similar results have been obtained by adding n-3 fatty acids as dietary supplements. This area is still in its infancy and more research will be required to realise the full potential of the role of lipids in Alzheimer's disease. Lipidomics research will broaden the scientific basis for optimising treatment and prevention.

In addition to these epidemic disorders, there are many other diseases that are directly caused by inherited defects in lipid metabolic enzymes and transporters. Examples are Smith-Lemli-Opitz syndrome, a defect in cholesterol biosynthesis, and sphingolipidoses such as Gaucher and Niemann-Pick disease that are storage diseases due to defects in lipid degradation. Lipids also play major roles in autoimmune diseases, such as Guillain-Barré Syndrome which is caused by anti-glycolipid antibodies. Finally, specific glycolipids act as (co-) receptors for bacteria, such as *Salmonella*, viruses such as HIV, and toxins such as cholera and Shiga toxin. The role of lipids in these disease states needs to be explored at the level of single molecules in order to identify new drug targets.

Dynamics and Supramolecular Organisation of Lipids

Two main features distinguish lipids from other biomolecules. First, unlike sugars or amino acids, the majority of lipids are *insoluble* in water. This fundamental physical property causes the lipids to be unsuitable for simple 'aqueous' biochemical methodology. The second rather unique property of lipids, particularly in an aqueous environment, is self-aggregation, i.e. biological lipids generally form aggregates of various sorts, mostly extended sheet-like structures known as bilayers. The bilayer, the structural basis of the cell membrane, is formed by 'amphipathic' lipid molecules, i.e. molecules that possess both a hydrophilic portion in contact with the water, and a lipophilic portion which remains isolated from the aqueous medium. Biological membranes are thus water-immiscible structures consisting of a microenvironment composed of lipids and proteins. These possess a considerable degree of freedom to diffuse, both rotationally and laterally, in the plane of the membrane.

The membrane forms of lipid aggregates are unique because they are held together by non-covalent bonds, formed by the hydrophobic effect. Not always appropriately understood, the hydrophobic effect arises not only from an affinity of the lipid hydrophobic moieties with each other, but mainly from the comparatively much larger affinity of water molecules between themselves and with the polar parts of amphipathic lipids. Still, the difference in physical properties of the various types of lipids can result in lateral compositional heterogeneities within specific membranes. Biophysical studies clearly show immiscible phases within lipid bilayers. There is now increasing evidence for the role of sphingolipid-cholesterol assemblies in the formation of dynamic platforms within cell membranes ('rafts') that function in signal transduction and membrane trafficking. Certain viruses such as HIV, influenza and Ebola virus coat themselves with a raft-like lipid membrane enriched in sphingolipid-cholesterol on exiting infected cells, and evidence is accumulating that implicates rafts in the cleavage of the Alzheimer precursor protein APP. More work is now needed on the physical and chemical principles underlying phase behaviour of lipid bilayers to understand how this modulates the biochemistry within membranes. The propensity for phase separation introduces a totally new aspect in membrane organisation and function.

The hydrophobicity and self-association of lipids are put to good use by cells and organisms. Hydrophobicity provides an efficient barrier to the diffusion of the mostly water-soluble biomolecules, so that the biological membrane constitutes the structural and functional limit of the cell, and of the intracellular organelles. In many vertebrates, including mammals, a layer of skin lipids, the so-called *stratum corneum*, provides an efficient means to avoid uncontrolled water evaporation. The myelin layer that insulates axons in nerve cells is another lipid principle at work in nerve conduction. Finally, inside the cell lipid droplets, aggregates of predominantly hydrophobic lipids such as triacylglycerols surrounded by specific proteins and amphipathic lipids, are the solution to the problem of storing a maximum of highly energetic fuel in a minimum of space. However, how the balance between storage and hydrolysis is regulated remains an issue to be solved.

Understanding Lipid Metabolism

The functions of thousands of different lipids are determined by their concentration at a specific site in time. The precipitous development of novel holistic analytical techniques, in particular mass spectrometry, will allow the identification and quantitative determination of virtually any lipid, with ever-increasing resolution in space and time. Lipidomic analysis should now be applied to well-understood human diseases of lipid metabolism to determine if it offers new advantages in both diagnosis and prognosis, as well as being a tool for assessing the progress of specific therapies. A clear example of the power of lipidomics in diagnosing human genetic diseases comes from the tandem mass spectrometric analysis of blood samples from newborns for different acylcarnitines; such an analysis unambiguously identifies lesions in specific steps of mitochondrial fatty acid oxidation. As a consequence, poorly understood diseases as well as new diseases will become important subjects for lipidomic analysis.

Lipidomics as a Gateway to New Biochemistry

There is significant evidence to indicate the existence of numerous lipid species of low abundance, about which we have essentially no information regarding structure, biosynthetic or degradative biochemistry, or encoding genes. Work on tetralinoleoyl-cardiolipin synthesis provides a recent example of how the elucidation of the structure of a minor lipid provided a gateway to experimental inquiry that successfully resulted in defining a new biosynthetic pathway of immense importance. Tetralinoleoyl-cardiolipin is essential for normal mitochondrial function, and its defective synthesis occurs in the X-linked genetic disease Barth syndrome. It is anticipated that lipidomics-directed mass spectrometry will stimulate the identification of new biochemical pathways and genes, whose importance in cellular and organism biology can be deduced using reverse genetic approaches. Also, uncovering new low abundance lipids and their biosynthetic and degradative biochemistry have the potential for revealing novel second messengers, which are often of very low abundance.

The use of lipidomics for diagnosis is a completely new area of research that could potentially revolutionise areas of biomedical research and practice.

The local concentration of a lipid is determined by a finely tuned process involving synthesis, transport and turnover. While metabolism is protein-catalysed, the exchange of lipids between different environments is primarily determined by the physical properties of the lipid (Fig.3), but here transport proteins also play important roles. Thus, to understand how the local lipid concentration is regulated, it is important to study the activity of enzymes and transporters, their topology and how they are regulated at the transcriptional and post-transcriptional level. It is only through such a detailed knowledge of the processes involved in lipid homeostasis that we will understand the design principles of the system, identify its most sensitive points, and be able to define life-style guidelines; these will protect against lipid-related disease or devise effective and efficient interventions when these are needed. Once again this stresses that the lipidome should not be viewed as an entity independent from the genome, transcriptome or metabolome. Efforts to integrate respective databases should be recognised as an important priority.

Lipid Signalling and Disease

Cell signalling encompasses the biochemical events following receptor engagement that lead to either positive or negative cell fates. Lipids can function as intracellular messengers that are generated by activation of signalling enzymes. For example, phosphorylation of the membrane lipid phosphatidylinositol can yield seven distinct inositol phospholipids phosphorylated at different positions of the inositol ring. Each of these lipids functions as a signal, and mutations in the responsible kinases and phosphatases have been related to numerous disease states including type-2 diabetes and cancer. In addition, phosphoinositides are involved in invasion by bacteria such as *Listeria monocytogenes* (meningitis, abortion) or *Shigella flexneri* (dysentery).

Cellular phospholipids are the source of many intracellular lipid messengers. Phospholipases A_2 release arachidonic acid which can be transformed into prostaglandins, thromboxanes or leukotrienes. These 'eicosanoids' play important roles at the origin of inflammatory sites in rheumatoid arthritis, cardiovascular and neurodegenerative diseases. Other highly bioactive lipids produced by phospholipases are platelet-activating-factor (PAF), a strong mediator of inflammation, the extracellular agonist lysophosphatidic acid (LPA), which is involved in mechanisms related to tumorigenesis including angiogenesis, and diacylglycerol, which regulates protein kinase C (PKC) activity. PKC has

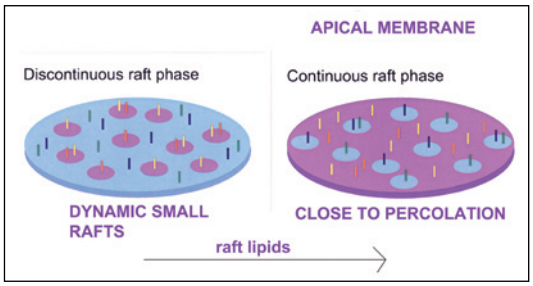

Figure 3: Lipid biophysics. Dynamic small rafts in a plasma membrane may coalesce during cell activation, or form the connected phase in membranes particularly rich in sphingolipids and sterols like the apical membrane of epithelial cells. As a consequence, raft proteins can now interact more efficiently, for example in signal transduction (courtesy of Kai Simons).

a number of functions including the suppression of apoptosis, which is also regulated via the ceramide/sphingosine-1-phosphate rheostat (signalling products of sphingolipid metabolism).

Finally, the last 15 years have witnessed the dramatic emergence of lipid-activated nuclear receptors.

Multiple non-membranous lipids, such as fatty acids, lysophospholipids, bile acids, and oxysterols, either imported into the cell or synthesised endogenously, are direct regulators of gene expression. They are independent of the classical transcriptional regulation of cholesterol homeostasis uncovered by Brown and Goldstein[2] and colleagues, which works via sensors that activate the proteolytic production of a transcription factor. These findings highlight the need for intensifying basic research for understanding lipid homeostasis and combating lipid-related diseases.

Most important is the issue of how specific lipid-protein interactions influence protein activity in cell membranes. Recent structures of membrane proteins are providing the first clues of how lipids can perform such functions.

Enabling Technologies

Because lipidomics is concerned with all lipids and their enzymes and genes, it faces the formidable challenge of having to develop the appropriate technologies. They must enable comprehensive measurements of the expression, location and regulation of lipids, enzymes and genes in time. Application of high-throughput mode is mandatory. The introduction of soft ionisation techniques such as electrospray ionisation (ESI) and matrix-assisted laser desorption/ionisation (MALDI) have revolutionised the field of lipid analysis making polar lipids accessible to mass spectrometric analysis. Now numerous methodologies have been developed for both the structural analysis of complex lipids as well as quantitative profiling of complex lipid mixtures. On the other hand, the relevant enzymes must be identified using (reverse) genetic, molecular biological and data mining approaches.

[2] Brown and Goldstein, Nobel lecture. More at www.nobelprize.org

Nanomedicine

The 19th century vision of the father of medicinal chemistry, Paul Erlich, of a magic bullet which targets the disease and avoids the healthy cells is close to coming to a realisation. It is the use of lipids as drug carriers in the form of nanocapsules and as drugs and pro-drugs themselves for their role in providing biocompatibility. The structural and chemical diversity of lipids derived from lipidomics offers a unique laboratory for rational drug discovery, development, and optimisation of efficacy. Several promising liposome-based systems, some containing bioactive lipids that are activated by phospholipases released by diseased tissues, are now on their way to the clinic for the treatment of life-threatening disorders such as cancer and inflammation.

Next, we need a broad range of imaging techniques to define comprehensively with high-resolution where exactly the relevant lipids, proteins and genes are situated in the body (Fig.4), cells and subcellular organelles. To this end, STED[2]-nanomicroscopy and single lipid molecule tracing must be further developed. Next to histochemical, cytochemical and physical imaging techniques, cell fractionation protocols must be developed to localise lipids with the goal of providing the same type of information that is routinely available for (glyco) proteins. With regard to the application of imaging in the clinic, high-content methods for protein and lipid imaging and automated methods for image analysis are mandatory[3].

Within the aim of understanding lipid function, we need to know better how lipids physically interact amongst themselves and with proteins. For this purpose solid state nuclear magnetic resonance (NMR) can serve as a valuable technology. While lipid phases themselves have already been studied by multiple techniques in model systems, only recently have correlation spectroscopy and multiphoton fluorescence microscopy of lipophilic probes such as Laurdan been successfully applied to characterise the physical state of the lipids in cellular systems. This will be especially relevant for a number of signalling lipids, such as ceramide, that have been suggested as changing the physical state of the membrane.

One other challenge is to devise novel sophisticated bioinformatics approaches within Europe. A global harmonising effort to develop improved information technology solutions for platform integration in the areas of lipidomics and lipid-related genomics, proteomics, and metabolomics will allow for cross-referencing the different types of data. Standard processing procedures for data handling need to be elaborated. All this falls into two broad categories. The first concerns the sorting of the literature into annotated pathways and the second relates to the management, processing and integration of the experimental output as generated by the individual scientist. The handling of such experimental output can be subdivided into three distinct parts: defining standard processing procedures for extracting results from the data, integrating these results across experimental approaches to obtain knowledge and to enrich the annotations of pathways, and finally constructing the knowledge base to hold the assembled information. *The ultimate challenge is to apply this knowledge in the clinic.*

Statements and Recommendations

To further develop diagnostic tools, preventive medicines and therapeutic drugs, a better understanding of the lipids in the whole human organism is required. The recommendations listed below address the need to accelerate research in the field of Structural Medicine in Europe with special emphasis on lipidomics.

Recommendation: Invest in Human Capital
The opportunities of lipid research and glycosciences within Structural Medicine can be realised only when sufficient resources in human capital are created through investment in adequate interdisciplinary, educational training and research programmes. A broad variety of disciplines in the context of the chemistry, (systems) biology and medicine of lipids and carbohydrates needs to be taught in training programmes ranging from summer schools to specialised PhD and MD/PhD programmes with the aim of satisfying clinical, academic and industrial needs. Europe needs to train researchers in the emerging field of lipidomics. Without new blood Europe will not be able to capitalise on the possibilities opening up in this area. Annual workshops in lipidomics should be organised. ESF should encourage its member organisations to promote funding programmes including PhD training in lipidomics.
ESF recommends investing in training and research programmes aimed at training biomedical scientists in lipid-related fields.

Recommendation: Enabling Technologies Must Serve Basic and Applied Lipidomics *in parallel*
A major goal for the future will be to develop technologies enabling lipidomics at several frontiers. The most important methodology will be mass spectrometry of the sophistication necessary to

[2] stimulated emission depletion microscopy
[3] See ESF/EMRC SPB 28 *Medical Imaging for Improved Patient Care* (September 2007). More at www.esf.org/spb28

do quantitative lipidomics analysis. The improvement of the techniques for lipidome analysis, i.e. sample preparation, lipid synthesis, analytical techniques, and bioinformatics methods demands the elaboration of standard operation procedures and standard processing procedures, respectively. All this pertains to functional, evolutionary, clinical, pharmaceutical, toxico- and nutrilipidomics. To establish priorities, a close dialogue must exist between technology developers and scientists involved in biology, nutrition and medicine. In this way conflicts between hypothesis-driven basic research that uses lipidomics, and the development of clinical screenings and analyses that employ lipidomics are avoided. The challenge is to set up such an infrastructure.

ESF recommends investing in further development of enabling technologies for lipidomics, while establishing and maintaining strong links between technology developers and the lipid scientific community. One pillar in these efforts is support for maintaining the recently created 'Lipidomics Expertise Platform', a forum for the exchange of lipidomics information and standard materials in Europe.

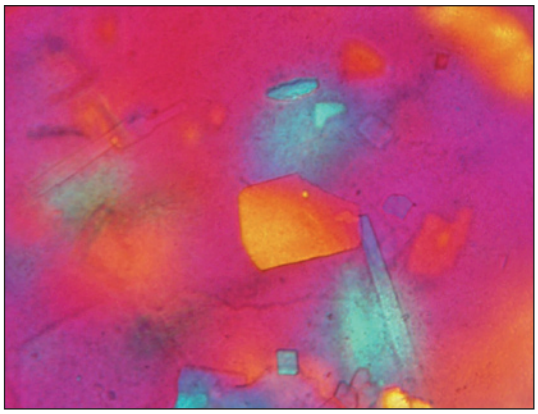

Figure 4: Gallstones. Cholesterol monohydrate crystals in mouse gallbladder bile under a polarised light microscope. This lipid metabolic disease is a fellow traveler of the obesity and metabolic syndrome epidemic (courtesy of Dr. A. Moschetta).

Recommendation: Harmonise Lipidomics Practices within the EU

Standardisation of lipidomic analysis is of utmost advantage. This could take the form of interlinking existing foci of lipidomics research or, alternatively, the assignment of dedicated (virtual) centres, for example within the network of centres for integrated structural biology that were proposed in the 2006 report of the European Strategy Forum on Research Infrastructures (ESFRI). In settings where the drive to advance technology is linked to solving scientific problems, centres must have a responsibility for conducting collaborative studies with extramural investigators that are linked to ongoing funding.

ESF recommends a strong coordinated interdisciplinary research effort in Europe to understand lipid function with respect to their roles in health and disease.

Recommendation: Intregrate Lipidomics-related Databases

A key task for a fast development of lipidomics will be to build a common, open access repository of the theoretical fundaments: lipid species maps as well as the genome, proteome, metabolome and signalome related to lipids. Such a database should provide the basis for bioinformatic tools that allow us to integrate all chemical, physical, biological and medical information relevant to a specific lipid-related issue. The central database would be beneficial for all different disciplines of lipidomics, which conversely contribute data and knowledge to this central repository increasing the basic knowledge of lipids. In addition, an integrative database is a prerequisite for strategies to gain further insight into the regulation of lipid metabolism, such as the correlation of lipid metabolic flux rates and mRNA and/or protein expression levels based on pathway models. This in turn would help to discover novel lipid biomarkers or patho-mechanisms and utilise this knowledge for the diagnosis, monitoring and cure of lipidome-related diseases.

ESF recommends an expansion of the tasks of the EMBL-EBI[3], Cambridge, under the ESFRI recommendations, by supporting initiatives aimed at integrating European lipid databases and their communication with other databases worldwide. This allows a holistic interpretation of the lipid data in the context of health and disease.

[3] European Bioinformatics Institute. More at www.ebi.ac.uk

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The European Medical Research Councils (EMRC) is the membership organisation for all the Medical Research Councils in Europe under the ESF. The mission of the EMRC is to promote innovative medical research and its clinical application towards improved human health and to strengthen medical research in Europe.

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