A cell contains up to 1000 different lipids. Nevertheless, lipids remain **the underestimated building blocks of life**. LipidX wants to change this state of affairs.

Project leader Gisou van der Goot is satisfied : «Without SystemsX.ch, we couldn't afford this mass-spectrometer.»

Photo thm

Thomas Müller

Epalinges. In many respects the shell of cells has remained a *terra incognita* for biological research despite the fact that biologists have been studying cells since the invention of the microscope. For the main part, however, their interest has focused on proteins and the hereditary substance DNA, firstly because life takes place there, secondly because this is where the information, the genome, sits.

But there is also another, third reason, why DNA and proteins have stood – and continue to stand – in the foreground: they are comparatively easy to examine. Lipids however, which are the components of the plasma membrane, are difficult to access experimentally. Their chemical structure – consisting of two hydrophobic fatty acid tails and a hydrophilic head – gives them high degrees of freedom. Furthermore, they do not crystallize as proteins and DNA do. Nonetheless, the vital importance of lipids stems from the fact that life would not be possible without them because lipids do the job of outlining a cell by separating it from its environment. They achieve this separation by forming a double membrane, a so-called bilayer, which is not rigid like a wall, but behaves rather like a two-dimensional liquid, similar to an oil film on water.

A thousand different types

«A single type of lipid would suffice to build a bilayer», explains Gisou van der Goot, «but neurons, for example, exhibit up to 1000 different lipids. Alas, we have no idea what the majority of them actually do». This is about to change. Engineer and biophysicist van der Goot is professor at the Global Health Institute at EPF Lausanne and she leads LipidX, one of SystemsX.ch's research, development and technology projects. In all, 14 research groups from six Swiss and one foreign university are looking to eliminate the blank spaces on the shells of cells.

Lipids have the unfair reputation of being nothing more than bricks in a wall, indispensable, but uninteresting. What has been clear for a long time already is that they actually constitute extremely intelligent «walls». Lipids not only separate the inside of the cell from the outside and divide cells into compartments. Certain lipids also structure the bilayer with so-called microdomains, thereby allowing different reactions to run off at different places and at different times in the same cell. Other lipids escort proteins to their workplace in the plasma membrane, where again different lipids help these membrane proteins to do their job.

Resistence against anoxia

Furthermore, as new research shows, lipids also perform physiological tasks of the utmost importance. In a recent article in «Science» Howard Riezman and Jean Claude Martinou, both professors at the University of Geneva, demonstrate that lipids play an important role in the resistance of animals to oxygen depletion (anoxia). It turns out that it is the length of some lipids called ceramides that is decisive for the protection against anoxia.

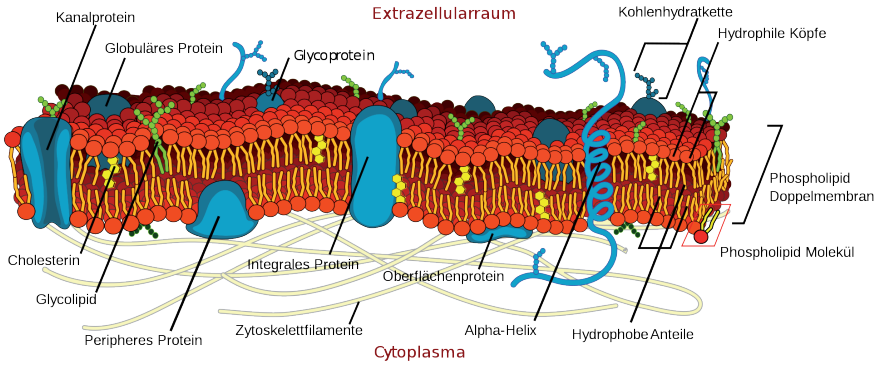
Riezman and Martinou owe this new knowledge to lipidomics. Analogous to genomics and proteomics that cata-

logue genes and proteins in a systematic way, the aim of researchers working on lipidomics is to characterize all lipids that our cells contain and produce.

A map of the cell

The still young and developing technology needed for this task is at the center of LipidX. «We want to draw a map of the cell that shows which lipids occur where and what they do», says Gisou van der Goot, outlining one of the principal purposes of LipidX. In a set of model organisms, such as yeast, fruit fly, worm, but also in vertebrate animal cells, LipidX researchers will systematically be investigating the 400 genes that govern the lipid metabolism. Using yeast, the first step of this investigation is to create mutants with only one of these genes missing, and then to look for a change in the lipid composition and determine the consequences.

This entails a lot of exacting, arduous work, some of which can fortunately be done, at least in part, by robots in the shape of high-throughput-mass-spectrometry equipment. «Without SystemsX.ch we couldn't afford this mass-spectrometer.», van der Goot says, as she looks forward to the new paths that LipidX will enable researchers to embark on.



The double membrane separates the cell from its environment. Illustration: Wikipedia

Introducing the most famous Lipid: Cholesterol

«Sunny side up» a cholestor bomb? Photo: Wikipedia

The best known and at the same time most disputed lipid in the general public is cholesterol. It increases the stability of the cell membranes and, together with proteins, participates in the signal transduction. The human body contains about 140 g of cholesterol, two of which are replaced by the body every day. Daily food intake contributes roughly a tenth of the replaced quantity.

Contrary to a widespread belief, there is no good or bad cholesterol. Nor is it fat, as is also widely assumed: it is simply vital to life. There is a recurring debate as to whether an increased cholesterol level in the blood actually increases the danger of cardiac infarcts, and, concomitantly, whether the frequent prescription of anti-lipidemic drugs really extends life. The cholesterol level is increased by so-called lipoproteins of low density (LDL), which transport cholesterol from the liver to the organ tissues. Therefore, LDL cholesterol-complexes are called «bad cholesterol», while the «good» HDL cholesterol-complexes (high density lipoproteins) are responsible for lowering cholesterol levels.

Also controversial is whether the cholesterol level in the brain is linked to Alzheimer disease. Increased cholesterol levels are suspected to promote the development of the so-called plaques in the brains of Alzheimer patients. Here, too, conclusive evidence is still outstanding. thm

«LipidX – Systems Biology of Biomembranes» at a glance

LipidX
Systems Biology of Biomembranes

Principal investigator	**Prof. Gisou van der Goot**
Involved research groups	**Global Health Institute, EPFL; Département de Biochimie (3); Université de Genève; Institute of Zoology, University of Zurich; Laboratory for Computational Systems Biotechnology, EPFL; Institute of Biochemistry, ETH Zürich; Institute of Chemical Sciences and Engineering, EPFL; ISREC, EPFL; Institute of Molecular Systems Biology, ETHZ; Institute of Computational Science, ETHZ; Microbiology and Molecular Medicine, Faculty of Medicine, University of Geneva; Center for Integrative Genomics and Department of Physiology, University of Lausanne; Department of Biochemistry and Department of Biological Sciences, National University of Singapore; Biozentrum, University of Basel.**
Number of research groups	**14**
Researchers : Administration	**59 : 0.4**
Biologists : Non-biologists	**4:1**
Overall Budget (2008-2011)	**20'738'370, thereof 8'138'000 CHF from SystemsX.ch**