# Lipids in the Limelight

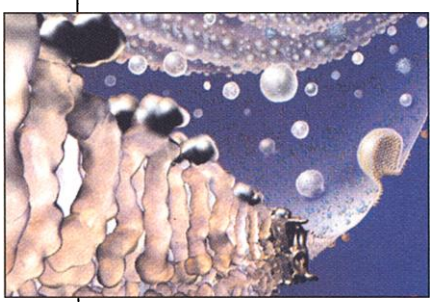
The term lipid can bring to mind many associations. Unfortunately, these are often negative, such as the contribution that excessive dietary fat makes to heart disease. But lipids are also essential components of cell membranes, and during the past several years, cell biologists have found that lipid molecules play many more dynamic roles as well, helping to control a majority of cellular activities. Consequently, lipids are major determinants of many pathologies in addition to heart disease. This issue of *Science* highlights a few of the recent emerging themes in lipid biology.

Despite a growing emphasis on lipids in cell signaling, the question of how cells respond to dietary fat remains near the top of the lipid research marquee. Chawla *et al.* (p. 1866) have proposed a general framework to understand how receptors in the nucleus may act as sensors for diet-derived lipids. The script calls for an elaborate gene network to prevent lipid overload.

The development of new drugs, such as the so-called Cox-2 inhibitors, for treating pain, fever, and inflammation underscores the rapid progress made in eicosanoid lipid biology. An update is provided by Funk (p. 1871), who focuses on two main actors in the field: the prostaglandins and leukotrienes. Derived from membrane lipids, these molecules are released and transported to a variety of target cells, where they can influence the immune response. Elucidating the molecular details of their actions may aid in the design of even better anti-inflammatory drugs.

The membrane-derived lysophospholipids, which affect processes including angiogenesis, neuronal survival, and immunity, are also involved in disease. The demonstration that cells bear surface receptors for these lipids shows that they can work from outside the cell as well as from inside. Hla *et al.* (p. 1875) provide a backstage view of how lysophospholipid receptor biology may present new opportunities for understanding complex diseases such as cancer and autoimmunity.

Lipid additions can be important for protein function. The developmentally important protein Hedgehog is a prime example. Its unique lipid modification by cholesterol and palmitoyl, as well as its action through a cell surface receptor that harbors a sterol-sensing domain, thicken the plot of this signaling story. Ingham (p. 1879) critiques recent Hedgehog history and ponders what roles the lipid adducts serve.



As described by Sato *et al.* (p. 1881), lipids may also help direct proteins to their proper locations in the cell. Many of the proteins that regulate vesicle trafficking bear a lipid-binding motif that targets them to distinct membrane-localized phospholipids, thus determining when and where the proteins perform.

In addition to directing vesicle trafficking, membrane lipids, particularly when organized in distinct microdomains known as caveolae and rafts, play other roles, such as transporting materials into and through cells and organizing the cell's signal transduction pathways. In a News article, Marx (p. 1862) takes a look at these functions and also at the ongoing controversy about how many are performed by caveolae as opposed to rafts.

New insights into lipid function can also be found in *Science*'s Signal Transduction Knowledge Environment (STKE). Hilgemann *et al.* set the stage for understanding why phosphatidylinositol 4,5-bisphosphate, once thought to only be a source for generating lipid signaling molecules, should now be considered a signaling molecule in its own right. And finally, Munnik and Musgrave raise the curtain on an unexpected role for phospholipase D, which may help direct vesicle transport along the cell's vast microtubule network.

–LISA CHONG AND JEAN MARX

CONTENTS

## NEWS



## REVIEWS AND VIEWPOINTS



***See also Perspective on p. 1845, Reports on pp. 1939 and 1942, and by Baron and Malhotra published online in* Science *this week (www.sciencexpress.org), and content in* Science's STKE *(stke.sciencemag.org; see p. 1783).***

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