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Special issue: Regulation of lipid metabolism in yeast

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The complexity and dynamic nature of the “lipidome” of eukaryotic cells are increasingly apparent. Taking into account the diversity within many lipid classes created by variability in such factors as acyl chain substitutions, degree of desaturation, hydroxylation, and phosphorylation, the number of molecular species in eukaryotic cells exceeds one thousand. Such estimates of the diversity of the lipidome do not even account for the various water-soluble turnover products of lipid metabolism, many of which are vital signaling molecules themselves. Furthermore, specialized lipids serve to modify proteins and to target and anchor them to specific membranes.

Understanding of the complex cellular roles played by lipids, as well as their precursors and turnover products, in signaling, membrane trafficking, and transcriptional networks continues to expand. The regulation of synthesis, turnover, and trafficking of lipids of all classes is extraordinarily complex, but major progress has been made recently in deciphering the mechanisms underlying these processes in a number of eukaryotic cell systems. In the context of these advances, the yeast model system has an important role to play. The powerful tools of yeast molecular and classical genetics enable the cellular functions of gene products to be probed individually and in combination with an ease not possible in any other eukaryotic organism. The advantages of using these genetic approaches in yeast have already been amply demonstrated in the dissection of complex cellular functions such as cell division and membrane trafficking.

The time is now ripe to fully exploit the advantages of the yeast system to explore the complex cellular roles of the constituents of the lipidome. As is discussed in a number of the papers in this special issue, yeast cells synthesize the same general classes of lipids found in other eukaryotes via pathways largely homologous to those in mammalian cells. In a number of cases, identification of yeast genes involved in various aspects of lipid metabolism has enabled identification of their mammalian counterparts. It is true that the lipids found in yeast exhibit some specific differences from the lipids found in mammalian cells. For example, yeast synthesizes ergosterol as its major sterol instead of cholesterol, and produces sphingolipids containing inositol rather than choline. Furthermore, yeast cells synthesize phosphatidylserine by a mechanism different from that employed by mammalian cells. It is also true that phosphatidylinositol (3,4,5)-triphosphate has not been observed in baker’s yeast, *Saccharomyces cerevisiae*, although it has recently been detected under specialized conditions in the fission yeast, *Schizosaccharomyces pombe*. Furthermore, some aspects of the signaling attributed to inositol polyphosphates and diacylglycerol documented in mammalian cells have not been observed in *S. cerevisiae*. Thus, caution is necessary in extending observations made in experiments in yeast to mammalian cells. Nevertheless, the yeast model system offers

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unparalleled opportunity to manipulate levels of gene products that control the synthesis, turnover, or localization of specific lipids. These genetic approaches can now be combined with an ever-increasing array of high-throughput biochemical and molecular methodologies allowing the lipidome, as a whole, to be probed with increasing accuracy and sensitivity. Similarly, advances in genome-wide technologies permit ever more sensitive analyses of the effects of specific changes in lipid metabolism on genome-wide transcription, protein–protein interactions, and activation of signaling pathways. Thus, the papers in this special issue are presented at a time of unprecedented opportunity for the functional analysis of the yeast lipidome.

These papers will be of interest not only to those interested in lipid metabolism in yeast, but to those interested in eukaryotic lipidomics in general. In this special issue, readers with a general interest in lipid metabolism and the roles of lipids in eukaryotic cell biology will find comprehensive reviews on subjects of great current interest. These articles include in-depth coverage of yeast phospholipids, sphingolipids, and lipid storage. The roles of lipids in endocytosis and many other aspects of cell biology are also discussed. Neutral lipid metabolism and fatty acid synthesis and regulation are presented in relationship to the broader contexts of cellular regulation and physiology. The complex regulation of phospholipid biosynthesis and turnover is also covered in a number of the articles in this issue. Topics related to lipid metabolism, such as formation and transport of glycosylphosphoinoside proteins and the transport and metabolism of glycerophosphoesters produced through phospholipid deacylation, are reviewed in detail. These papers are presented in this comprehensive issue at a time when there is increasing interest in the roles of lipids and their secondary metabolites in cell signaling, membrane trafficking, and membrane identity. The articles presented here clearly illustrate the tremendous potential of the yeast model system to contribute to our overall understanding and progress in all of these crucial areas of biomedical research.

We thank our colleagues for preparing these excellent reviews, and thank the referees who provided constructive criticisms for improving the presentation of the reviews. We hope that our readers find this special issue to be a source of inspiration for future investigations.