

The Mysteries of Sphingolipids

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Sphingolipids are a diverse class of membrane lipids that make up a high percentage of the eukaryotic plasma membranes lipids and have been recently been implicated in important signaling pathways. Despite discovery in the 19th century, their name, derived from “Sphinx” because of their enigmatic properties, still applies. We do not have a complete understanding of the enzymology of their biosynthesis, nor their functions, although we know that metabolites in the pathway are implicated in the regulation of various pathways including cellular differentiation, apoptosis and stress responses. There is a huge diversity of sphingolipids with various head groups and fatty acyl chains. We are now beginning to get the first insights into how the synthesis of this diverse family of lipids is controlled. In addition, recently, a new concept has emerged, termed the raft hypothesis, which postulates that sphingolipids, together with cholesterol, form specialized membrane domains with increased lipid order that function in membrane protein sorting and signal transduction. This hypothesis has become widely accepted, even though it has not been seriously put to test. In this lecture, I will discuss a few aspects of sphingolipid biosynthesis, its function in the heat shock response and discuss some critical issues and ways that one might put to test the raft hypothesis.

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