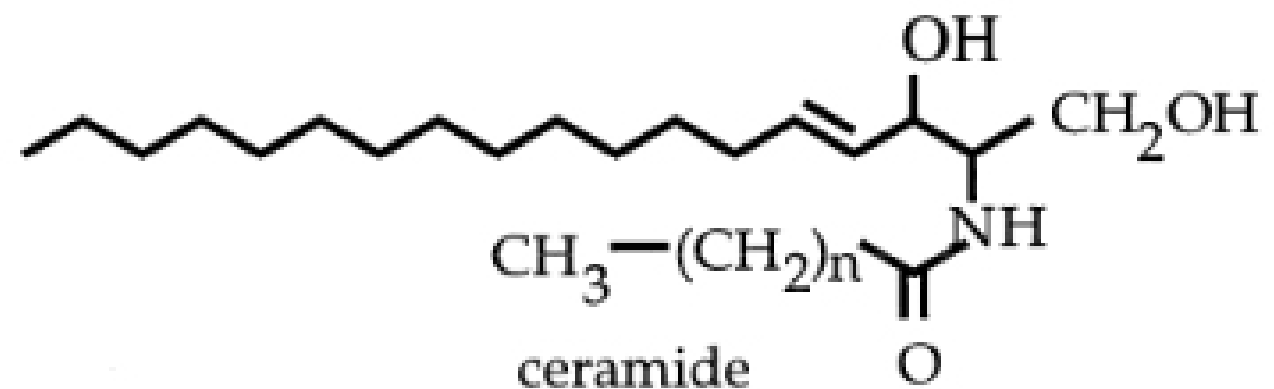
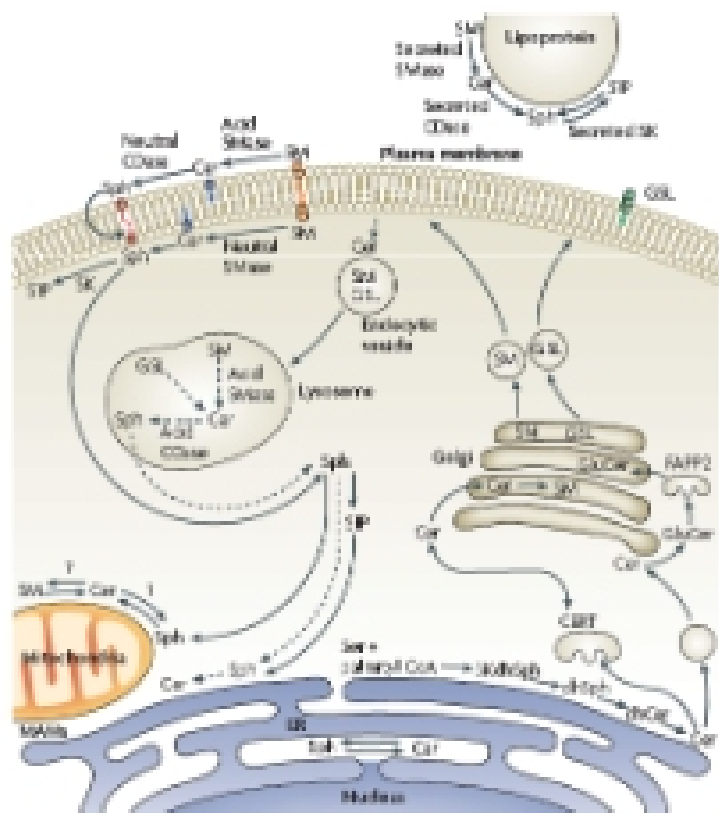


# Lipid Second Messengers: Lessons from Sphingolipids

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# Lipids Overview

- Functional classes of lipids:
  1. Structural lipids → membrane lipids (5-10% dry mass); barriers around cells and cellular compartments.
  2. Storage lipids → 80% of adipocyte mass; passive role in cell until enzymatically oxidized.
  3. Messenger lipids → active role in metabolic traffic; potent signals; intracellular messengers.

# Examples of Lipid Second Messengers

**Table 1.** Lipid second messengers (Prokazova, et al, 2007).

Second messenger	Generation pathway	Specific signal	Physiological response
IP <sub>3</sub> , DAG	Hydrolysis of PtdIns(4,5)P <sub>2</sub> by phospholipases C <sub>β</sub> and C <sub>γ</sub>	Activation of G protein-coupled receptors by hormones, activation of receptor tyrosine kinases by growth factors	Vasoconstriction, vasorelaxation, proliferation, migration
PtdIns(3,4,5)	Phosphorylation of PtdIns(4,5)P <sub>2</sub> by PI3K	Cytokines, ligands of surface antigens	Cell survival
Ceramide	Hydrolysis of sphingomyelin by neutral, Mg <sup>2+</sup> -dependent, and acidic sphingomyelinase	Cytokines, growth factors, antibodies to CD molecules, oxLDL, thermal shock, hypoxia/reperfusion, UV radiation, drugs, lipopolysaccharides	Apoptosis, endothelial dysfunction
Sphingosine	Hydrolysis of ceramide by neutral ceramidase	Second messenger function is not established unambiguously	Arrest of cell division, apoptosis
S1P	Phosphorylation of sphingosine by sphingosine kinase	Second messenger function is not established unambiguously	Cell growth, cell survival