



## ***Can we dispense with sphingolipids?***

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Sphingolipids (SL) are ubiquitous minor lipids in mammalian cell membranes, yet there is little data on the behavior of cells under SL-restriction conditions. We have prepared mammalian cells in which the activity of the main enzyme in SL biosynthesis (serine-palmitoyl CoA transferase, or SPT) has been suppressed, either genetically or chemically, so that their SL contents can be directly controlled through changes in the culture medium SL supply. We observe that the cells resist extreme changes of SL concentration in the medium with moderate changes in SL concentration in the membranes. A 250-fold decrease in SL levels in the medium still allowed cell division, with only a 7-fold decrease in membrane SL concentration. Important physical properties of the membranes, such as fluidity (measured using laurdan fluorescence), or mechanical resistance to penetration (AFM force spectroscopy), revealed only small changes as a result of SL restriction. Lipidomic analysis of the cell plasma membranes indicated a number of changes in phospholipid composition that could compensate the loss of sphingomyelin, so that the membrane biophysical parameters would remain constant.