

CDB SEMINAR

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Functional analysis of lipid metabolism genes affecting developmental signaling pathways

Summary

Sphingolipids are major components of cell membrane, and are involved in various cellular processes by making membrane raft or working as signaling molecules. As other membrane lipids, sphingolipids are not evenly distributed. The membrane lipid composition is quite different among different cell types, and even among intracellular organelles in the same cell. However, the significance of lipid composition in cell membrane is not well understood. In a forward genetic screen for mutations that alter intracellular Notch receptor trafficking in *Drosophila melanogaster*, we recovered mutants that disrupt genes encoding serine palmitoyltransferase (SPT, a rate limit enzyme of sphingolipids) and acetyl-CoA carboxylase (ACC, a rate limit enzyme of fatty acids). SPT and ACC mutations potentially disrupt all sphingolipids and all phospholipids synthesis, respectively. Both mutants caused Notch and other proteins to accumulate abnormally in endosomal compartments. In mosaic animals, mutant tissues exhibited an unusual non-cell-autonomous effect whereby mutant cells are functionally rescued by secreted activities emanating from adjacent wildtype tissue. Strikingly, both mutants displayed prominent tissue overgrowth phenotypes that are partially attributable to altered Notch and Wnt signaling. Our analysis of the mutants suggest that accurate lipid composition is essential for proper intracellular traffcking and normal development.

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