

Molecular mechanism of moisturizing factor, ceramides, as a lipid signaling molecule

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Ceramide, the backbone of membrane sphingolipids, is now recognized as an intracellular lipid second messenger that regulates various signal transduction systems including apoptosis. In the yeast *Saccharomyces cerevisiae*, accumulation of intracellular ceramide causes strong growth defect. In this study, we screened yeast mutant strains showing abnormal sensitivity against ceramide accumulation. It was found that deletion of *IRA2* gene encoding GTPase-activating protein or *PDE2* gene encoding cyclic AMP phosphodiesterase, which negatively regulate Ras-cAMP-PKA signaling pathway, causes high sensitivity against the growth inhibition induced by ceramide accumulation. On the contrary, deletion of *RAS2* gene encoding small GTPase causes resistance against the growth inhibition. These results suggested functional relationship between ceramide signaling and Ras-cAMP-PKA pathway.