The involvement of sphingolipids in apoptosis induced by acetic acid in yeast

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The yeast *Saccharomyces cerevisiae* can undergo programmed cell death in response to different stimuli, exhibiting typical apoptotic markers such as externalization of phosphatidylserine, DNA fragmentation, chromatin condensation, cytochrome *c* release from mitochondria and production of reactive oxygen species (ROS). Changes in sphingolipid metabolism have been linked to apoptosis and oxidative stress in both yeast and mammalian cells. Indeed, ceramides have been detected in mitochondria and accumulate upon stress treatments, increasing the permeability of the mitochondria to cytochrome *c* and leading to the generation of ROS. We aimed to characterize the relative contribution of biosynthesis versus catabolism of ceramides to the apoptotic cell death induced by acetic acid in yeast. Yeast cells lacking Lag1p, Lac1p (unable to generate ceramide by de novo synthesis), Isc1p (unable to generate ceramide by degradation of inositolphosphosphingolipids), Ydc1p and Ypc1p (unable to breakdown ceramide) were generated by homologous recombination. Our results show that lag1 and isc1 mutant cells exhibited a higher resistance to acetic acid that was correlated with lower levels of mitochondrial ROS production and reduced alterations of the mitochondrial membrane potential. Associated with these events, there was less translocation of cytochrome *c* to the cytosol in response to acetic acid than in the wild-type strain. Our results suggest that ceramide production contributes to cell death induced by acetic acid, especially through the hydrolysis of inositolphosphosphingolipids catalyzed by Isc1p.

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