The role of cardiolipin in mitochondrial function: Implications for Barth Syndrome

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In eukaryotic cells, the acyl species of the phospholipid cardiolipin (CL) are more highly unsaturated than those of the other membrane phospholipids. Defective acylation of CL with unsaturated fatty acids and decreased total CL are associated with Barth syndrome, an X-linked cardio- and skeletal myopathy attributed to a defect in the gene G4.5 (also known as tafazzin). We constructed a yeast mutant (taz1) containing a null mutation in the homolog of the human G4.5 gene. The yeast taz1Δ mutant was temperature sensitive for growth on ethanol as sole carbon source, but grew normally on glucose or glycerol plus ethanol. Total CL content was reduced in the taz1Δ mutant, and monolyso-CL accumulated. The predominant CL acyl species found in wild type cells, C18:1 and C16:1 were markedly reduced in the mutant, while CL molecules containing saturated fatty acids were present. Interestingly, CL synthesis increased in the mutant, while expression of the CL structural genes CRD1 and PGS1 did not, suggesting that de novo biosynthetic enzyme activities are regulated by CL acylation. These results indicate that the taz1Δ mutant is an excellent genetic tool to study CL remodeling and may serve as a model system for the study of Barth syndrome.

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\text{A} & \text{B} & \text{C} & \text{D} \\
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Structure of cardiolipin. In the acid form of authentic cardiolipin, X and Y are hydrogens while A, B, C and D are fatty acyl groups (Schlame et al., 2000).

**List of recent publications**


