Katedry biochémie a genetiky
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Vás pozývajú na **38**. prednášku v rámci Kuželových seminárov:

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

ktorá sa uskutoční

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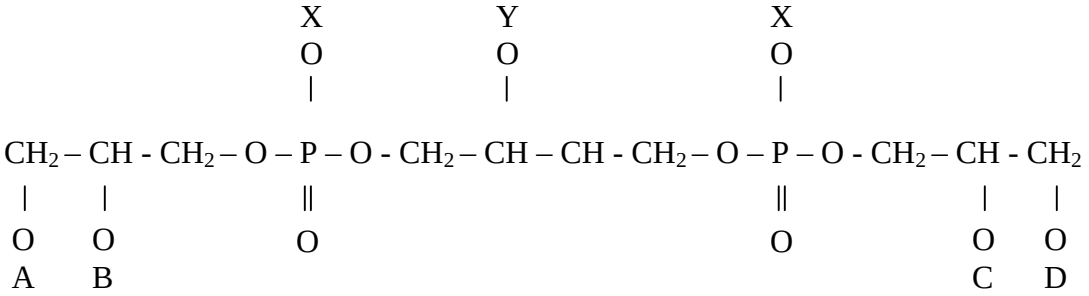
In eukaryotic cells, the acyl species of the phospholipid cardiolipin (CL) are more highly unsaturated than those of the other membrane phospholipids. Defective acylation of CL with unsaturated fatty acids and decreased total CL are associated with Barth syndrome, an X-linked cardio- and skeletal myopathy 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 *taz1D* 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 *taz1D* 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 *taz1D* mutant is an excellent genetic tool to study CL remodeling and may serve as a model system for the study of Barth syndrome.



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

Shamir, A., Shaltiel, G., Greenberg, M.L., Belmaker, R.H., and Agam, G. (2003). The effect of lithium on expression of genes for inositol biosynthetic enzymes in mouse hippocampus: a comparison with the yeast model. Mol. Brain Res. 115: 104-110.

Ding, D.B., and Greenberg, M.L. (2003). Lithium and valpronate decrease the membrane phosphatidylinositol/phosphatidylcholine ratio. Mol. Microbiol. 47: 373-381.

Koshkin, V., and Greenberg, M.L. (2002). Cardiolipin prevents rate-dependent uncoupling and provides osmotic stability in yeast mitochondria. Biochem. J. 364: 317-322.

Vaden, D.L., Ding, D., Peterson, B., and Greenberg, M.L.. (2001). Lithium and valproate decrease inositol mass and increase expression of the yeast *INO1* and *INO2* genes for inositol biosynthesis. J. Biol. Chem. 276: 15466-15471.

Jiang, F., Ryan, M.T., Schlame, M., Zhao, M., Gu, Z., Klingenberg, M., Pfanner, N., and Greenberg, M.L. (2000). Absence of cardiolipin in the crd1 null mutant results in decreased mitochondrial membrane potential and reduced mitochondrial function. J. Biol. Chem. 275: 22387-22394.

Schlame, M., Rua, D., and Greenberg, M.L. (2000). The biosynthesis and functional role of cardiolipin. Prog. Lipid Res. 39: 257-288.

Koshkin, V., and Greenberg, M.L. (2000). Oxidative phosphorylation in cardiolipin-lacking yeast mitochondria. Biochem. J. 347: 687-691.