

2012. Nuclear envelope phosphatase 1-regulatory subunit 1 (formerly TMEM188) is the metazoan Spo7p ortholog and functions in the lipin activation pathway. *J. Biol. Chem.* V. 287. P. 3123.
- Harris T.E., Finck B.N.* 2011. Dual function lipin proteins and glycerolipid metabolism. *Trends Endocrinol. Metab.* V. 22. P. 226.
- Heier C., Kühnlein R.P.* 2018. Triacylglycerol metabolism in *Drosophila melanogaster*. *Genetics*. V. 210. P. 1163.
- Hu M., Wang F., Li X., Rogers C.Q., Liang X., Finck B.N., Mitra M.S., Zhang R., Mitchell D.A., You M.* 2012. Regulation of hepatic lipin-1 by ethanol: Role of AMP-activated protein kinase/steryl regulatory element-binding protein 1 signaling in mice. *Hepatology*. V. 55. P. 437.
- Khalil M.B., Sundaram M., Zhang H.Y., Links P.H., Raven J.F., Manmontri B., Sariahmetoglu M., Tran K., Reue K., Brindley D.N., Yao Z.* 2009. The level and compartmentalization of phosphatidate phosphatase-1 (lipin-1) control the assembly and secretion of hepatic VLDL. *J. Lipid Res.* V. 50. P. 47.
- Khayyo V.I., Hoffmann R.M., Wang H., Bell J.A., Burke J.E., Reue K., Airola M.V.* 2020. Crystal structure of a lipin/Pah phosphatidic acid phosphatase. *Nat. Commun.* V. 11. P. 1.
- Langner C.A., Birkenmeier E.H., Ben-Zeef O., Schotz M.C., Sweet H.O., Davisson M.T., Gordon J.I.* 1989. The fatty liver dystrophy (fld) mutation. A new mutant mouse with a developmental abnormality in triglyceride metabolism and associated tissue-specific defects in lipoprotein lipase and hepatic lipase activities. *J. Biol. Chem.* V. 264. P. 7994.
- Lin Y.P., Carman G.M.* 1989. Purification and characterization of phosphatidate phosphatase from *Saccharomyces cerevisiae*. *J. Biol. Chem.* V. 264. P. 8641.
- Loewen C.J.R., Gaspar M.L., Jesch S.A., Delon C., Ktistakis N.T., Henry S.A., Levine T.P.* 2004. Phospholipid metabolism regulated by a transcription factor sensing phosphatidic acid. *Science*. V. 304. P. 1644.
- Makarova M., Gu Y., Chen J.S., Beckley J.R., Gould K.L., Olfertenko S.* 2016. Temporal regulation of lipid activity diverged to account for differences in mitotic programs. *Curr. Biol.* V. 26. P. 237.
- Mall M., Walte T., Gorjánácz M., Davidson I.F., Nga Ly-Hartig T.B., Ellenberg J., Mattaj I.W.* 2012. Mitotic lamin disassembly is triggered by lipid-mediated signaling. *J. Cell Biol.* V. 198. P. 981.
- Pascual F., Carman G.M.* 2013. Phosphatidate phosphatase, a key regulator of lipid homeostasis. *Biochim. Biophys. Acta. Mol. Cell Biol. Lipids*. V. 1831. P. 514.
- Péterfy M., Phan J., Xu P., Reue K. et al.* 2001. Lipodystrophy in the fld mouse results from mutation of a new gene encoding a nuclear protein, lipin. *Nat. Genet.* V. 27. P. 121.
- Peterson T.R., Sengupta S.S., Harris T.E., Carmack A.E., Kang S.A., Balderas E., Guertin D.A., Madden K.L., Carpenter A.E., Finck B.N., Sabatini D.M.* 2011. mTOR complex 1 regulates lipin 1 localization to control the SREBP pathway. *Cell*. V. 146. P. 408.
- Phan J., Reue K.* 2005. Lipin, a lipodystrophy and obesity gene. *Cell Metab.* V. 1. P. 73.
- Ren H., Federico L., Huang H., Sunkara M., Drennan T., Frohman M.A., Smyth S.S., Morris A.J.* 2010. A phosphatidic acid binding/nuclear localization motif determines lipin1 function in lipid metabolism and adipogenesis. *Mol. Biol. Cell*. V. 21. P. 3171.
- Reue K., Dwyer J.R.* 2009. Lipin proteins and metabolic homeostasis. *J. Lipid Res.* V. 50. P. 109.
- Reue K., Wang H.* 2019. Mammalian lipin phosphatidic acid phosphatases in lipid synthesis and beyond: metabolic and inflammatory. *J. Lipid Res.* V. 60. P. 728.
- Santos-Rosa H., Leung J., Grimsey N., Peak-Chew S., Siniossoglou S.* 2005. The yeast lipin Smp2 couples phospholipid biosynthesis to nuclear membrane growth. *EMBO J.* V. 24. P. 1931.
- Schweitzer G.G., Collier S.L., Chen Z., McCommis K.S., Pittman S.K., Yoshino J., Matkovich S.J., Hsu F.F., Chast R., Eaton J.M., Harris T.E., Weihl C.C., Finck B.N.* 2019. Loss of lipin-1-mediated phosphatidic acid phosphohydrolase activity in muscle leads to skeletal myopathy in mice. *FASEB J.* V. 33. P. 652.
- Siniossoglou S., Santos-Rosa H., Rappsilber J., Mann M., Hurt E.* 1998. A novel complex of membrane proteins required for formation of a spherical nucleus. *EMBO J.* V. 17. P. 6449.
- Siniossoglou S.* 2013. Phospholipid metabolism and nuclear function: roles of the lipin family of phosphatidic acid phosphatases. *Biochim. Biophys. Acta. Mol. Cell Biol. Lipids*. V. 1831. P. 575.
- Soto-Cardalda A., Fakas S., Pascual F., Choi H.S., Carman G.M.* 2012. Phosphatidate phosphatase plays role in zinc-mediated regulation of phospholipid synthesis in yeast. *J. Biol. Chem.* V. 287. P. 968.
- Ugrankar R., Liu Y., Provaznik J., Schmitt S., Lehmann M.* 2011. Lipin is a central regulator of adipose tissue development and function in *Drosophila melanogaster*. *Mol. Cell. Biol.* V. 31. P. 1646.
- Watahiki A., Shimizu K., Hoshikawa S., Chiba M., Kitamura H., Egusa H., Fukumoto S., Inuzuka H.* 2020. Lipin-2 degradation elicits a proinflammatory gene signature in macrophages. *Biochem. Biophys. Res. Commun.* V. 524. P. 477.
- Zhang P., Reue K.* 2014. Lipin-1 flexes its muscle in autophagy. *Cell Cycle*. V. 13. P. 3789.

Lipins: Characteristics and Functional Role in the Organism

S. S. Saidakova^{a, b, *}, K. N. Morozova^{a, b}, and E. V. Kiseleva^b

^aDepartment of Cytology and Genetics, Novosibirsk State University, Novosibirsk, 630090 Russia

^bFederal Research Center Institute of Cytology and Genetics SB RAS, Novosibirsk, 630090 Russia

*e-mail: custodian.of.midnight@gmail.com

The family of lipin proteins includes enzymes participating in the phospholipid biosynthesis pathway (Kennedy pathway) which are able to dephosphorylate phosphatidic acid to diacylglycerol. In addition, lipins may be trans-

ported from the cytoplasm to the nucleus and function as coactivators of gene expression. This dual function justifies the high interest in the study of these proteins. The purpose of this review is to give a general idea of the structure, functions, and regulation mechanisms of various lipin orthologs and isoforms in the tissues of eukaryotic organisms and to summarize the latest data obtained by researchers in this field. A separate section is devoted to human diseases caused by excess or deficiency of lipin.

Keywords: lipin, lipids, phosphatidate phosphatase, *fld* mice, lipodystrophy, transcriptional cofactor