

脂蛋白脂酶调控因子研究进展

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摘要 脂蛋白脂酶(Lipoprotein lipase, LPL)是脂质代谢的关键酶,其正常调控对于机体向组织提供脂质营养至关重要。作为LPL重要的调控因子,糖基化磷脂酰肌醇锚定高密度脂蛋白结合蛋白1(Glycosylphosphatidylinositol- anchored high density lipoprotein-binding protein 1, GPIHBP1)能与LPL结合起脂解平台的作用,并作为载体参与LPL向毛细血管内皮细胞的转运。另外,近年来也鉴定出其他几个LPL活性调控因子,包括microRNAs、A型重复排序蛋白相关受体(Sortilin-related receptor with A-type repeats, SorLA)和载脂蛋白(Apolipoproteins, apo)。这些LPL调控因子的成功鉴定,有助于人们深入认识机体脂解代谢和乳糜微粒血症发生的内在机制。文章重点综述了LPL的调控因子GPIHBP1的研究进展,同时也对其他几个调控因子的研究进展进行了讨论。

关键词: 脂蛋白脂酶 糖基化磷脂酰肌醇锚定高密度脂蛋白结合蛋白1 调控因子

Abstract: Lipoprotein lipase (LPL) is an essential enzyme in the lipid metabolism, and proper regulation of LPL is important for controlling the delivery of lipid nutrients to tissues. Recent studies have identified glycosylphosphatidylinositol-anchored high density lipoprotein-binding protein 1(GPIHBP1) as the important regulation factor of LPL that serves as a binding platform for lipolysis on the vascular lumen and an endothelial cell transporter transporting LPL from the interstitial spaces to the capillary lumen. In addition, several other regulation factors of LPL have also been identified including microRNAs, SorLA (Sortilin-related receptor with A-type repeats), and apolipoproteins that are potentially important for regulating LPL activity. These discoveries provide new directions for understanding basic mechanisms of lipolysis and hyperlipidemia. In this update, we focused on summarizing recent progresses on GPIHBP1, the endothelial cell LPL transporter. We also highlighted the recent progresses on several other regulation factors of LPL that are relevant to the regulation of LPL activity.

Keywords: LPL, GPIHBP1, regulation factors

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- [1] Brunzell JD, Deeb SS. Familial lipoprotein lipase deficiency, apo C-II deficiency, and hepatic lipase deficiency. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. The metabolic and molecular bases of inherited disease. 8th ed. New York: McGraw-Hill, 2001: 2789-2816.
- [2] Olivecrona T, Olivecrona G. The ins and outs of adipose tissue. In: Ehnholm C, ed. Cellular Lipid Metabolism. Springer: Berlin Heidelberg, 2009: 315-369.
- [3] Wang H, Eckel RH. Lipoprotein lipase: from gene to obesity. Am J Physiol Endocrinol Metab, 2009, 297(2): E271- E288.
- [4] Davies BS, Beigneux AP, Fong LG, Young SG. New wrinkles in lipoprotein lipase biology. Curr Opin Lipidol, 2012, 23(1): 35-42. 

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- [5] 杨宇虹, 穆云祥, 赵郁, 刘新宇, 赵莉莉, 汪军梅, 解用虹. 中国人群脂蛋白脂肪酶基因突变与高脂血症的相关性研究. 遗传学报, 2007, 34(5): 381-391. [浏览](#)
- [6] 崔璐璐, 王敏, 黄青阳. 脂蛋白酯酶基因Pvu II多态与中国人群脂蛋白脂肪酶基因突变与高脂血症的相关性研究. 遗传, 2010, 32(10): 1031-1036. [浏览](#)
- [7] Goldberg IJ, Soprano DR, Wyatt ML, Vanni TM, Kirchgessner TG, Schotz MC. Localization of lipoprotein lipase mRNA in selected rat tissues. *J Lipid Res*, 1989, 30(10): 1569-1577.
- [8] Bessesen DH, Richards CL, Etienne J, Goers JW, Eckel RH. Spinal cord of the rat contains more lipoprotein lipase than other brain regions. *J Lipid Res*, 1993, 34(2): 229-238.
- [9] Davies BS, Beigneux AP, Barnes RH II, Tu YP, Gin P, Weinstein MM, Nobumori C, Nyrén R, Goldberg I, Olivecrona G, Bensadoun A, Young SG, Fong LG. GPIHBP1 is responsible for the entry of lipoprotein lipase into capillaries. *Cell Metab*, 2010, 12(1): 42-52. [crossref](#)
- [10] Bengtsson G, Olivecrona T. Lipoprotein lipase: mechanism of product inhibition. *Eur J Biochem*, 1980, 106(2): 557-562. [crossref](#)
- [11] Ahn J, Lee H, Chung CH, Ha T. High fat diet induced downregulation of microRNA-467b increased lipoprotein lipase in hepatic steatosis. *Biochem Biophys Res Commun*, 2011, 414(4): 664-669. [crossref](#)
- [12] Chen T, Li Zb, Tu J, Zhu WG, Ge JH, Zheng XY, Yang L, Pan XP, Yan H, Zhu JH. MicroRNA-29a regulates pro-inflammatory cytokine secretion and scavenger receptor expression by targeting LPL in oxLDL-stimulated dendritic cells. *FEBS Lett*, 2011, 585(4): 657-663. [crossref](#)
- [13] Klinger SC, Glerup S, Raarup MK, Mari MC, Nyegaard M, Koster G, Prabakaran T, Nilsson SK, Kjaergaard MM, Bakke O, Nykjær A, Olivecrona G, Petersen CM, Nielsen MS. SorLA regulates the activity of lipoprotein lipase by intracellular trafficking. *J Cell Sci*, 2011, 124(7): 1095-1105. [crossref](#)
- [14] Perdomo G, Kim DH, Zhang T, Qu S, Thomas EA, Toledo FG, Slusher S, Fan Y, Kelley DE, Dong HH. A role of apolipoprotein D in triglyceride metabolism. *J Lipid Res*, 2010, 51(6): 1298-1311. [crossref](#)
- [15] Lee JH, Giannikopoulos P, Duncan SA, Wang J, Johansen CT, Brown JD, Plutzky J, Hegele RA, Glimcher LH, Lee AH. The transcription factor cyclic AMP-responsive element-binding protein H regulates triglyceride metabolism. *Nat Med*, 2011, 17(7): 812-815. [crossref](#)
- [16] Beigneux AP, Davies BS, Gin P, Weinstein MM, Farber E, Qiao X, Peale F, Bunting S, Walzem RL, Wong JS, Blaner WS, Ding ZM, Melford K, Wongsiriroj N, Shu X, de Sauvage F, Ryan RO, Fong LG, Bensadoun A, Young SG. Glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1 plays a critical role in the lipolytic processing of chylomicrons. *Cell Metab*, 2007, 5(4): 279-291. [crossref](#)
- [17] Young SG, Davies BS, Fong LG, Gin P, Weinstein MM, Bensadoun A, Beigneux AP. GPIHBP1: an endothelial cell molecule important for the lipolytic processing of chylomicrons. *Curr Opin Lipidol*, 2007, 18(4): 389-396. [crossref](#)
- [18] Ioka RX, Kang MJ, Kamiyama S, Kim DH, Magoori K, Kamataki A, Ito Y, Takei YA, Sasaki M, Suzuki T, Sasano H, Takahashi S, Sakai J, Fujino T, Yamamoto TT. Expression cloning and characterization of a novel glycosylphosphatidylinositol-anchored high density lipoprotein-binding protein, GPI-HBP1. *J Biol Chem*, 2003, 278(9): 7344-7349. [crossref](#)
- [19] Beigneux AP, Weinstein MM, Davies BS, Gin P, Bensadoun A, Fong LG, Young SG. GPIHBP1 and lipolysis: an update. *Curr Opin Lipidol*, 2009, 20(3): 211-216. [crossref](#)
- [20] Beigneux AP, Gin P, Davies BS, Weinstein MM, Bensadoun A, Ryan RO, Fong LG, Young SG. Glycosylation of Asn-76 in mouse GPIHBP1 is critical for its appearance on the cell surface and the binding of chylomicrons and lipoprotein lipase. *J Lipid Res*, 2008, 49(6): 1312-1321. [crossref](#)
- [21] Gin P, Yin LY, Davies BSJ, Weinstein MM, Ryan RO, Bensadoun A, Fong LG, Young SG, Beigneux AP. The acidic domain of GPIHBP1 is important for the binding of lipoprotein lipase and chylomicrons. *J Biol Chem*, 2008, 283(43): 29554-29562. [crossref](#)
- [22] Beigneux AP, Gin P, Davies BS, Weinstein MM, Bensadoun A, Fong LG, Young SG. Highly conserved cysteines within the Ly6 domain of GPIHBP1 are crucial for the binding of lipoprotein lipase. *J Biol Chem*, 2009, 284(44): 30240-30247. [crossref](#)
- [23] Beigneux AP, Davies BS, Tat S, Chen J, Gin P, Voss CV, Weinstein MM, Bensadoun A, Pullinger CR, Fong LG, Young SG. Assessing the role of the glycosylphosphatidylinositol-anchored high density lipoprotein-binding protein 1 (GPIHBP1) three-finger domain in binding lipoprotein lipase. *J Biol Chem*, 2011, 286(22): 19735-19743. [crossref](#)
- [24] Weinstein MM, Yin LY, Beigneux AP, Davies BS, Gin P, Estrada K, Melford K, Bishop JR, Esko JD, Dallinga-Thie GM, Fong LG, Bensadoun A, Young SG. Abnormal patterns of lipoprotein lipase release into the plasma in GPIHBP1-deficient mice. *J Biol Chem*, 2008, 283(50): 34511-34518. [crossref](#)
- [25] Davies BS, Goulbourne CN, Barnes RH II, Turlo KA, Gin P, Vaughan S, Vaux DJ, Bensadoun A, Beigneux AP, Fong LG, Young SG. Assessing mechanisms of GPIHBP1 and lipoprotein lipase movement across endothelial cells. *J Lipid Res*, 2012, 53(12): 2690-2697. [crossref](#)
- [26] Olafsen T, Young SG, Davies BS, Beigneux AP, Kenanova VE, Voss C, Young G, Wong KP, Barnes RH II, Tu YP, Weinstein MM, Nobumori C, Huang SC, Goldberg IJ, Bensadoun A, Wu AM, Fong LG. Unexpected expression pattern for glycosylphosphatidylinositol-anchored HDL-binding protein 1 (GPIHBP1) in mouse tissues revealed by positron emission tomography scanning. *J Biol Chem*, 2010, 285(50): 39239-39248. [crossref](#)
- [27] Nielsen MS, Brejning J, García R, Zhang HF, Hayden MR, Vilaró S, Gliemann J. Segments in the C-terminal folding domain of lipoprotein lipase important for binding to the low density lipoprotein receptor-related protein and to heparan sulfate proteoglycans. *J Biol Chem*, 1997, 272(9): 5821-5827. [crossref](#)
- [28] Wang J, Hegele RA. Homozygous missense mutation (G56R) in glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1 (GPI-HBP1) in two siblings with fasting chylomicronemia (MIM 144650). *Lipids Health Dis*, 2007, 6: 23. [crossref](#)

- [29] Beigneux AP, Bensadoun A, Gin P, Peter J, Walzem RL, Weinstein MM, Davies BS, Kuiven-hoven JA, Kastelein JJ, Fong LG, Dallinga-Thie GM, Young SG. Chylomicronemia with a mutant GPIHBP1 (Q115P) that cannot bind lipoprotein lipase. *Arterioscler Thromb Vasc Biol*, 2009, 29(6): 956-962. [crossref](#)
- [30] Franssen R, Young SG, Peelman F, Hertecant J, Sierts JA, Schimmel AW, Bensadoun A, Kastelein JJ, Fong LG, Dallinga-Thie GM, Beigneux AP. Chylomicronemia with low post-heparin lipoprotein lipase levels in the setting of GPIHBP1 defects. *Circ Cardiovasc Genet*, 2010, 3(2): 169-178. [crossref](#)
- [31] Coca-Prieto I, Kroupa O, Gonzalez-Santos P, Magne J, Olivecrona G, Ehrenborg E, Valdivielso P. Childhood-onset chylomicronaemia with reduced plasma lipoprotein lipase activity and mass: identification of a novel GPIHBP1 mutation. *J Intern Med*, 2011, 270(3): 224-228. [crossref](#)
- [32] Charriere S, Peretti N, Bernard S, Di Filippo M, Sassolas A, Merlin M, Delay M, Debard C, Lefai E, Lachaux A, Moulin P, Marçais C. GPIHBP1 C89F neomutation and hydrophobic C-terminal domain G175R mutation in two pedigrees with severe hyperchylomicronemia. *J Clin Endocrinol Metab*, 2011, 96(10): 1675-1679. [crossref](#)
- [33] Olivecrona G, Ehrenborg E, Semb H, Makoveichuk E, Lindberg A, Hayden MR, Gin P, Davies BS, Weinstein MM, Fong LG, Beigneux AP, Young SG, Olivecrona T, Hernell O. Mutation of conserved cysteines in the Ly6 domain of GPIHBP1 in familial chylomicronemia. *J Lipid Res*, 2010, 51(6): 1535-1545. [crossref](#)
- [34] Surendran RP, Visser ME, Heemelaar S, Wang J, Peter J, Defesche JC, Kuivenhoven JA, Hosseini M, Péterfy M, Kastelein JJ, Johansen CT, Hegele RA, Stroes ES, Dallinga-Thie GM. Mutations in LPL, APOC2, APOA5, GPIHBP1 and LMF1 in patients with severe hypertriglyceridaemia. *J Intern Med*, 2012, 272(2): 185-196. [crossref](#)
- [35] Rios JJ, Shastry S, Jasso J, Hauser N, Garg A, Bensadoun A, Cohen JC, Hobbs HH. Deletion of GPIHBP1 causing severe chylomicronemia. *J Inher Metab Dis*, 2012, 35(3): 531-540. [crossref](#)
- [36] Davies BS, Waki H, Beigneux AP, Farber E, Weinstein MM, Wilpitz DC, Tai LJ, Evans RM, Fong LG, Tontonoz P, Young SG. The expression of GPIHBP1, an endothelial cell binding site for lipoprotein lipase and chylomicrons, is induced by peroxisome proliferator-activated receptor- γ . *Mol Endocrinol*, 2008, 22(11): 2496-2504. [crossref](#)
- [37] Holmstrøm K, Pedersen AW, Claesson MH, Zocca MB, Jensen SS. Identification of a microRNA signature in dendritic cell vaccines for cancer immunotherapy. *Hum Immunol*, 2010, 71(1): 67-73. [crossref](#)
- [38] Milenkovic D, Deval C, Gouranton E, Landrier JF, Scalbert A, Morand C, Mazur A. Modulation of miRNA expression by dietary polyphenols in apoE deficient mice: a new mechanism of the action of polyphenols. *PLoS One*, 2012, 7(1): e29837.
- [39] Tian GP, Chen WJ, He PP, Tang SL, Zhao GJ, Lv YC, Ouyang XP, Yin K, Wang PP, Cheng H, Chen Y, Huang SL, Fu YC, Zhang DW, Yin WD, Tang CK. MicroRNA-467b targets LPL gene in RAW 264.7 macrophages and attenuates lipid accumulation and proinflammatory cytokine secretion. *Biochimie*, 2012, 94(12): 2749-2755.
- [40] Nielsen MS, Gustafsen C, Madsen P, Nyengaard JR, Hermey G, Bakke O, Mari M, Schu P, Pohlmann R, Dennes A, Petersen CM. Sorting by the cytoplasmic domain of the amyloid precursor protein binding receptor SorLA. *Mol Cell Biol*, 2007, 27(19): 6842-6851. [crossref](#)
- [41] Xian XD, Liu TT, Yu J, Wang YH, Miao YF, Zhang JJ, Yu Y, Ross C, Karasinska JM, Hayden MR, Liu G, Chui DH. Presynaptic defects underlying impaired learning and memory function in lipoprotein lipase-deficient mice. *J Neurosci*, 2009, 29(14): 4681-4685. [crossref](#)
- [42] Wang H, Astarita G, Taussig MD, Bharadwaj KG, DiPatrizio NV, Nave KA, Piomelli D, Goldberg IJ, Eckel RH. Deficiency of lipoprotein lipase in neurons modifies the regulation of energy balance and leads to obesity. *Cell Metab*, 2011, 13(1): 105-113. [crossref](#)
- [43] Pennacchio LA, Olivier M, Hubacek JA, Cohen JC, Cox DR, Fruchart JC, Krauss RM, Rubin EM. An apolipoprotein influencing triglycerides in humans and mice revealed by comparative sequencing. *Science*, 2001, 294(5540): 169-173. [crossref](#)
- [44] Pollin TI, Damcott CM, Shen HQ, Ott SH, Shelton J, Horenstein RB, Post W, McLenithan JC, Bielak LF, Peyser PA, Mitchell BD, Miller M, O'Connell JR, Shuldiner AR. A null mutation in human APOC3 confers a favorable plasma lipid profile and apparent cardioprotection. *Science*, 2008, 322(5908): 1702-1705. [crossref](#)
- [45] Omori Y, Imai J, Watanabe M, Komatsu T, Suzuki Y, Kataoka K, Watanabe S, Tanigami A, Sugano S. CREB-H: a novel mammalian transcription factor belonging to the CREB/ATF family and functioning via the box-B element with a liver-specific expression. *Nucleic Acids Res*, 2001, 29(10): 2154-2162. [crossref](#)
- [46] McConathy WJ, Alaupovic P. Studies on the isolation and partial characterization of apolipoprotein D and lipoprotein D of human plasma. *Biochemistry*, 1976, 15(3): 515-520. [crossref](#)

- [1] 钱琰琰, 王慧君, 马端. 特异AT序列结合蛋白2(SATB2)的研究进展[J]. *遗传*, 2011,33(9): 947-952
- [2] 杨宇晖, 梁旭方, 方荣, 彭敏燕, 黄志东. 鳕脂蛋白脂酶基因SNP及其与食性驯化相关性分析[J]. *遗传*, 2011,33(9): 996-1002
- [3] 杜纪坤, 黄青阳, 李守华, 熊国梅. 脂蛋白脂酶基因HindIII酶切多态性与2型糖尿病的关联研究[J]. *遗传*, 2007,29(8): 929-929-933
- [4] 杜纪坤, 黄青阳. 脂蛋白脂酶基因的研究进展[J]. *遗传*, 2007,29(1): 8-16
- [5] 李国华, 张, 沅, 孙东晓, 李, 宁. 奶牛乳铁蛋白基因5非翻译区PCRSSCP多态性分析[J]. *遗传*, 2004,26(6): 827-830
- [6] 赵迎社, 杨中汉, 冯建生, 蒋建伟, 吴美玉, 周天鸿. 高脂血症患者脂蛋白脂酶基因外显子4区域变异的研究 [J]. *遗传*, 2002,24(5): 519-522

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