

解供能,而 lipin1 作为脂肪酸氧化基因的转录辅激活因子又能增加脂肪酸的氧化,从而最终提供能量,使机体适应空腹禁食状态。Bou Khalil 等^[18]研究发现,肝脏 lipin1 α 或 lipin1 β 的表达会上调极低密度脂蛋白-甘油三酯的合成效率,降低载脂蛋白 B100 的降解。

综上, lipin 作为 PAP1 在甘油脂类的生物合成中发挥关键作用,同时 lipin1 在细胞核中作为转录辅激活因子影响脂肪酸氧化基因的表达,与肥胖及糖、脂代谢紊乱的发生关系密切,可能成为治疗肥胖及其糖、脂代谢紊乱相关疾病的外周新靶点,这也将成为研究者关注的热点与重点。

参 考 文 献

- [1] Shea J, Diamandis EP, Sharma AM, et al. The obesity epidemic [J]. Clin Chem, 2012, 58(6): 968-973.
- [2] Nadra K, de Preux Charles AS, Médard JJ, et al. Phosphatidic acid mediates demyelination in Lpin 1 mutant mice [J]. Genes Dev, 2008, 22(12): 1647-1661.
- [3] Donkor J, Zhang P, Wong S, et al. A conserved serine residue is required for the phosphatidate phosphatase activity but not the transcriptional coactivator functions of lipin-1 and lipin-2 [J]. J Biol Chem, 2009, 284(43): 29968-29978.
- [4] Wang H, Zhang J, Qiu W, et al. Lipin-1 γ isoform is a novel lipid droplet-associated protein highly expressed in the brain [J]. FEBS Lett, 2011, 585(12): 1979-1984.
- [5] Reue K, Brindley DN. Thematic review series: glycerolipids. Multiple roles for lipins/phosphatidate phosphatase enzymes in lipid metabolism [J]. J Lipid Res, 2008, 49(12): 2493-2503.
- [6] Van Harmelen V, Rydén M, Sjölin E, et al. A role of lipin in human obesity and insulin resistance: relation to adipocyte glucose transport and GLUT4 expression [J]. J Lipid Res, 2007, 48(1): 201-206.
- [7] Donkor J, Sparks LM, Xie H, et al. Adipose tissue lipin-1 expression is correlated with peroxisome proliferator-activated receptor alpha gene expression and insulin sensitivity in healthy young men [J]. J Clin Endocrinol Metab, 2008, 93(1): 233-239.
- [8] Lin J, Wu H, Tarr PT, et al. Transcriptional co-activator PGC-1 α drives the formation of slow-twitch muscle fibres [J]. Nature, 2002, 418(6899): 797-801.
- [9] Kim DK, Kim JR, Koh M, et al. Estrogen-related receptor γ (ERR γ) is a novel transcriptional regulator of phosphatidic acid phosphatase, LIPIN1, and inhibits hepatic insulin signaling [J]. J Biol Chem, 2011, 286(44): 38035-38042.
- [10] Samuel VT, Petersen KF, Shulman GI. Lipid-induced insulin resistance: unravelling the mechanism [J]. Lancet, 2010, 375(9733): 2267-2277.
- [11] Burgdorf C, Hänsel L, Heidbreder M, et al. Suppression of cardiac phosphatidate phosphohydrolase 1 activity and lipin mRNA expression in Zucker diabetic fatty rats and humans with type 2 diabetes mellitus [J]. Biochem Biophys Res Commun, 2009, 390(1): 165-170.
- [12] Mlinar B, Pfeifer M, Vrtacnik-Bokal E, et al. Decreased lipin 1 beta expression in visceral adipose tissue is associated with insulin resistance in polycystic ovary syndrome [J]. Eur J Endocrinol, 2008, 159(6): 833-839.
- [13] Loos RJ, Rankinen T, Pérusse L, et al. Association of lipin 1 gene polymorphisms with measures of energy and glucose metabolism [J]. Obesity (Silver Spring), 2007, 15(11): 2723-2732.
- [14] Aulchenko YS, Pullen J, Kloosterman WP, et al. LIPIN2 is associated with type 2 diabetes, glucose metabolism, and body composition [J]. Diabetes, 2007, 56(12): 3020-3026.
- [15] Zhang P, O'Loughlin L, Brindley DN. Regulation of lipin-1 gene expression by glucocorticoids during adipogenesis [J]. J Lipid Res, 2008, 49(7): 1519-1528.
- [16] Phan J, Reue K. Lipin, a lipodystrophy and obesity gene [J]. Cell Metab, 2005, 1(1): 73-83.
- [17] Manmontri B, Sariahmetoglu M, Donkor J, et al. Glucocorticoids and cyclic AMP selectively increase hepatic lipin1 expression, and insulin acts antagonistically [J]. J Lipid Res, 2008, 49(5): 1056-1067.
- [18] Bou Khalil M, Sundaram M, Zhang HY, et al. The level and compartmentalization of phosphatidate phosphatase-1 (lipin-1) control the assembly and secretion of hepatic VLDL [J]. J Lipid Res, 2009, 50(1): 47-58.

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· 网上快讯 ·

血糖控制不佳可增加 2 型糖尿病患者肾循环中一氧化氮的活性 [Diabetes Care, 2013, 36(12): 4071-4075.]

已有实验研究显示血糖可促进内皮细胞释放一氧化氮,而后者参与糖尿病模型肾脏高灌注的发生。为此,研究者对血糖控制与 2 型糖尿病患者肾脏一氧化氮活性的关系进行研究。研究共纳入 113 例 2 型糖尿病患者,记录其肾血流和肾小球滤过率,计算功能型一氧化氮活性、尿一氧化氮分泌及血浆 L-精氨酸与不对称二甲基精氨酸 (ADMA) 比值。HbA1c 处于最高三分位者肾血流增加[低、中、高三分位

者分别为 (576 ± 17) vs. (585 ± 22) vs. (627 ± 33) ml/(min \cdot m²), $P = 0.05$],而肾小球滤过率没有差异。同时, HbA1c 水平较高者肾血流对一氧化氮合酶抑制剂的反应增加 (-55 ± 7) vs. (-64 ± 8) vs. (-86 ± 8) ml/min, $P = 0.04$], L-精氨酸与 ADMA 比值及尿一氧化氮分泌也增加。与实验研究的结果一致,血糖控制不佳的患者肾脏可出现高灌注及一氧化氮活性增加。肾的一氧化氮系统可能成为改善糖尿病患者血流动力学的新靶点。

(刘欣摘译)