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乳酸脱氢酶：子痫前期的潜在调控因子

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【摘　要】子痫前期（pre-eclampsia，PE）是一种严重威胁母婴安全的妊娠并发症，其发病机制尚未完全阐明。近年研究表明，糖酵解关键酶乳酸脱氢酶（lactate dehydrogenase，LDH）在PE发生发展中有重要作用。本文系统综述了PE患者血清及胎盘中LDH及其同工酶水平的异常改变对PE发病的影响；并深入分析LDH各亚基通过调控缺氧、炎症、自噬异常及细胞损伤等多重途径参与胎盘功能障碍的分子机制；最后，还探讨了LDH代谢产物乳酸在PE发病中的影响。LDH不仅是PE的潜在生物标志物，其介导的非代谢功能调控以及代谢重编程可能为PE防治提供新靶点。

【关键词】乳酸脱氢酶；子痫前期；发病机制
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Lactate dehydrogenase: a potential regulatory molecule in preeclampsia

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【**Abstract**】Preeclampsia（PE）is a severe pregnancy complication that poses significant risks to maternal and fetal health，and its pathogenesis remains unclear. Recent studies have shown that lactate dehydrogenase（LDH），a key enzyme in glycolysis，plays a pivotal role in the development and progression of PE. This article reviews the abnormal changes in the levels of LDH and its isozymes in serum and placental tissue and their impact on the pathogenesis of PE and analyzes the molecular mechanisms by which LDH subunits contribute to placental dysfunction through multiple pathways including hypoxia，inflammation，autophagy dysregulation，and cellular damage. In addition，this article discusses the role of lactate，a metabolic product of LDH activity，in the pathogenesis of PE. LDH can be used as a potential biomarker for PE，and the regulation of non-metabolic functions and metabolic reprogramming mediated by LDH provide new targets for the prevention and treatment of PE.

【**Key words**】lactate dehydrogenase；preeclampsia；pathogenesis

子痫前期（pre-eclampsia，PE）是妊娠特有的以高血压、蛋白尿为特征的多系统、多器官损伤的疾病，亦是孕产妇死亡和严重并发症的主要原因之一，其发病率占妊娠女性的2%~8%[1]。研究表明，子痫前期的病理基础为胎盘滋养细胞侵袭能力受损导致子宫螺旋动脉重铸不良进而引发胎盘缺血缺氧，其可能与免疫调节异常[2]、代谢紊乱[3]以及遗传与表观因素调控异常[4]等多种因素密切相关。然而迄今为止，子痫前期的病因和发病机制仍未完全阐明，缺乏有效的防治策略。近年来研究认为：胎盘发育早期滋养细胞所处的低氧环境对其生物学功能的塑造具有决定性的作用[5-7]。当细胞处于低氧环境或因细胞生长活跃导致相对低氧状态时代谢会发生改变，常规的葡萄糖氧化磷酸化所产生的能量便不足以供给细胞。此时，葡萄糖会通过无氧糖酵解途径、经由乳酸脱氢酶A（lactate dehydrogenase A，LDHA）分解成为乳酸，以提供细胞的主要能量来源。乳酸脱氢酶作为糖酵解途径的关键酶限速酶，其异常表达与子痫前期的发病及其严重程度有密切相连。近年来，多项小型临床表明，妊娠期母体外周血乳酸脱氢酶（lactate dehydrogenase，LDH）或LDHA水平与PE严重程度呈现明显的相关性[8-13]，并显示子痫前期孕妇血清LDH或LDHA水平对其疾病严重程度以及不良妊娠结局有一定的预测价值[14-15]。本篇综述系统梳理了LDH可能参与子痫前期发病的分子机制，为防治子痫前期提供新的理论依据和可能的治疗靶点。

1　乳酸脱氢酶

LDH由M亚基（LDHA，基因定位：11p15.1）和H亚基（LDHB，基因定位：12p12.1）组成。通过改变LDH的M、H亚基的组合可以形成2种同源四聚体同工酶，即LDHA（也称为A4/LDH5）和LDHB（也称为B4/LDH1），以及3种异四聚体异构体，即LDH2（H3M1），LDH3（H2M2）和LDH4（H1M3）[16]（图1）。

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所有 LDH 亚型相对分子质量均为 35 kDa，均属于可催化丙酮酸与乳酸双向转化的同工酶。此外，LDH 广泛存在于各组织及细胞中，但由于各亚基的活性位点周围带电残基数量不同，从而影响异构体与底物的亲和力，使得 LDH 不同亚型的相对丰度呈现组织特异性分布[17]；其中 LDH1 和 LDH2 在主要分布于心脏和红细胞，LDH3 在大脑和肾脏中占主导地位，LDH4 和 LDH5 则主要定位于在骨骼肌和肝脏[18]。

LDH 是糖酵解途径中的关键酶，主要定位于细胞质中。在有氧条件下，LDHB 主导丙酮酸向乳酸的转化，生成的丙酮酸可进一步氧化为乙酰辅酶 A 并进入线粒体三羧酸循环（tricarboxylic acid cycle，TCA）以产生大量三磷酸腺苷（adenosine triphosphate，ATP）；当细胞缺氧时，丙酮酸无法完全氧化进入 TCA 循环，此时 LDHA 在细胞质中将丙酮酸还原为乳酸，通过少量而快速地生成 ATP 以维持缺氧条件下的基础能量供应[17]（图 1）。另外，尽管 LDHA 与 LDHB 对底物的亲和力存在差异，但单独敲除任一亚基后，细胞仍能维持乳酸与丙酮酸间的正常转化[19]，这表明二者均具有催化双向反应的功能，其功能差异主要体现在底物亲和力及作用条件的不同。

2 乳酸脱氢酶同工酶水平在子痫前期中呈现差异化改变

目前研究表明，LDH 在子痫前期母体血清及胎盘组织中的总表达量明显升高，但其同工酶亚型的升高比例存在异质性。尽管 LDH 水平与子痫前期严重程度、妊娠结局及并发症发生率呈正相关，并常作为子痫前期发病多指标联合预测体系中的辅助参数，但其作为单一指标对子痫前期发病及围产期不良结局的预测效能有限，而研究提示联合检测血清总 LDH 与同工酶谱（LDH1-LDH5）可明显提升子痫前期的预测准确性[10]。其中，①Saleem FR 等[10]发现正常妊娠时孕妇血清的 LDH 以 LDHB（20%~25%）和 LDH2 为主，而子痫前期患者血清中 LDH4 表达明显增高；②Makkonen M 等[20]检测出重度子痫前期患者外周血出现 LDH2 降低伴 LDH3 升高；③Sammour MB 等[21]的研究显示，与正常妊娠相比，严重子痫前期患者的血清和胎盘提取物中的 LDHA 明显增加；④ Neal JL 等[22]进一步证实胎盘内皮细胞存在 LDHA 基因表达上调。

因此，子痫前期患者血清及胎盘中存在 LDHA 与 LDHB 同工酶差异化改变，即 LDHA 表达上调与 LDHB 表达下调，这一特征性分子表达差异为阐明乳酸脱氢酶参与子痫前期发病的分子机制提供了重要线索。

3 LDH 参与子痫前期发病的可能机制

子痫前期的发病机制尚不明确，目前研究多认为是一种由缺血缺氧、炎症、应激等多种分子机制共同交叠引起的“产科综合征”。其中，早发型子痫前期与胎盘发育缺陷相关，而晚发型子痫前期则与母体血流灌注不足及母体心血管疾病易感性相关。LDH 作为糖酵解关键酶，可能从多种途径参与子痫前期的发病。

3.1 缺血及缺氧

妊娠早期，绒毛外滋养细胞（extravillous trophoblast，EVT）侵入子宫肌层从而限制子宫内膜血流，随后通过子宫螺旋动脉逐渐重铸，维持胎儿快速生长发育所需的能量[23]。而子痫前期患者母胎界面由于 EVT 侵袭能力受损，子宫螺旋动脉重铸障碍的缺氧可持续至妊娠终止，引发母胎界面代谢紊乱[24]。

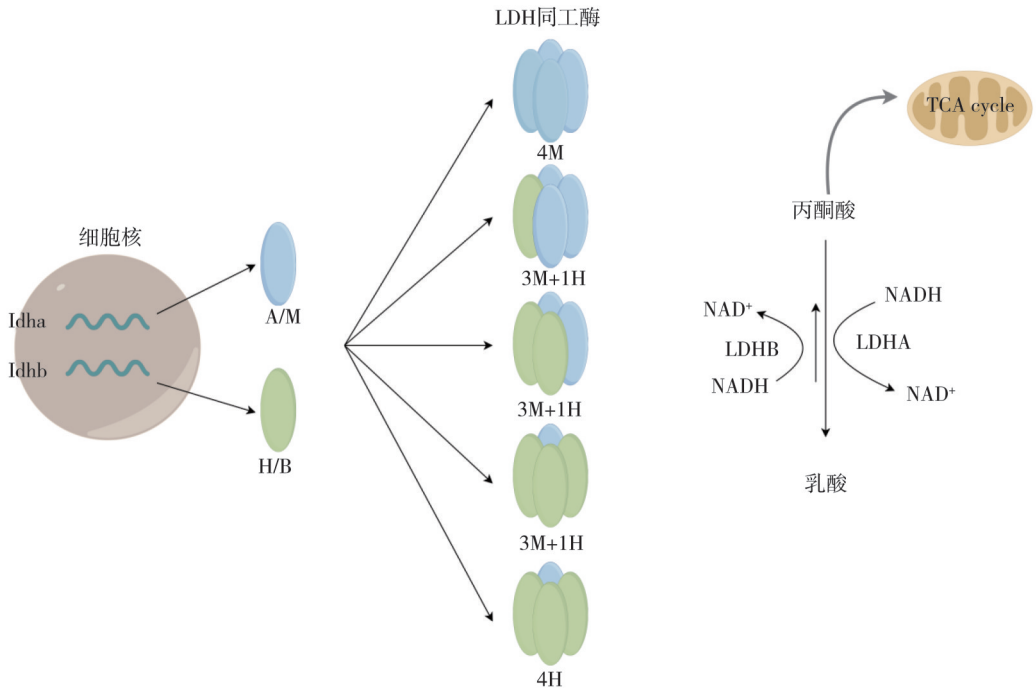


图 1 LDH 同工酶及其反应式

LDHA作为明确的缺氧诱导基因，其表达受缺氧诱导因子-1α（hypoxia-Inducible factor-1 alpha，HIF-1α）调控：HIF-1α的升高或失活均可诱导LDHA表达上调[20]。HIF-1α是细胞应答缺氧的核心转录因子，在正常氧气浓度下通过脯氨酰羟化酶（prolyl hydroxylase domain-containing enzyme，PHD）介导迅速降解，而缺氧状态下PHD活性受到抑制，从而激活HIF-1α[25]。正常妊娠早期HIF-1α水平升高，孕晚期逐渐降低，但子痫前期患者血液及胎盘组织中HIF-1α在孕中晚期仍持续高表达[26]。而Liu B等[27]的研究报道了缺氧通过甲基化修饰调控HIF-1α与缺氧反应元件（hypoxia response element，HRE）结合，诱导LDHA转录表达。同时LDHA也可与HIF-1α形成复合物，通过抑制羟基化依赖的蛋白酶体降解增强HIF-1α稳定性，从而进一步激活糖酵解基因转录[28]。

3.2 免疫失调与炎症

免疫调节在胚胎成功着床及母胎界面形成过程中具有决定性作用，但子痫前期胎盘组织存在明显的免疫紊乱与炎症激活[29]。正常妊娠状态下，蜕膜中的T细胞亚群、B细胞、自然杀伤细胞细胞及巨噬细胞共同协调胚胎植入并维持胎儿免疫耐受；当这些免疫细胞发生功能失调时，会诱发炎症反应、氧化应激和内皮功能障碍，从而促进子痫前期的发病。

子痫前期患者外周血中出现T细胞的数量及相对比例的明显失衡。研究发现，相较于正常孕妇，子痫前期患者外周血中全身效应T细胞数量增加并呈现辅助性T细胞1型（T helper 1 cells，Th1）极化倾向；同时，其胸腺中成熟幼稚型调节性T细胞（regulatory T cells，Tregs）及新近胸腺迁出细胞（recent thymic emigrants，RTE）比例明显降低，而记忆型Tregs比例升高，提示外周Treg细胞分化过程可能发生异常[30-31]。

LDHA在调控T细胞方面发挥重要作用。肿瘤相关研究表明，LDHA可能是活化T细胞的特征性代谢标志物[32]。LDHA通过介导未成熟胸腺细胞抗原-1（immature thymocyte antigen-1，IMT-1）从胞质向细胞膜表面的易位参与T细胞胸腺选择[33-34]；而LDHA的功能缺失会通过干扰蛋白激酶B（protein kinase B，Akt）调控的叉头框蛋白O1（forkhead box protein O1，Foxo1）依赖性基因程序终止机制，导致T细胞活化、增殖、迁移及Th17分化受损[35]。此外，LDHA还参与调控$CD8^+$ T细胞向T记忆干细胞（T memory stem cells，Tscm）的定向分化[36-37]。因此，LDHA可能通过调控T细胞功能参与子痫前期发病。

3.3 自噬

自噬作为维持细胞稳态的核心调控机制，通过选择性清除受损细胞器（如线粒体）、异常折叠蛋白及胞内病原体等过程，在应激条件下保障细胞代谢平衡与功能完整性[38]。研究证实自噬动态失衡与子痫前期病理进程明显相关：自噬活性降低或溶酶体降解功能障碍会损害绒毛外滋养细胞侵袭能力，导致子宫螺旋动脉重塑异常，进而引发胎盘缺血缺氧及炎症级联反应[39-41]；然而矛盾的是，子痫前期患者胎盘滋养细胞与内皮细胞却呈现自噬标志物自噬接头蛋白p62（sequestosome-1，p62）和微管相关蛋白1轻链3-Ⅱ（microtubule-associated protein 1 light chain 3-Ⅱ，LC3-Ⅱ）的异常高表达[42-43]，提示自噬流阻滞可能参与疾病进展，由此衍生出通过调控自噬通路干预子痫前期发展的治疗策略[40-44]。

LDH各亚型对自噬有潜在的调控作用。早期研究提示自噬水平与LDHA表达呈正相关[45]，抑制LDHA活性可明显降低细胞自噬活性[46]；而Hu L等[47]在结直肠癌细胞模型中发现敲低LDHA反而诱导自噬水平升高。近年研究更强调LDHB在自噬溶酶体功能调控中的核心地位：直接抑制LDHB可促进自噬体向溶酶体的定向转运，进而促进感染进一步发展[48]；硫化氢通过干扰LDHB与ATP6V1A的相互作用抑制自噬溶酶体成熟，进而阻断肿瘤病理性血管重塑[49]；但也有研究指出肿瘤细胞可通过上调LDHB维持基础自噬通量，从而支持其异常增殖[50]。这些发现提示LDH在细胞自噬调控网络中具有关键作用，但其具体分子机制研究仍然较少。

3.4 细胞损伤

LDH主要定位于细胞质中，当细胞凋亡、崩解后LDH由细胞内释放到循环中，基于此，LDH检测已被纳入溶血、肝酶升高及血小板减少综合征（hemolysis，elevated liver enzymes，and low platelets syndrome，HELLP syndrome）评估溶血严重程度的辅助诊断标准，为临床鉴别与病情监测提供重要依据[51]。而目前临床实践中也将其作为细胞损伤的生物标志物，应用于评估除子痫前期以外的肿瘤、中毒等疾病严重程度。

3.5 乳酸堆积

当母胎界面发生慢性缺氧时，滋养细胞中LDH活性增强也促进了母胎界面和母体循环中乳酸的异常增多；而乳酸则可能从能量代谢[52]、细胞侵袭[53]、血管生成[54]、氧化应激[55]、免疫反应[56]等多个方面影响胎儿生长发育和母体健康。

近年来的研究认为，细胞内乳酸过度堆积与肿瘤、代谢性疾病及神经退行性疾病等多种疾病发生发展有关。肿瘤相关研究发现，细胞内乳酸堆积和乳酰化与肿瘤的恶性程度相关：一方面乳酸生成为肿瘤细胞快速增殖提供能量[57-58]；另一方面乳酸还可以通过诱导巨噬细胞M2型极化或影响活性氧产生，为肿瘤的生长和发展提供有利的免疫条件[59]。同时已有研究证明，乳酸水平异常与子痫前期的发生发展有关：子痫前期患者妊娠早期血清中的乳酸水平与子痫前期发病存在高度相关性，并可用于早孕期预测子痫前期[60]；子痫前期患者的母胎界面存在明确的代谢紊乱，滋养细胞内乳酸水平随子痫前期的严重程度加重而上升[61]。但现有报道仅局限于研究乳酸水平与子痫前期的发病的相关性，尚未就乳酸影响子痫前期发病的具体分子机制进行报道。

4 结语与展望

近年来的研究表明LDH与子痫前期发病间存在明显关联。PE患者母体血清及胎盘组织中LDH总活性的明显升高，且伴有LDHA/LDHB比例失衡[62]。现有研究已揭示LDH可能通过缺血缺氧、免疫失调、炎症激活、自噬紊乱及乳酸代谢异常等多种病理途径参与子痫前期的发病，本研究系统探讨了LDH潜在参与子痫前期发病的分子途径。

尽管LDH参与子痫前期发病的研究取得了一定进展，但仍存在一些亟待解决的科学问题：首先，现有关于LDH亚

型表达谱的临床研究存在结论异质性，这种差异可能源于样本来源（循环系统与胎盘组织）或疾病分期的不同；其次，目前对 LDH 调控网络的探究主要集中于缺氧应答机制，而表观遗传修饰、转录后调控等分子层面的调控作用尚未明确；最后，LDH 通过分泌乳酸影响炎症、表观遗传修饰等分子机制，进而参与子痫前期发病的分子机制仍有待进一步研究。未来研究可以进一步围绕上述方向深入探讨 LDH 参与 PE 发病的具体分子机制，为开发子痫前期的新型防治策略提供理论依据。

参 考 文 献

[1] Gestational hypertension and preeclampsia: ACOG practice bulletin, number 222[J]. Obstet Gynecol, 2020, 135(6): 237-260.

[2] Deer E, Herrock O, Campbell N, et al. The role of immune cells and mediators in preeclampsia[J]. Nat Rev Nephrol, 2023, 19(4): 257-270.

[3] Hu M, Li J, Baker PN, et al. Revisiting preeclampsia: a metabolic disorder of the placenta[J]. Febs J, 2022, 289(2): 336-354.

[4] Ashraf UM, Hall DL, Rawls AZ, et al. Epigenetic processes during preeclampsia and effects on fetal development and chronic health[J]. Clin Sci (Lond), 2021, 135(19): 2307-2327.

[5] Liu ZZ, Yu Y, Zhang XY, et al. Transcriptomic profiling in hypoxia-induced trophoblast cells for preeclampsia[J]. Placenta, 2023, 136: 8-17.

[6] Perlman BE, Merriam AA, Lemenze A, et al. Implications for preeclampsia: hypoxia-induced Notch promotes trophoblast migration[J]. Reproduction, 2021, 161(6): 681-696.

[7] Wang Z, Zhao G, Zibrila AI, et al. Acetylcholine ameliorated hypoxia-induced oxidative stress and apoptosis in trophoblast cells *via* p38 MAPK/NF-κB pathway[J]. Mol Hum Reprod, 2021, 27(8): gaab045.

[8] Kasraeian M, Asadi N, Vafaei H, et al. Evaluation of serum biomarkers for detection of preeclampsia severity in pregnant women[J]. Pak J Med Sci, 2018, 34(4): 869-873.

[9] Deeksha HS, Pajai S, Reddy Eleti M, et al. A comprehensive review on serum lactate dehydrogenase (LDH) and uric acid in preeclampsia: implications for maternal health and disease severity[J]. Cureus, 2024, 16(3): e56928.

[10] Saleem FR, Chandru S, Biswas M. Evaluation of total LDH and its isoenzymes as markers in preeclampsia[J]. J Med Biochem, 2020, 39(3): 392-398.

[11] Tsoi SCM, Zheng J, Xu F, et al. Differential expression of lactate dehydrogenase isozymes (LDH) in human placenta with high expression of LDH-A4Isozyme in the endothelial cells of pre-eclampsia villi[J]. Placenta, 2001, 22(4): 317-322.

[12] Han Q, Zheng W, Guo XD, et al. A new predicting model of preeclampsia based on peripheral blood test value[J]. Eur Rev Med Pharmacol Sci, 2020, 24(13): 7222-7229.

[13] Pergialiotis V, Panagiotopoulos M, Bellos I, et al. Serum LDH values in hypertensive disorders of pregnancy and their association with maternal and neonatal morbidity: a meta-analysis[J]. Int J Clin Pract, 2021, 75(12): e14986.

[14] Nasir SK, Khalil RY, Mahmood MB, et al. Serum lactate dehydrogenase level in preeclampsia and its correlation with disease severity, maternal and perinatal outcomes[J]. BMC Womens Health, 2025, 25(1): 108.

[15] Reddy Eleti M, Agrawal M, Dewani D, et al. Serum LDH levels in normotensive and preeclamptic-eclamptic pregnant women and its correlation with fetomaternal outcome[J]. Cureus, 2023, 15(4): e37220.

[16] Sharma D, Singh M, Rani R. Role of LDH in tumor glycolysis: regulation of LDHA by small molecules for cancer therapeutics[J]. Semin Cancer Biol, 2022, 87: 184-195.

[17] Claps G, Faouzi S, Quidville V, et al. The multiple roles of LDH in cancer[J]. Nat Rev Clin Oncol, 2022, 19(12): 749-762.

[18] Gallo M, Sapio L, Spina A, et al. Lactic dehydrogenase and cancer: an overview[J]. Front Biosci (Landmark Ed), 2015, 20(8): 1234-1249.

[19] Urbańska K, Orzechowski A. Unappreciated role of LDHA and LDHB to control apoptosis and autophagy in tumor cells[J]. Int J Mol Sci, 2019, 20(9): E2085.

[20] Makkonen M, Penttilä IM, Castrén O. Serum lactic acid dehydrogenase and isoenzymes during pregnancy and labor[J]. Acta Obstet Gynecol Scand, 1980, 59(2): 97-102.

[21] Sammour MB, Ramadan MA, Kahail FK, et al. Serum and Placental lactic dehydrogenase and alkaline phosphatase isoenzymes in normal pregnancy and in pre-eclampsia[J]. Acta Obstet Gynecol Scand, 1975, 54(5): 393-400.

[22] Neal JL, Lowe NK, Corwin EJ. Serum lactate dehydrogenase profile as a retrospective indicator of uterine preparedness for labor: a prospective, observational study[J]. BMC Pregnancy Childbirth, 2013, 13: 128.

[23] Li Q, Sharkey A, Sheridan M, et al. Human uterine natural killer cells regulate differentiation of extravillous trophoblast early in pregnancy[J]. Cell Stem Cell, 2024, 31(2): 181-195.

[24] Torres-Torres J, Espino-Y-Sosa S, Martinez-Portilla R, et al. A narrative review on the pathophysiology of preeclampsia[J]. Int J Mol Sci, 2024, 25(14): 7569.

[25] Vatte S, Ugale R. HIF-1, an important regulator in potential new therapeutic approaches to ischemic stroke[J]. Neurochem Int, 2023, 170: 105605.

[26] Shi J, Wang J, Jia N, et al. A network pharmacology study on mechanism of resveratrol in treating preeclampsia *via* regulation of AGE-RAGE and HIF-1 signalling pathways[J]. Front Endocrinol (Lausanne), 2022, 13: 1044775.

[27] Liu B, Wen H, Yang J, et al. Hypoxia affects HIF-1/LDH-a signaling pathway by methylation modification and transcriptional regulation in Japanese flounder (*Paralichthys olivaceus*)[J]. Biology (Basel), 2022, 11(8): 1233.

[28] Wang F, Chen L, Kong D, et al. Canonical Wnt signaling promotes HSC glycolysis and liver fibrosis through an LDH-A/HIF-1α transcriptional complex[J]. Hepatology, 2024, 79(3): 606-623.

[29] Phoswa WN, Khaliq OP, Eche S. A review on inflammasomes and immune checkpoints in pre-eclampsia complicated with tuberculosis and human immune deficiency virus[J]. Int J Environ Res Public Health, 2023, 20(17): 6627.

[30] Wagner MI, Jöst M, Spratte J, et al. Differentiation of ICOS+ and ICOS- recent thymic emigrant regulatory T cells (RTE T regs) during normal pregnancy, pre-eclampsia and HELLP syndrome[J]. Clin Exp Immunol, 2016, 183(1): 129-142.

[31] Peng X, Chinwe Oluchi-Amaka I, Kwak-Kim J, et al. A comprehensive review of the roles of T-cell immunity in preeclampsia[J]. Front Immunol, 2025, 16: 1476123.

[32] Tang Y, Gu S, Zhu L, et al. LDHA: The Obstacle to T cell responses against tumor[J]. Front Oncol, 2022, 12: 1036477.

[33] Peng M, Yin N, Chhangawala S, et al. Aerobic glycolysis promotes T helper 1 cell differentiation through an epigenetic mechanism [J]. Science, 2016, 354(6311): 481-484.

[34] Fujishiro Y, Kishi H, Matsuda T, et al. Lactate dehydrogenase A-dependent surface expression of immature thymocyte antigen-1: an implication for a novel trafficking function of lactate dehydrogenase-a during T cell development[J]. Eur J Immunol, 2000, 30(2): 516-524.

[35] Xu K, Yin N, Peng M, et al. Glycolytic ATP fuels phosphoinositide 3-kinase signaling to support effector T helper 17 cell responses[J]. Immunity, 2021, 54(5): 976-987.

[36] Hermans D, Gautam S, García-Cañaveras JC, et al. Lactate dehydrogenase inhibition synergizes with IL-21 to promote $CD8^+$ T cell stemness and antitumor immunity[J]. Proc Natl Acad Sci USA, 2020, 117 (11): 6047-6055.

[37] Lv Y, Tang W, Xu Y, et al. Apolipoprotein L3 enhances $CD8^+$ T cell antitumor immunity of colorectal cancer by promoting LDHA-mediated ferroptosis[J]. Int J Biol Sci, 2023, 19(4): 1284-1298.

[38] Debnath J, Gammoh N, Ryan KM. Autophagy and autophagy-related pathways in cancer[J]. Nat Rev Mol Cell Biol, 2023, 24(8): 560-575.

[39] Nakashima A, Cheng SB, Ikawa M, et al. Evidence for lysosomal biogenesis proteome defect and impaired autophagy in preeclampsia[J]. Autophagy, 2020, 16(10): 1771-1785.

[40] Huang Z, Cheng S, Jash S, et al. Exploiting sweet relief for preeclampsia by targeting autophagy-lysosomal machinery and proteinopathy[J]. Exp Mol Med, 2024, 56(5): 1206-1220.

[41] Ren HG, Dai RC, Nik Nabil WN, et al. Unveiling the dual role of autophagy in vascular remodelling and its related diseases[J]. Biomed Pharmacother, 2023, 168: 115643.

[42] Melland-Smith M, Ermini L, Chauvin S, et al. Disruption of sphingolipid metabolism augments ceramide-induced autophagy in preeclampsia[J]. Autophagy, 2015, 11(4): 653-669.

[43] Sun JD, Yu MQ, Du WZ, et al. The cGAS-STING pathway promotes the development of preeclampsia by upregulating autophagy: Mechanisms and implications[J]. Int Immunopharmacol, 2024, 128: 111531.

[44] Ma F, Ding N, Xie L, et al. Inhibition of autophagy *via* 3-methyladenine alleviates the progression of preeclampsia[J]. Acta Biochim Biophys Sin (Shanghai), 2024, 57(3): 356-364.

[45] Kania E, Pająk B, O'Prey J, et al. Verapamil treatment induces cytoprotective autophagy by modulating cellular metabolism[J]. Febs J, 2017, 284(9): 1370-1387.

[46] Zhang QY, Qin Y, Sun XD, et al. Sodium butyrate blocks the growth of colorectal cancer by inhibiting the aerobic glycolysis mediated by SIRT4/HIF-1α[J]. Chem Biol Interact, 2024, 403: 111227.

[47] Hu L, Huang S, Chen G, et al. Nanodrugs incorporating LDHA siRNA inhibit M2-like polarization of TAMs and amplify autophagy to assist oxaliplatin chemotherapy against colorectal cancer[J]. ACS Appl Mater Interfaces, 2022, 14(28): 31625-31633.

[48] Fan S, Wu K, Zhao M, et al. LDHB inhibition induces mitophagy and facilitates the progression of CSFV infection[J]. Autophagy, 2021, 17 (9): 2305-2324.

[49] Wang X, Huang XY, Zhang YY, et al. Hydrogen sulfide attenuates disturbed flow-induced vascular remodeling by inhibiting LDHB-mediated autophagic flux[J]. Redox Biol, 2025, 79: 103456.

[50] Shi L, Yan H, An S, et al. SIRT5-mediated deacetylation of LDHB promotes autophagy and tumorigenesis in colorectal cancer[J]. Mol Oncol, 2019, 13(2): 358-375.

[51] Illsinger S, Janzen N, Sander S, et al. Preeclampsia and HELLP syndrome: impaired mitochondrial function in umbilical endothelial cells [J]. Reprod Sci, 2010, 17(3): 219-226.

[52] Kyllo HM, Wang D, Lorca RA, et al. Adaptive responses in uteroplacental metabolism and fetoplacental nutrient shuttling and sensing during placental insufficiency[J]. Am J Physiol Endocrinol Metab, 2023, 324(6): 556-568.

[53] Liang X, Tang SL, Song YJ, et al. Effect of 2-deoxyglucose-mediated inhibition of glycolysis on migration and invasion of HTR-8/SVneo trophoblast cells[J]. J Reprod Immunol, 2023, 159: 104123.

[54] Song J, Lee K, Park SW, et al. Lactic acid upregulates VEGF expression in macrophages and facilitates choroidal neovascularization[J]. Invest Ophthalmol Vis Sci, 2018, 59(8): 3747-3754.

[55] Li QX, Chen HT, Li ZY, et al. Glucocorticoid caused lactic acid accumulation and damage in human chondrocytes *via* ROS-mediated inhibition of Monocarboxylate Transporter 4[J]. Bone, 2022, 155: 116299.

[56] Zhou HC, Xin-Yan Yan, Yu WW, et al. Lactic acid in macrophage polarization: the significant role in inflammation and cancer[J]. Int Rev Immunol, 2022, 41(1): 4-18.

[57] Boufaied N, Chetta P, Hallal T, et al. Obesogenic high-fat diet and MYC cooperate to promote lactate accumulation and tumor microenvironment remodeling in prostate cancer[J]. Cancer Res, 2024, 84(11): 1834-1855.

[58] Ippolito L, Morandi A, Giannoni E, et al. Lactate: a metabolic driver in the tumour landscape[J]. Trends Biochem Sci, 2019, 44(2): 153-166.

[59] Lopez Krol A, Nehring HP, Krause FF, et al. Lactate induces metabolic and epigenetic reprogramming of pro-inflammatory Th17 cells [J]. EMBO Rep, 2022, 23(12): e54685.

[60] Dasgupta S, Subramani E, Mitra I, et al. Discovery of novel metabolic signatures for early identification of women at risk of developing gestational hypertension[J]. Metabolomics, 2023, 19(5): 50.

[61] Bloxam DL, Bullen BE, Walters BNJ, et al. Placental glycolysis and energy metabolism in preeclampsia[J]. Am J Obstet Gynecol, 1987, 157(1): 97-101.

[62] Ackerman WE, Buhimschi CS, Brown TL, et al. Transcriptomics-based subphenotyping of the human placenta enabled by weighted correlation network analysis in early-onset preeclampsia with and without fetal growth restriction[J]. Hypertension, 2023, 80(6): 1363-1374.

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