·综　述·

组蛋白乳酸化在消化系统肿瘤中的研究进展及展望

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［**摘要**］组蛋白乳酸化修饰是一种新型的组蛋白翻译后修饰，通过乳酸分子与组蛋白赖氨酸残基的共价结合，在细胞代谢重编程中发挥关键作用，尤其在消化系统肿瘤的发生、发展中具有重要意义。近年来，组蛋白乳酸化在多种恶性肿瘤中的作用机制逐渐被揭示，显示其在肿瘤生物学中的广泛影响和临床潜力。本文重点梳理组蛋白乳酸化在消化系统肿瘤中的研究进展，具体分析其在胃癌、肝癌、结肠癌等主要消化道肿瘤中的作用机制。研究表明，乳酸化通过直接修饰组蛋白赖氨酸残基，调节肿瘤细胞的基因表达和染色质构象，进而促进肿瘤的增殖、侵袭和转移。乳酸化通过影响组蛋白与DNA的结合方式，改变染色质的开放性，增强癌基因的转录活性。此外，调控乳酸化水平或抑制乳酸化相关酶，如乳酸脱氢酶抑制剂、乳酸生成抑制剂及特定组蛋白乳酸化酶的靶向治疗，能够有效地抑制肿瘤的发生与发展，并在临床前模型中展示出潜在的治疗效果。本文从不同类型的消化道癌症出发，系统总结组蛋白乳酸化的作用机制，旨在为基于乳酸化修饰的靶向治疗策略提供新的研究方向和理论支持。

［**关键词**］组蛋白乳酸化；乳酸；翻译后修饰；肿瘤
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Research progress and prospect of histone lactylation in digestive system tumors

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［**Abstract**］Histone lactylation is a novel type of post-translational modification, where a lactate molecule covalently binds to the lysine residues of histones. This modification plays a key role in cellular metabolic reprogramming, particularly in digestive system tumorigenesis and progression. In recent years, the role of histone lactylation in various malignancies has been increasingly recognized, highlighting its broad impact on tumor biology and clinical potential. This article focused on the research progress of histone lactylation in digestive system cancers, specifically analyzing its mechanisms in major gastrointestinal cancers such as gastric cancer, liver cancer, and colon cancer. Studies have shown that lactylation modifies histone lysine residues directly, regulating tumor cell gene expression and chromatin conformation, thereby promoting tumor proliferation, invasion, and metastasis. Lactylation affects histone-DNA interactions, altering chromatin openness and enhancing the transcriptional activity of oncogenes. In addition, targeted therapies that modulate lactation levels or inhibit lactation-related enzymes, such as lactate dehydrogenase inhibitors, lactate

production inhibitors, and specific histone lactonases, are effective in inhibiting tumorigenesis and progression and have demonstrated potential therapeutic efficacy in preclinical models. This article systematically summarized the mechanisms of histone lactylation in various types of gastrointestinal cancers, offering new research directions and theoretical support for targeted therapeutic strategies based on lactylation modification.

［**Key words**］Histone lactylation; Lactate; Post-translational modification; Tumor

乳酸是能量产生过程中重要的中间产物。20世纪，Warburg等[1]发现在有氧条件下糖酵解依然可以生成乳酸，这一现象被称为“Warburg效应”。至今已有大量研究表明乳酸不是代谢废物，其可通过影响组蛋白和DNA的表观遗传状态来调节基因表达、代谢过程。近年来乳酸已被证明可以作为组蛋白乳酸化的前体，与组蛋白赖氨酸残基发生共价结合，影响基因的转录，发挥促肿瘤功能[2]。越来越多的证据表明靶向组蛋白乳酸化的治疗策略可能有效地干预肿瘤进程并延长患者的生存期。因此，本文综述组蛋白乳酸化在消化系统肿瘤中的发生机制及潜在作用的研究的最新进展，旨在为靶向组蛋白乳酸化的治疗策略提供新的思路。

1 表观遗传学及组蛋白修饰

表观遗传学涉及多种修饰方式和调控机制，包括DNA甲基化、RNA修饰、组蛋白修饰以及非编码RNA调控等，它彰显基因调控复杂而精细的网络，有助于人们深入理解基因型与表型之间的关系，并探索其在疾病治疗中的应用潜力[3-5]。

组蛋白修饰作为基因表达调控的重要机制，是生物学和医学的研究热点。组蛋白是染色质的主要成分，是构成核小体的基本单位。核小体是由DNA缠绕在由8个组蛋白分子组成的八聚体上形成的。组蛋白的N端和C端尾部可经历多种翻译后修饰，如乙酰化、磷酸化、甲基化、乳酸化。这些修饰可改变组蛋白尾部的电荷和结构，影响其与DNA的结合能力，调节染色质的结构状态和基因的转录活性[6]。

2 组蛋白乳酸化修饰

早期研究普遍认为正常组织细胞在缺氧条件下抑制氧化磷酸化，增强糖酵解以刺激乳酸的生成。然而，Warburg等[1]发现大多数肿瘤细胞即使在有氧条件下，也倾向于通过糖酵解生成乳酸来获取能量，而非依赖线粒体氧化磷酸化，可见乳酸在肿瘤细胞代谢中具有普遍作用，这为肿瘤细胞代谢研究提供了新的方向。2019年，Zhao等[2]证实了组蛋白乳酸化的存在。该研究发现，乳酸通过乳酸脱氢酶（lactate dehydrogenase，LDH）催化生成乙酰辅酶A，介导组蛋白赖氨酸乳酸化，从而调控染色质结构和基因转录。该修饰受糖酵解代谢（己糖激酶、磷酸果糖激酶等）和丙酮酸脱氢酶活性的双重调控。这些代谢酶通过影响乳酸生成和代谢，间接调节组蛋白乳酸化水平。尽管目前尚未明确发现专门的“组蛋白乳酸化酶”，但有研究[7-8]表明，乳酸化修饰可能由一些转移酶家族的某些酶（如乙酰转移酶等）催化，类似于乙酰化修饰的过程。乳酸不仅是能量代谢中的重要中间产物，作为一种多功能生物信号分子广泛调控细胞内外的代谢过程，还参与免疫调节、抗炎反应及基因表达等多种生物学效应。乳酸化修饰通过调节染色质的开放性和基因转录活性，参与多种生理及病理条件下的基因表达调控，尤其在癌症等多种疾病的发生和发展中发挥重要作用（表1）。因此，组蛋白乳酸化作为一种新的表观遗传修饰，为理解乳酸在细胞代谢和疾病发生中的作用提供了全新的视角。

3 组蛋白乳酸化修饰在消化系统肿瘤中的作用及机制研究进展

3.1 在胃癌领域的研究进展

胃肠道肿瘤是全球癌症死亡的主要原因之一，胃癌更是位居全球三大癌症之列[9]。研究发现，胃癌中存在2 375个赖氨酸乳酸化位点，其在胃肿瘤中显著富集，并与患者的不良预后相关[10]。在分子机制方面，葡萄糖转运蛋白3（glucose transporter 3，GLUT3）通过激活乳酸脱氢酶A（lactate dehydrogenase A，LDHA），增强糖酵解，诱导组蛋白乳酸化，改变组蛋白与DNA的结合方式，调节癌基因的表达并抑制抑癌基因的启动子区域，促进胃癌细胞的增殖、侵袭和迁移[11]。同时，氨基酸-tRNA合成酶作为乳酸转移酶可介导组蛋白乳酸化，激活转录因子YAP，上调细胞周期调控蛋白和胚胎干细胞标志物，同时抑制细胞凋亡信号转导通路，从而加速胃癌细胞的生长和转移[12]。此外，组蛋白乳酸化可调节肿瘤免疫细胞活性，影响免疫反应，但具体机制还有待研究[13]。

研究人员开发新型计算模型识别组蛋白乳酸化位点[14]，将其作为胃癌预后标志物预测患者治疗反应与预后。但检测标准和实验流程缺乏

表1 组蛋白乳酸化与消化系统肿瘤关系的概述

Tab. 1 Overview of histone lactylation in relation to tumors of the digestive system

Type of disease	Cells type	Lactylation sites	Relevant molecule or pathway	Downstream effect	Reference
Gastric cancer	Tumor cell	Not mentioned	GLUT3, LDHA	Promoting proliferation, migration, and invasion of tumor cells	[11]
	Tumor cell	Not mentioned	AARS, YAP	Inhibition of apoptotic signaling and accelerates tumor cell growth	[12]
Liver cancer	Tumor stem cell, tumor cell	H3K9, H3K56, H3K14	Demethylzeylasteral, RJA, glycolysis/glycolysis-related cellular pathways	Inhibition of proliferation of hepatocellular carcinoma stem cells, tumor cells	[19-20]
	Tumur cell	H3K124	CENPA/YY1 complex, CCND1, NRP2, YY1	Promoting tumor growth	[21]
	Tumur cell	Not mentioned	ESM1, GP73	Promoting angiogenesis in the tumor microenvironment for hepatocellular carcinoma growth and metastasis	[22-23]
	Macrophage	H3K18	SRSF, MYB, GLUT1, LDHA, HK-1	Promoting polarization of M2-type macrophages to create an immunosuppressive microenvironment	[24]
	Tumor infiltrating lymphocytes	Pantothenoylation	NR6A1, OSBP2, UNC119B; WNT, MAPK, MTOR, NOTCH signaling pathway	Promotion of immunosuppressive TME	[25]
Pancreatic cancer	Tumor cell	Not mentioned	P53, KRAS, SLC16, Raf/MEK/ERK signaling pathway	Promoting tumor cell proliferation, invasion metastasis	[28-31]
	Tumor cell, immune cell	Not mentioned	NUSAP1, c-Myc, HIF-1α, LDHA	Promotion of tumor cell proliferation and metastasis, immune escape	[32-33]
	Tumor cell	H4K12	Nectin-2	Enhancement of immune escape of tumor cells	[34]
	Tumor cell	H3K18	TTK, BUB1B, AMPK pathway	Promoting tumor proliferation and inhibition of apoptosis	[35-36]
Colorectal cancer	Not mentioned	Not mentioned	SMC4, PGAM1, HK2, PFKL, ALDOC, ABC transporter proteins	Tumor growth promotion, angiogenesis and immune escape, immunosuppressive TME	[39]
	Neutrophil	H3K18	GPR37, CXCL1, CXCL5; Hippo corridor	Promoting TME neutrophil recruitment	[40]
	Tumor cell	Not mentioned	LINC00152, YY1, IL-8, TNF-α; NF-κB passage	Promoting migration and invasion of tumor cells	[41]
	Macrophage	H3K18	RARγ, TRAF6, TNF-α, IL-6; NF-κB, STAT3 pathway	Promoting tumor growth	[42]
	Tumor cell	H3K18	NOP2/NSUN2, ENO1	Promoting proliferation and metastasis of tumor cells	[43]
	Tumor cell	Not mentioned	KAT8, eEF1A2	Promoting proliferation and metastasis of tumor cells	[44]
	Tumor cell	Not mentioned	circATXN7, NF-κB	Promoting immune escape of tumor cells	[45]
	Tumor cell	Not mentioned	RUBCNL, BECN1, PtdIns3K complexes	Promoting maturation and function of autophagosomes	[46]

GLUT3: Glucose transporter 3; LDH: Lactate dehydrogenase, which is composed of LDHA\LDHB\LDHC; AARS: Aminoacyl-tRNA synthetase; CENPA: Centromere protein A; YY1: YY1 transcription factor; CCND1: Cyclin D1; NRP2: Neuropilin-2; ESM1: Endothelial cell specific molecule 1; GP73: Golgi protein-73; SRSF: Serine/arginine splicing factor 1; GLUT: Facilitative glucose transporter; HK: Hexokinase; NR6A1: Nuclear receptor subfamily 6 group A member 1; OSBP2: Oxysterol binding protein 2; UNC119B: Unc-119 lipid binding chaperone B; WNT: Wingless/integrated; MAPK: Mitogen-activated protein kinase; MTOR: Mammalian target of rapamycin; NOTCH: Notch protein; TME: Tumor microenvironment; SLC: Solute carrier family; NUSAP1:Nucleolar and spindle-associated protein 1; HIF: Hypoxia-inducible factor; TTK: TTK protein kinase; BUB1B: Mitotic checkpoint serine/threonine kinase; SMC4: Structural maintenance of chromosomes 4; PGAM1: Phosphoglycerate mutase 1; GPR37: G protein-coupled receptor 37; CXCL1: Chemokine (C-X-C motif) ligand 1; CXCL5: chemokine (C-X-C motif) ligand 5; LINC00152: Long intergenic non-coding RNA 152; IL-8: Interleukin-8; TNF-α: Tumor necrosis factor-α; RARγ: RAR-related orphan receptor, including ROR-α, -β and -γ; TRAF6: TNF receptor-associated factor 6; IL-6: Interleukin-6; NF-κB: Nuclear factor kappa-light-chain-enhancer of activated B cells; STAT3: Signal transducer and activator of transcription 3; NOP2/NSUN2: NOP2/Sun RNA methyltransferase 2; ENO1: Enolase 1; KAT8: Lysine acetyltransferase 8; eEF1A2: Eukaryotic translation elongation factor 1 Alpha 2; RUBCNL: Rubicon like autophagy enhancer; BECN1: Beclin 1.

统一规范，影响研究结果的可靠性与重复性。GLUT3、LDHA、氨基酸-tRNA合成酶和YAP信号转导通路调节乳酸生成与组蛋白乳酸化，促进胃癌细胞生长、转移，为靶向治疗提供方向。这些乳酸化标志物可评估免疫治疗反应，助力制定个体化治疗策略。但目前组蛋白乳酸化在胃癌中的作用机制尚未明晰，仍需进一步研究。

3.2 在肝癌领域的研究进展

原发性肝癌是全球的第六大常见癌症，也是癌症死亡的第三大主因，其中75%~85%为肝细胞癌（hepatocellular carcinoma，HCC）[15]。Han等[16]研究表明，HCC中组蛋白乳酸化水平显著高于癌旁组织，为探究HCC发展机制提供思路。在蛋白质相互作用调控方面，该研究发现赖氨酸的乳酸化修饰涉及泛素化调控。USP14作为去泛素化酶，能维持蛋白质的稳定性，影响与其他蛋白质的相互作用、翻译后修饰、复合物形成和细胞内定位，促进上皮-间质转化并加速肝癌的进展[17]。在糖酵解代谢调控上，Fan等[18]证实H3K56la通过调节糖酵解代谢及干细胞相关基因的表达，增强肝癌干细胞（liver cancer stem cell，LCSC）的自我更新能力和耐药性。去甲泽拉木醛和蜂王浆酸通过调节糖酵解途径，降低乳酸生成，抑制H3K9、H3K56、H3K14的乳酸化，减少LCSC、肝癌细胞中促肿瘤基因的转录水平，抑制肝癌发生[19-20]。组蛋白乳酸化还会影响特定基因转录活性。Liao等[21]发现组蛋白H3的变体着丝粒蛋白A（centromere protein A，CENPA）在赖氨酸124位点的乳酸化能够促进其与转录因子1（yin-yang 1，YY1）结合形成复合物，增强细胞周期蛋白D1、神经毡蛋白2和YY1的转录活性，推动HCC的增殖。同时，组蛋白乳酸化上调内皮细胞特异性分子1的转录和高尔基体蛋白73的表达，促进肿瘤微环境（tumor microenvironment，TME）中的血管生成，促进HCC的生长和转移[21-23]。此外，组蛋白乳酸化与免疫微环境密切相关。Cai等[24]发现富含丝氨酸/精氨酸的剪接因子（serine/arginine splicing factor 1，SRSF）通过与转录因子MYB的3'-非翻译区结合，促进葡萄糖转运蛋白1、己糖激酶1和LDHA的表达及乳酸水平上升，诱导H3K18la，进而促进M2型巨噬细胞的极化，形成免疫抑制性微环境。Wu等[25]筛选及鉴定出乳酸化特异性基因*NR6A1*、*OSBP2*和*UNC119B*与WNT、MAPK、MTOR和NOTCH信号转导通路密切相关。*NR6A1*激活信号转导通路的下游靶基因；*OSBP2*影响细胞膜脂质的组成，调节信号转导通路活性；*UNC119*调节蛋白质与细胞膜的结合，影响细胞信号转导，这些基因通过影响多条信号转导通路抑制自然杀伤细胞和肿瘤浸润淋巴细胞的浸润，推动HCC的进展。

组蛋白乳酸化在HCC的病理学机制中扮演关键角色，为临床应用提供多种可能性，其通过靶向乳酸化修饰，选择性抑制剂1C8增强PD-1单克隆抗体的疗效[24]。USP14和ABCF1的乳酸化位点可作为潜在的HCC诊断指标[16, 26]，靶向CENPA-YY1-CCND1/NRP2轴及乳酸化特异性基因*NR6A1*、*OSBP2*和*UNC119B*，或成为HCC新的治疗靶点。

3.3 在胰腺癌领域的研究进展

胰腺癌死亡率位居全球前列，胰腺导管腺癌（pancreatic ductal adenocarcinoma，PDAC）早期诊断棘手，生存率极低[27]。研究[28-30]表明，PDAC的进展与糖酵解代谢途径密切相关。在PDAC中，*P53*和*KRAS*基因突变激活Raf/MEK/ERK信号转导通路，增强糖酵解和乳酸产生，LDHA高表达也促使乳酸积累，导致肿瘤组织及TME酸化。溶质运载蛋白16（solute carrier family 16，SLC16）转运乳酸，调节胰腺癌细胞乳酸化，助力肿瘤细胞适应酸性环境、持续增殖，并增强其侵袭转移能力[31]。Chen等[32]发现核仁纺锤体相关蛋白1（nucleolar and spindle associated protein 1，NUSAP1）通过与*c-Myc*基因和缺氧诱导因子-1α结合，形成转录调节复合物，增强LDHA的表达，促进糖酵解和乳酸生成，进而通过Kla稳定NUSAP1，形成NUSAP1-LDHA-糖酵解-乳酸的前馈环，促进肿瘤细胞的增殖和转移。其中缺氧诱导因子-1α在缺氧环境下可促进乳酸化，帮助肿瘤细胞适应高乳酸引起的酸性环境，支持其生长和侵袭[33]。此外，乳酸还可转运至免疫细胞，引起细胞内酸化，抑制其糖酵解功能，致使抗肿瘤能力受损，促进肿瘤细胞的免疫逃逸[29-30]。Wang等[34]证实H4K12la通过调节免疫相关分子连接蛋白2（nectin-2）的表达，增强癌细胞的免疫逃逸能力。不仅如此，乳酸化修饰还可影响相关基因和分子的转录活性。研究[35-36]表明，H3K18la的增加激活PDAC细胞中的特定激酶（TTK、BUB1B），其

通过影响AMPK信号转导通路等调节细胞能量代谢、调控有丝分裂检查点促进细胞增殖，维持染色体稳定性，推动肿瘤进展。Huang等[37]发现乳酸通过促进烟酰胺单核苷酸腺苷转移酶1（nicotinamide nucleotide adenylyltransferase 1，NMNAT1）乳酸化促进核内NAD^+合成，并抑制p38 MAPK-DDIT3信号转导通路，增强肿瘤细胞在葡萄糖缺乏时的存活能力。

基于胰腺癌中组蛋白乳酸化机制研究，临床上开辟了多种新应用途径。糖酵解途径抑制剂显示出显著改善治疗效果的潜力，有望与现有疗法产生协同效应[38]。鉴于LDHA高表达与肿瘤侵袭性、转移性及耐药性相关，检测LDHA水平已用于指导治疗方案调整。同时，靶向乳酸化修饰（如SLC16A1及相关信号转导通路）、调节免疫系统（如Raf/MEK/ERK信号转导通路和nectin-2），为靶向和免疫治疗提供新可能。此外，乳酸化相关的预后标志物（如NMNAT1和H3K18la）为早期诊断和个体化治疗提供了新工具。

3.4 在结直肠癌（colorectal cancer，CRC）领域的研究进展

CRC是全球常见癌症，在癌症相关死亡原因中位居第二[15]。组蛋白乳酸化在CRC发展中发挥着关键作用，而糖酵解代谢途径对其至关重要。Sun等[39]在CRC中发现4号染色体结构维护蛋白（structural maintenance of chromosomes 4，SMC4）下调时，与磷酸甘油酸变位酶1协同，增加糖酵解关键酶（HK2、PFKL、ALDOC等）的表达，通过组蛋白乳酸化增加转运蛋白的表达，促进乳酸生成并形成酸性TME。而Zhou等[40]发现糖酵解增强促进组蛋白乳酸化关键分子G蛋白偶联受体37（G protein-coupled receptor 37，GPR37）表达，其通过激活Hippo信号转导通路，调节LDHA表达及糖酵解，增加H3K18la，促进趋化因子如CXC族趋化因子配体1（CXC chemokine ligand 1，CXCL1）和CXC族趋化因子配体5（CXC chemokine ligand 5，CXCL5）的表达，使CRC肝转移TME中的中性粒细胞募集。组蛋白乳酸化还可调控肿瘤相关基因及分子影响CRC的发展进程。Wang等[41]用肠杆菌脂多糖处理肠癌细胞后发现其在LINC00152的启动子上引入组蛋白乳酸来增加其转录活性并上调其表达水平，进而下调核因子活化B细胞κ轻链增强子（nuclear factor kappa-light-chain-enhancer of activated B cells，NF-κB）信号转导通路炎性细胞因子表达，促进癌细胞迁移和侵袭。Li等[42]发现，H3K18la水平上调可降低维甲酸受体γ（retinoic receptor γ，RARγ）的基因转录活性，进而降低其在巨噬细胞的表达，从而促进IL-6产生，激活STAT3信号转导通路，促进肿瘤生长；此外，其还可激活NOP2/Sun RNA甲基转移酶(NOP2/Sun domain family member 2，NSUN2）的转录，增强5-甲基胞嘧啶修饰，促进α-烯醇化酶表达，支持肿瘤细胞的代谢重编程和适应代谢压力，推动肿瘤细胞的增殖和转移[43]。Xie等[44]发现赖氨酸乙酰转移酶8（lysine acetyltransferase 8，KAT8）催化乳酸基团转移到组蛋白赖氨酸残基上，改变其电荷状态，促进转录因子结合和基因转录，增强肿瘤细胞增殖、转移能力及代谢重编程；此外，KAT8还增强了eEF1A2的活性，促进蛋白质合成，进而增强mRNA翻译促进癌细胞生长。此外，Zhou等[45]研究结果显示，在*KRAS*突变型的CRC患者中肿瘤细胞产生的组蛋白乳酸化激活circATXN7转录使其表达上调，与NF-κB p65亚基结合，抑制其在细胞核转录活性。而NF-κB的抑制影响免疫应答和炎症反应，加剧CRC免疫逃逸。此外，组蛋白乳酸化促进自噬增强子基因*RUBCNL*的转录，介导磷脂酰肌醇-3-激酶复合物的募集和功能，促进自噬体的成熟及肿瘤细胞的适应性生存[46]。

组蛋白乳酸化在CRC中展现出重要的临床应用前景。SMC4、GPR37、NSUN2、KAT8等分子机制揭示其可能成为CRC的新的免疫治疗靶点。肠杆菌脂多糖调节LINC00152的表达促进肿瘤生长给肿瘤治疗提供利用细菌治疗癌症的新思路。此外，有研究[46]发现抑制组蛋白乳酸化可促进自噬或其他途径增强CRC细胞对贝伐珠单抗的敏感性，为治疗开拓新的路径。Huang等[47]研究的乳酸化相关生物标志物模型给临床提供了新的预后预测工具，在个性化治疗和靶向干预方面发挥了重要作用。

4 总结与展望

本文综合探讨组蛋白乳酸化作为新兴研究领域的重要性及其在多种消化系统肿瘤中的研究进展。总体而言，组蛋白乳酸化可调控基因的转录活性并参与调节与肿瘤相关的多条信号转导通

路，如NF-κB、Wnt/β-catenin和磷脂酰肌醇3-激酶（phosphoinositide 3-kinase，PI3K）/蛋白激酶B（protein kinase B，AKT）[41-42]，影响肿瘤细胞的增殖、侵袭和转移。此外，组蛋白乳酸化还对TME产生影响，包括调节免疫细胞的活化状态和肿瘤细胞的行为，导致肿瘤耐药[25]。然而，当前研究仍面临着多重挑战。首先，组蛋白乳酸化的具体调控机制尚不明确，且大多研究集中于单一模型或实验条件，缺乏标准化的检测方法和全面机制的探讨。其次，个体化治疗方面的研究仍较为薄弱，尚未明确如何基于乳酸化特征来制订治疗方案。乳酸化水平及其调控因子在不同个体中的差异可能会影响疗效，因此，未来的研究应重点关注乳酸化的全面调控机制，探索如何根据这些机制确立个体化的治疗策略。同时，由于现有数据主要来自实验室，缺乏临床验证，未来还需着重开发标准化的检测方法，并在临床试验中验证乳酸化在疾病诊断和治疗中的应用。

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曾丹丹：文章结构起草，文章撰写及修改。罗文凤：文献检索与汇总。叶甲舟：资料分析与解释。林燕：文章内容审阅及修改。梁嵘：指导文章选题，文章校对及修订。

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