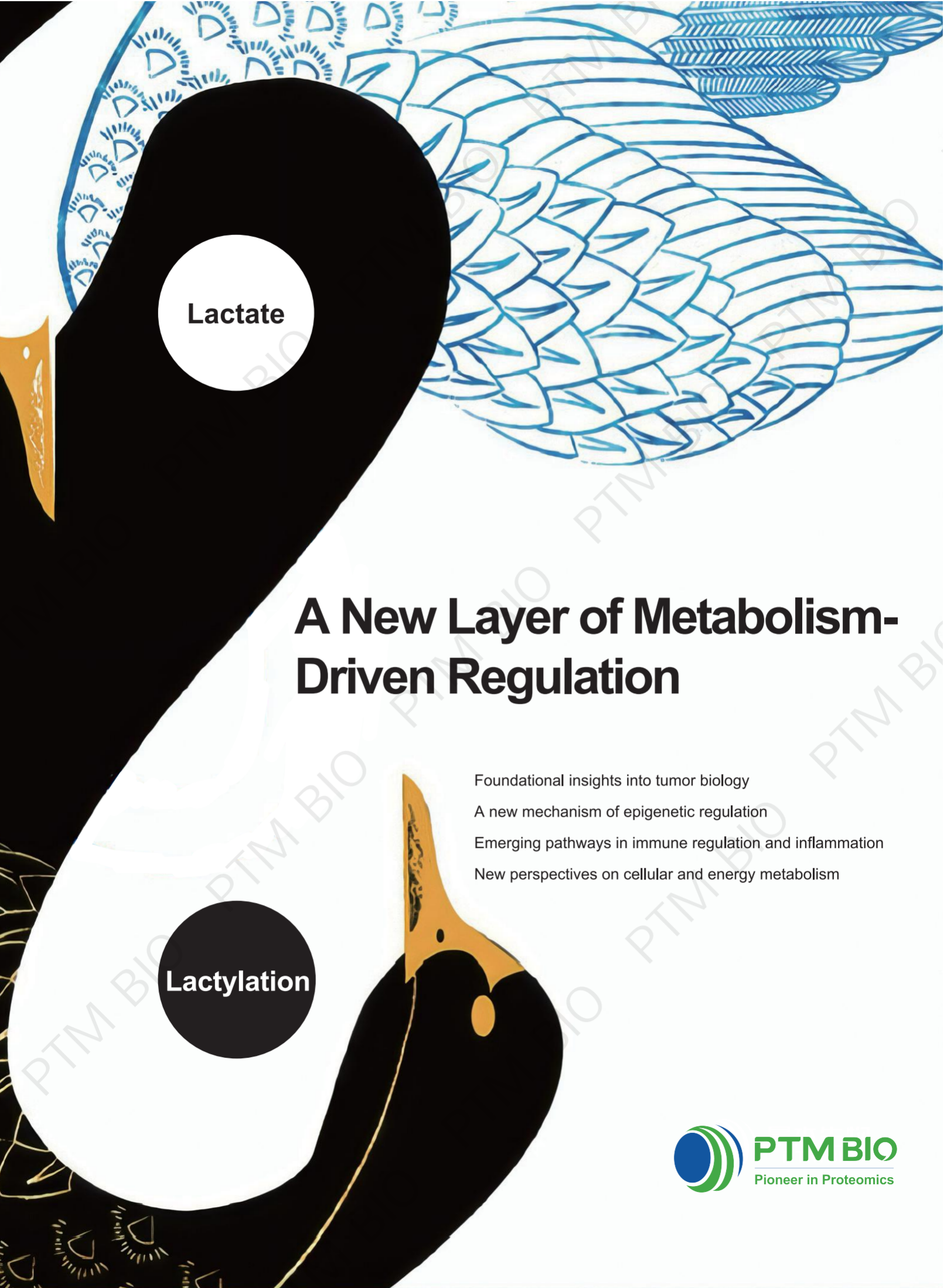




Lactate

A New Layer of Metabolism-Driven Regulation

Lactylation

Foundational insights into tumor biology

A new mechanism of epigenetic regulation

Emerging pathways in immune regulation and inflammation

New perspectives on cellular and energy metabolism



PTM BIO
Pioneer in Proteomics

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Chapter 1 | Discovery of Lactylation

1. First Report of Lactylation ▶▶▶

Lactate is a major carbon-containing metabolite produced during glycolysis. For many years, it was mainly regarded as an energy-related metabolic byproduct, while its regulatory roles in biology were not fully appreciated.

In 2019, Prof. Yingming Zhao's team at the University of Chicago published a landmark study in *Nature* titled "**Metabolic regulation of gene expression by histone lactylation.**" The study revealed that lactate accumulated during metabolism can serve as an endogenous substrate for lysine lactylation on histones.

This discovery uncovered a new layer of metabolism-driven epigenetic regulation, expanded our understanding of metabolic control of gene expression, and sparked growing interest in lactylation research.

nature

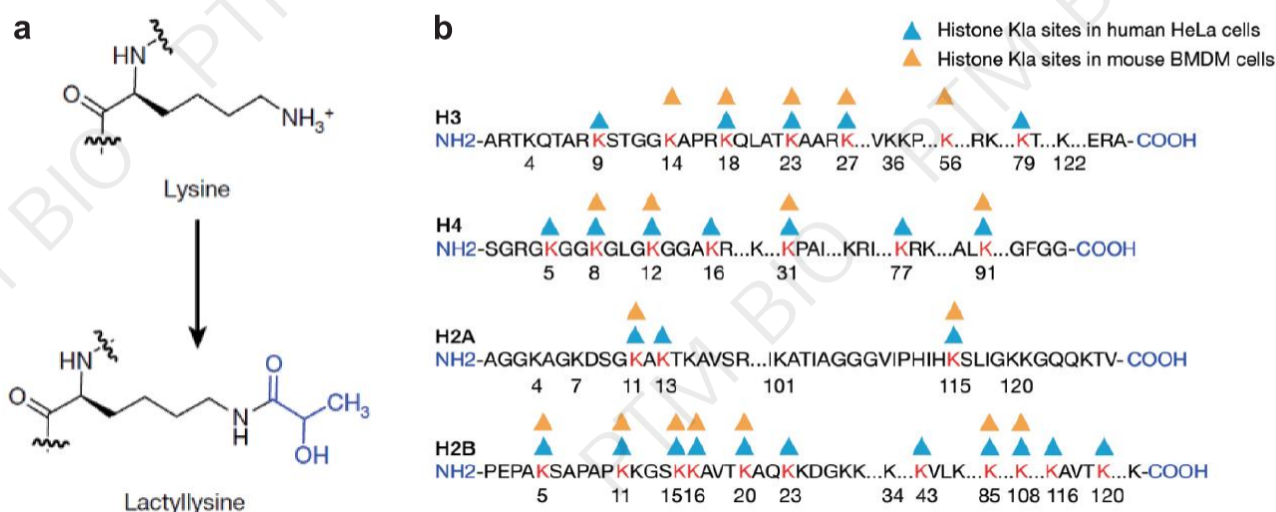
Article | Published: 23 October 2019

Metabolic regulation of gene expression by histone lactylation

2. Key Findings ▶▶▶

① Identification and Validation

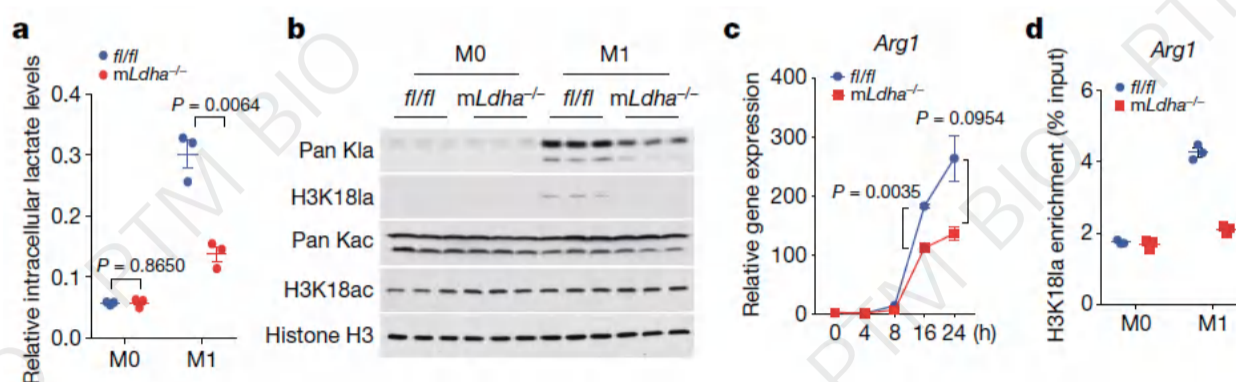
Mass spectrometry identified lactylation on core histone peptides from MCF-7 cells. Using PTM BIO's Pan anti-Kla antibody, Catalog No. **PTM-1401**, the study detected **26 histone lactylation sites in HeLa cells** and **16 sites in BMDMs**, confirming the broad presence of histone lactylation through isotope labeling and multiple validation experiments.



② Histone Lactylation Is Derived from Glycolysis

This study proposed an initial biochemical regulatory model for histone lactylation. The acetyltransferase **p300** catalyzes the transfer of lactyl groups from lactyl-CoA to histones.

Lactate generated through endogenous glycolysis serves as a key metabolic source and regulatory factor for histone lactylation, linking cellular metabolic state directly to chromatin regulation.

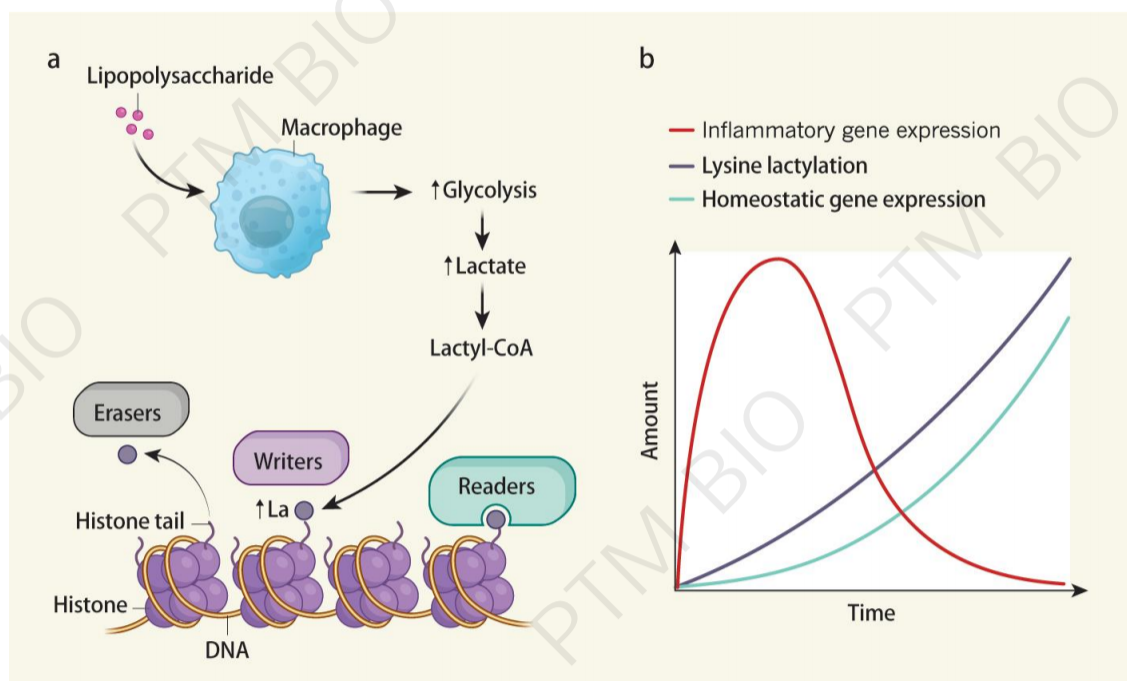


③ Physiological and Pathological Functions of Lactylation

The study also revealed potential physiological and pathological functions of lactylation.

During the late stage of **M1 macrophage polarization**, histone lactylation levels increase and promote the expression of genes involved in tissue repair and wound-healing processes.

Based on these findings, the authors proposed a new working model called the '**lactate timer**', in which histone lactylation dynamically coordinates the expression of inflammatory genes and homeostatic genes over time.



3. Discovery of D-lactylation ▶▶▶

Lactate exists as two optical isomers: **L-lactate** and **D-lactate**. Whether these two lactate isomers give rise to distinct lactylation forms has long remained unclear.

In July 2024, Prof. Yingming Zhao's team reported in *Nature Chemical Biology* the study '**Lysine L-lactylation is the dominant lactylation isomer induced by glycolysis**.' This work identified three isomeric forms of lysine lactylation-related modifications, including **L-lactylation**, **D-lactylation**, and **N-ε-carboxyethylation** (K_{L-la} , K_{D-la} and K_{ce}).

The study revealed that **L-lactylation** and **D-lactylation** are derived from **L-lactate** and **D-lactate**, respectively, and may play distinct roles in cellular metabolism and regulation.

nature chemical biology

Article

<https://doi.org/10.1038/s41589-024-01680-8>

Lysine L-lactylation is the dominant lactylation isomer induced by glycolysis

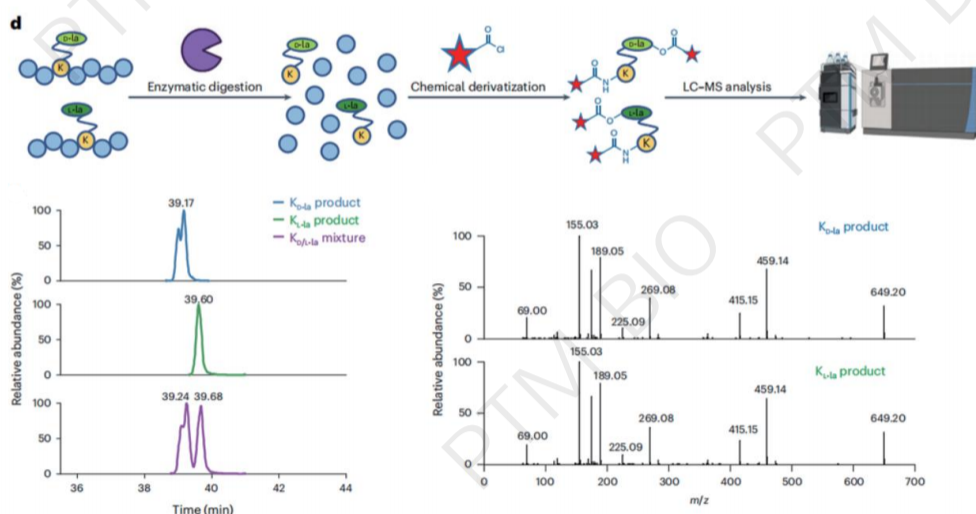
4. Key Findings ▶▶▶

① Identification and Differentiation of K_{L-la} , K_{D-la} and K_{ce}

K_{L-la} , K_{D-la} and K_{ce} have identical molecular weights and highly similar chemical structures, making them difficult to distinguish by conventional mass spectrometry.

To address this challenge, PTM BIO developed highly specific antibodies against K_{L-la} , K_{D-la} and K_{ce} , enabling initial discrimination of these three modifications by immunoblotting.

The study further established a chemical derivatization-assisted PTM analysis strategy, allowing the three isomeric modifications to generate distinguishable derivative products. After antibody-based enrichment and separation, the modified peptides were analyzed by HPLC-MS/MS, enabling accurate identification of K_{L-la} , K_{D-la} and K_{ce} .

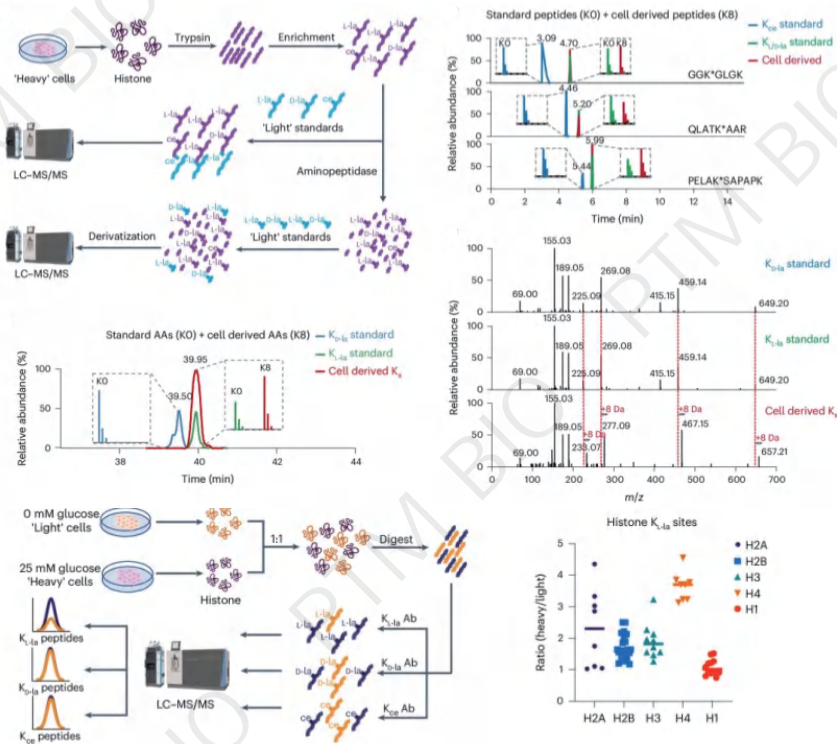


② K_{L-la} is the Dominant Form of Lactylation

Using **SILAC-based quantitative proteomics**, the researchers applied three modification-specific antibodies targeting K_{L-la} , K_{D-la} and K_{ce} (**PTM-1401RM**, **PTM-ZC288**, **PTM-1701RM**).

By introducing a chemical derivatization strategy that expands the chiral recognition window at the peptide level, the study successfully established a workflow to distinguish peptides carrying these three isomeric modifications.

The results showed that, in cells, histone lactylation is predominantly present as K_{L-la} .

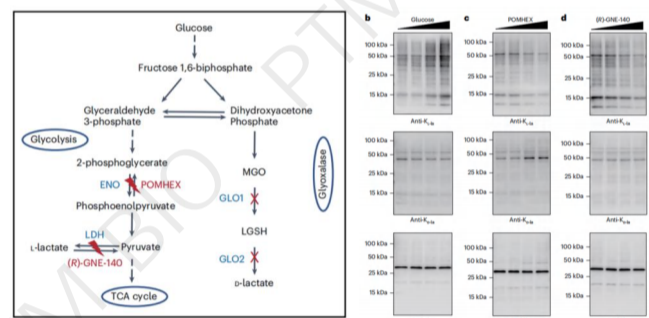


③ K_{L-la} , K_{D-la} and K_{ce} Are Independently Regulated

Using different metabolic inhibitors to perturb glycolysis and related metabolic pathways, the study found that K_{L-la} , K_{D-la} and K_{ce} are regulated differently during glycolytic metabolism and exist as distinct modification types.

Inhibition of the enolase pathway reduced the formation of cellular K_{D-la} and K_{ce} , while having little effect on glycolysis-sensitive K_{L-la} .

These findings suggest that different lactylation-related isomers are controlled by distinct metabolic routes and may have different biological functions.



Chapter 2 | Applications of Lactylation Research

The discovery of lactylation has opened new directions for understanding how the metabolite lactate contributes to cancer biology, immunology, and other disease-related processes.

PTM BIO provides **L-/D-lactylation-specific antibodies** and comprehensive lactylation analysis services to support research in the following areas.

① Regulatory Mechanisms

Key questions in lactylation research include identifying the enzymes responsible for generating lactyl-CoA, defining the site-specific functions of histone lactylation, and uncovering the potential writers, erasers, and readers of lactylation.

② Physiological and Pathological Functions

Many physiological and pathological processes depend heavily on glycolysis and lactate production, including tumor progression, ischemic cardiovascular and cerebrovascular diseases, immune cell activation, and anaerobic exercise metabolism.

Investigating how lactylation participates in these processes provides important insights into disease mechanisms and future translational applications.

Research Focus 1 | Tumor Microenvironment ▶▶

In the tumor microenvironment, lactate generated through glycolysis was once considered merely a metabolic waste product. Recent studies now show that lactate actively contributes to tumor progression.

Key roles of lactate in the tumor microenvironment include:

- Serving as an intracellular fuel substrate under high-lactate conditions
- Promoting tumor invasion and metastasis
- Supporting tumor angiogenesis
- Contributing to immunosuppression

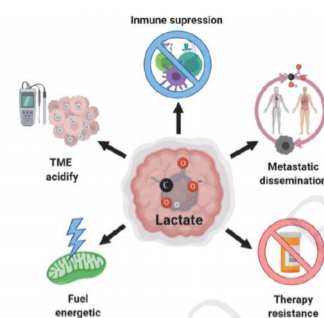


Figure. Multiple Functions of Lactate in the Tumor Microenvironment

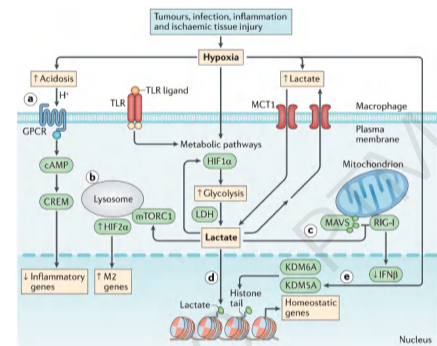
Title	Year	Journal
Alanyl-tRNA synthetase, AARS1, is a lactate sensor and lactyltransferase that lactylates p53 and contributes to tumorigenesis	2024	Cell
Metabolic regulation of homologous recombination repair by MRE11 lactylation	2024	Cell
Functional reprogramming of neutrophils within the brain tumor microenvironment by hypoxia-driven histone lactylation	2025	Cancer Discov
Histone lactylation-driven feedback loop modulates cholesterol-linked immunosuppression in pancreatic cancer	2025	Gut
Lactylome analysis suggests lactylation-dependent mechanisms of metabolic adaptation in hepatocellular carcinoma	2023	Nat Metab
A tumor-derived lactate/ENO1 lactylation feedback loop facilitates osimertinib resistance of lung adenocarcinoma	2026	Drug Resistance Updates
Lactylation of METTL16 promotes cuproptosis via m ⁶ A-modification on FDX1 mRNA in gastric cancers	2023	Nat Commun

Research Focus 2 | Inflammation and Immune Regulation ▶▶

Lactate is not only an important regulator of tumor immunity and antiviral responses, but also a key mediator linking hypoxia, enhanced glycolysis, and immune cell function.

Lactate produced under hypoxic and glycolytic conditions can regulate immune cell activation and cellular homeostasis through multiple mechanisms. The discovery of lactylation further highlights its role in epigenetic regulation of macrophage activation.

Understanding how lactylation coordinates hypoxia-driven signaling with canonical inflammatory pathways is becoming an important direction in inflammation and immune regulation research.



Title	Year	Journal
AARS1 and AARS2 sense lactate to regulate cGAS as global lysine lactyltransferases	2024	Nature
Long-term histone lactylation connects metabolic and epigenetic rewiring in innate immune memory	2025	Cell
Histone lactylation drives CD8+T cell metabolism and function	2024	Nat Immunol
Nonenzymatic lysine D-lactylation induced by glyoxalase II substrate SLG dampens inflammatory immune responses	2025	Cell Res
Global lactylome reveals lactylation-dependent mechanisms underlying TH17 differentiation in experimental autoimmune uveitis	2023	Sci Adv

Research Focus 3 | Cardiovascular Disease ▶▶

Blood lactate is a product of anaerobic metabolism and a marker of insufficient oxidative capacity. Clinical studies have associated elevated lactate with hypertension, suggesting that impaired oxidative metabolism or mitochondrial dysfunction may contribute to disease progression.

Lactate levels are also used clinically for diagnosis and prognosis in acute cardiovascular conditions, including acute coronary syndrome, cardiogenic shock, and cardiac surgery.

Under ischemic conditions caused by vascular obstruction, lactate accumulation may participate in the onset and progression of cardiovascular and cerebrovascular diseases. The molecular mechanisms behind these clinical observations remain to be further explored.

Title	Year	Journal
TRAP1 drives smooth muscle cell senescence and promotes atherosclerosis via HDAC3-primed histone H4 lysine 12 lactylation	2024	Eur Heart J
Gut microbiota-derived butyric acid regulates calcific aortic valve disease pathogenesis by modulating GAPDH lactylation and butyrylation	2025	iMeta
March2 Alleviates Aortic Aneurysm/Dissection by Regulating PKM2 Polymerization	2025	Circ Res
α-myosin heavy chain lactylation maintains sarcomeric structure and function and alleviates the development of heart failure	2023	Circ Res
Lactate promotes endothelial-to-mesenchymal transition via Snail1 lactylation after myocardial infarction	2023	Sci Adv

Research Focus 4 | Neurological Disorders

Lactate levels are closely associated with multiple neurological disorders, including Alzheimer's disease, Parkinson's disease, and stroke. During brain disease progression, energy metabolism is often disrupted, leading to imbalanced lactate production and metabolism, which may affect normal neuronal function.

Lactate has also emerged as a potential biomarker for neurological disease diagnosis and prognosis. For example, in acute stroke, measuring lactate levels in blood or cerebrospinal fluid may help assess disease severity and predict patient recovery.

A deeper understanding of lactylation in neurological disorders may provide new therapeutic opportunities for neuroprotection and neural repair.

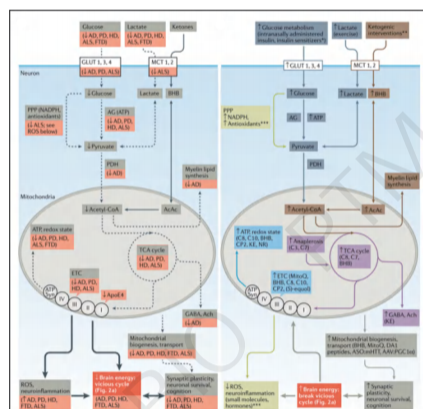


Figure. Multiple Roles of Lactate in Neurological Disorders

Title	Year	Journal
Astrocytic LRP1 enables mitochondria transfer to neurons and mitigates brain ischemic stroke by suppressing ARF1 lactylation	2024	Cell Metab
A positive feedback inhibition of isocitrate dehydrogenase 3β on paired-box gene 6 promotes Alzheimer-like pathology	2024	STTT
Physical exercise mediates cortical synaptic protein lactylation to improve stress resilience	2024	Cell Metab

Research Focus 5 | D-lactylation

As a newly reported modification type, D-lactylation remains a largely unexplored area with substantial research potential. Recent studies suggest that D-lactylation and L-lactylation may differ in their regulatory mechanisms and biological functions. Clinical evidence also indicates that abnormal D-lactate metabolism is closely associated with the development and progression of multiple diseases.

Key Disease-Related Directions: Gastrointestinal Disorders

D-lactate levels are markedly elevated in the urine of patients with short bowel syndrome. Gut microbiota-derived D-lactate can enter the liver through the portal vein, altering the morphology and function of hepatic Kupffer cells and enhancing pathogen capture and clearance;

Neurological Disorders

Accumulation of D-lactate has been associated with acute neurological injury, suggesting a potential role for D-lactate metabolism in brain dysfunction

Tumor Immunity

D-lactate may regulate M2 tumor-associated macrophages and reshape the immunosuppressive tumor microenvironment in hepatocellular carcinoma.

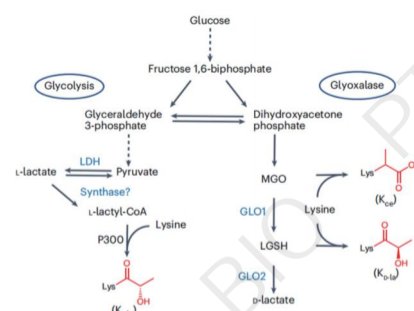


Figure. Diverse D-Lactate-Derived Modifications in Cellular Metabolism

Title	Year	Journal
Lysine L-lactylation is the dominant lactylation isomer induced by glycolysis	2024	Nat Chem Bio
Nonenzymatic lysine D-lactylation induced by glyoxalase II substrate SLG dampens inflammatory immune responses	2025	Cell Res

Milestones in Lactylation Research

2019

First Discovery and Validation of Histone Lactylation

nature

Article | Published: 23 October 2019

Metabolic regulation of gene expression by histone lactylation

Lactylation Links Metabolism to Epigenetic Regulation

nature metabolism

Glis1 facilitates induction of pluripotency via an epigenome-metabolome-epigenome signalling cascade

2020

Lactylation in Tumor Growth

Genome Biology

Histone lactylation drives oncogenesis by facilitating m⁶A reader protein YTHDF2 expression in ocular melanoma

Lactylation in Tissue Repair

TLR signaling adapter BCAP regulates inflammatory to reparatory macrophage transition by promoting histone lactylation

2021

Lactylation Atlas in Rice

AGRICULTURAL FOOD CHEMISTRY

Comprehensive Analysis of Lysine Lactylation in Rice (*Oryza sativa*) Grains

Lactylation in Mitochondrial Dysfunction

Cell

Erythroid mitochondrial retention triggers myeloid-dependent type I interferon in human SLE

2022

Lactylation in Alzheimer's Disease

Cell Metabolism

Positive feedback regulation of microglial glucose metabolism by histone H4 lysine 12 lactylation in Alzheimer's disease

Lactylation-Mediated Liver Cancer Suppression

Pharmacological Research

Demethylzylasteral targets lactate by inhibiting histone lactylation to suppress the tumorigenicity of liver cancer stem cells

Lactylation in Treg-Driven Tumorigenesis

Cell Reports

Tumor metabolite lactate promotes tumorigenesis by modulating MOESIN lactylation and enhancing TGF- β signaling in regulatory T cells

2023

Lactylation Reveals New Mechanisms and Therapeutic Potential in Heart Failure

Cell Research

 α -myosin heavy chain lactylation maintains sarcomeric structure and function and alleviates the development of heart failureLactylation-Mediated m⁶A Regulation in Gastric Cancer Cuproptosis

nature communications

Lactylation of METTL16 promotes cuproptosis via m⁶A-modification on *FDX1* mRNA in gastric cancer

2024

p53 Lactylation Promotes Tumorigenesis

Cell

Alanyl-tRNA synthetase, AARS1, is a lactate sensor and lactyltransferase that lactylates p53 and contributes to tumorigenesis

Lactylation Regulates cGAS-Mediated Innate Immunity

nature

AARS1 and AARS2 sense L-lactate to regulate cGAS as global lysine lactyltransferases

Lactylation Links Cancer Metabolism to DNA Damage Repair

Cell

Metabolic regulation of homologous recombination repair by MRE11 lactylation

2025

Lactylation: Bridging Metabolism and Epigenetics in Innate Immune Memory

Cell

Long-term histone lactylation connects metabolic and epigenetic rewiring in innate immune memory

Excessive Exercise Exacerbates Liver Injury via

Cell Metabolism

Muscle-derived small extracellular vesicles induce liver fibrosis during overtraining

Excessive Exercise Impairs Cognition via Lactylation

Cell Metabolism

Excessive vigorous exercise impairs cognitive function through a muscle-derived mitochondrial pretender

2026

Oral GLP-1 Receptor Agonists: Targeting Lactylation for the Treatment of Alzheimer's Disease

Cell Metabolism

Oral GLP-1 receptor agonist promotes astrocyte-neuron lactate and lipid transfer with neuroprotective effects**Ubiquitination-Lactylation Crosstalk: A Novel Mechanism Driving Hepatocellular Carcinoma Progression and Immune Evasion**

Original research

JOSD1 drives hepatocellular carcinoma malignancy by modulating the ubiquitination-lactylation switch on PGAM1

Mitochondrial lactate venting limits oxidative stress

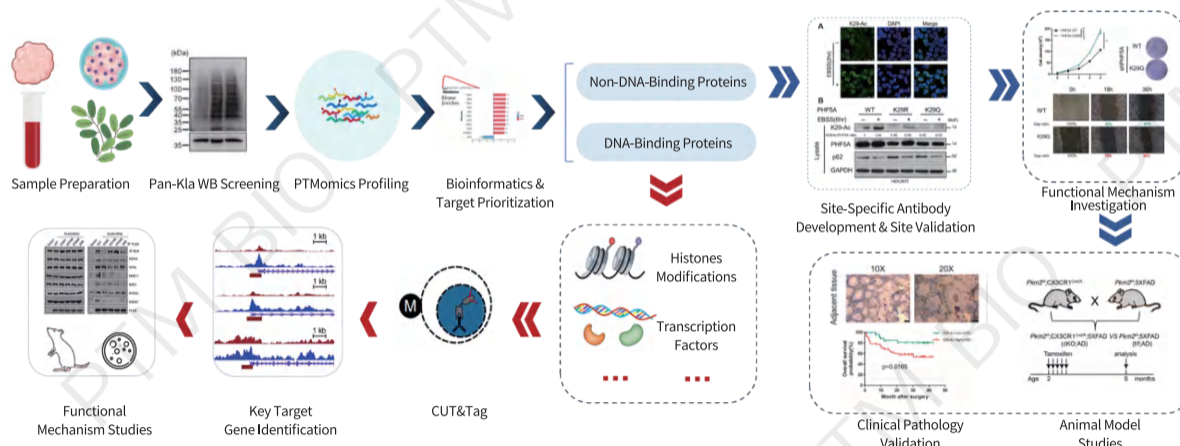
Cell Metabolism

Mitochondrial lactate venting limits oxidative stress

Powering 100+ high-impact lactylation discoveries with advanced PTMomics and antibody technologies.

Chapter 3 | Integrated Tools for Lactylation Research

1. Research Strategy



2. Lactylation Antibodies

PTM BIO provides a comprehensive portfolio of lactylation antibodies, including **pan L-/D-lactylation antibodies**, **L-/D-lactylation site-specific antibodies**, **multi-site histone lactylation antibodies**, and **pan L-/D-lactylation control antibodies**.

These antibody tools support multiple experimental applications, including **WB, IP, IHC, IF, ICC, ChIP, CUT&Tag, and flow cytometry**.

L-lactylation Antibodies

Product Name	Catalog No.	Target	Reactivity	Applications
Anti-L-Lactyl-Histone H2A.Z (Lys11) Rabbit mAb	PTM-1422RM	H2A.ZK11la, Lactylation	H, M, R	WB, IHC-P, ICC/IF, ChIP
Anti-L-Lactyl-Histone H2B (Lys120) Rabbit pAb	PTM-1423	H2BK120la, Lactylation	H, M, R	WB
Anti-L-Lactyl-Histone H2B (Lys15) Rabbit mAb	PTM-1426RM	H2BK15la, Lactylation	H, M	WB, ChIP
Anti-L-Lactyl-Histone H2B (Lys16) Rabbit mAb	PTM-1424RM	H2BK16la, Lactylation	H, M, R	WB
Anti-L-Lactyl-Histone H3 (Lys14) Rabbit mAb	PTM-1414RM	H3K14la, Lactylation	H, M, R	WB, ChIP, ICC/IF
Anti-L-Lactyl-Histone H3 (Lys14) Rabbit pAb	PTM-1414	H3K14la, Lactylation	H, M, R	WB, ChIP
Anti-L-Lactyl-Histone H3 (Lys18) Rabbit mAb	PTM-1406RM	H3K18la, Lactylation	H, M, R	WB, IHC-P, ICC/IF, IP
Anti-L-Lactyl-Histone H3 (Lys18) Rabbit mAb-ChIP Grade	PTM-1427RM	H3K18la	H, M	WB, ChIP, CUT&Tag
Anti-L-Lactyl-Histone H3 (Lys23) Rabbit mAb	PTM-1413RM	H3K23la	H, M, R	WB, IHC-P, ICC/IF, ChIP
Anti-L-Lactyl-Histone H3 (Lys27) Rabbit pAb	PTM-1428	H3K27la	H, M	WB, ChIP
Anti-L-Lactyl-Histone H3 (Lys56) Rabbit mAb	PTM-1421RM	H3K56la, Lactylation	H	WB, FC
Anti-L-Lactyl-Histone H3 (Lys9) Rabbit mAb	PTM-1419RM	H3K9la, Lactylation	H, M, R	WB, IHC-P, ICC/IF, ChIP
Anti-L-Lactyl-Histone H4 (Lys12) Rabbit mAb	PTM-1411RM	H4K12la, Lactylation	H, M, R	WB, IHC-P, IP, ChIP
Anti-L-Lactyl-Histone H4 (Lys16) Rabbit mAb	PTM-1417RM	H4K16la, Lactylation	H, M, R	WB, IHC-P, ICC/IF, ChIP
Anti-L-Lactyl-Histone H4 (Lys5) Mouse mAb	PTM-1409	H4K5la, Lactylation	H, M, R	WB, FC
Anti-L-Lactyl-Histone H4 (Lys5) Rabbit mAb	PTM-1407RM	H4K5la, Lactylation	H, M, R	WB, ICC/IF, FC, IP
Anti-L-Lactyl-Histone H4 (Lys5) Rabbit pAb	PTM-1407	H4K5la, Lactylation	H, M, R	WB
Anti-L-Lactyl-Histone H4 (Lys8) Rabbit mAb	PTM-1415RM	H4K8la, Lactylation	H, M, R	WB, ChIP, CUT&Tag
Anti-L-Lactyl Lysine Rabbit mAb	PTM-1401RM	Kla, Lactylation	H, M, R	WB, IHC-P, IP, ICC/IF, FC, ChIP
Anti-L-Lactyl Lysine Rabbit pAb	PTM-1401	Kla, Lactylation	H, M, R	WB, FC
Anti-L-Lactyl Lysine Rabbit pAb-BSA and Azide free	PTM-1425	Kla, Lactylation	H, R	WB, IHC-P
Anti-L-lactyllysine antibody conjugated agarose beads	PTM-1404	Lactylation	ALL	IAC

*H-Human, M-Mouse, R-Rabbit

D-lactylation Antibodies

Product Name	Catalog No.	Target	Reactivity	Applications
Anti-D-Lactyl Lysine Rabbit pAb(PTM-ZC288)	PTM-1429	Kla, D-Kla, D-lactylation	ALL	WB
Anti-D-Lactyl Lysine Rabbit mAb	PTM-1429RM	Kla, D-Kla, D-lactylation	H	WB
*H-Human				

① PTMab® Custom Antibody Development Advantages

Proprietary Rabbit
Monoclonal Antibody
Platform

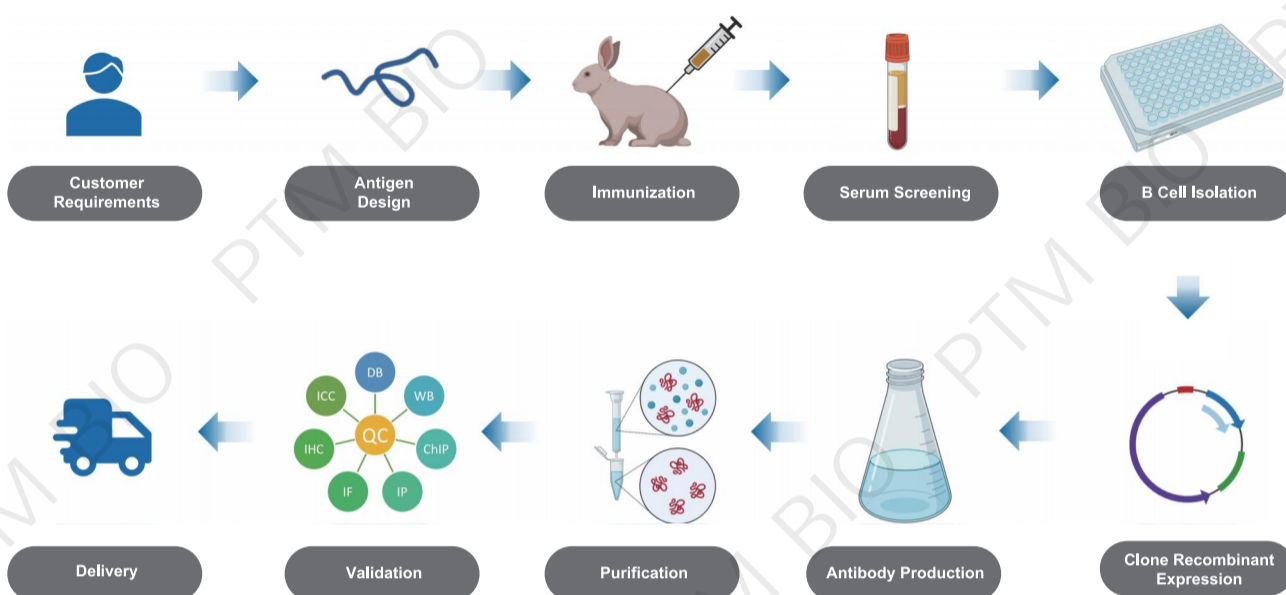
Advanced Antigen
Design

Expertise in
Novel Acylation
Antibodies

Mature Custom
Development
Workflow

Professional
Technical and
Project
Management
Team

② PTMab® Custom Antibody Development Workflow



3.L-/D-lactylation PTMomics Analysis ▶▶▶

Leveraging PTM BIO' s proprietary pan L-/D-lactylation antibodies and advanced mass spectrometry platforms, PTM BIO provides high-quality L-/D-lactylation PTMomics analysis.

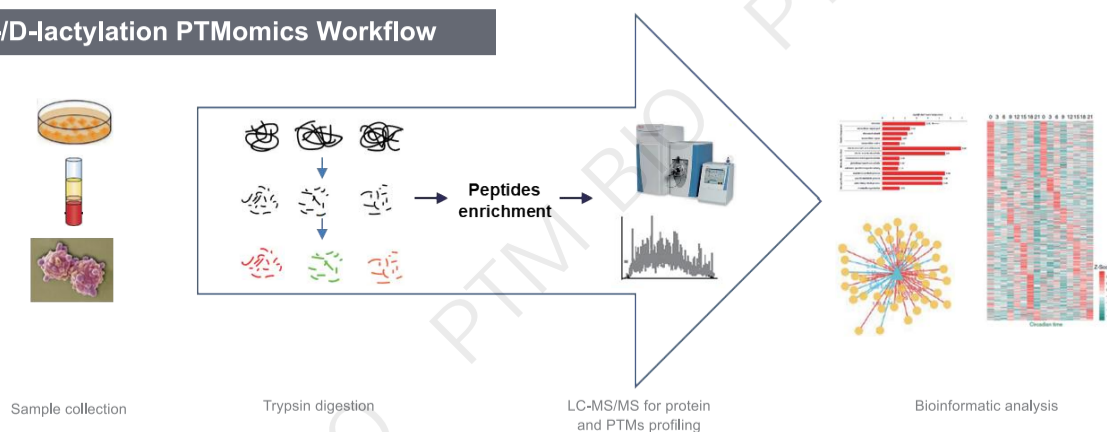
Our platform integrates state-of-the-art MS systems, including Orbitrap Astral, timsTOF HT, timsTOF Pro/Pro2, Orbitrap Exploris 480, Q Exactive HF-X, and Orbitrap Fusion Lumos, together with advanced analytical technologies such as Deep Insight Proteomics and 4D PTMomics.

This integrated workflow enables accurate and comprehensive profiling of L-/D-lactylation, supporting mechanistic studies across cancer biology, immunology, metabolism, neuroscience, and translational research.

① L-/D-lactylation PTMomics Services

- L-/D-lactylation site identification
- Quantitative L-/D-lactylation analysis
- L-/D-lactylome profiling

② L-/D-lactylation PTMomics Workflow

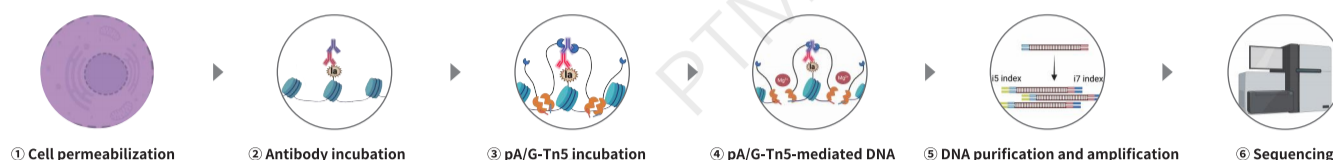


4.CUT&Tag Service ▶▶▶

CUT&Tag — Cleavage Under Targets and Tagmentation — is a highly efficient, high-resolution method for profiling **protein–DNA interactions**.

The technology uses hyperactive **Tn5 transposase** to simultaneously fragment DNA and insert sequencing adapters near antibody-bound target sites. This simplified workflow reduces sample input requirements, shortens turnaround time, and improves experimental efficiency.

CUT&Tag is well suited for studying **histone modifications, transcription factors, chromatin-associated proteins, and epigenetic regulatory mechanisms**.



Chapter 4 | Applications and Case Studies of Lactylation Research

Case Study 1 ▶▶▶

AARS1 and AARS2 Sense L-Lactate to Regulate cGAS as Global Lysine Lactyltransferases



Key Findings

1. L-lactate suppresses cGAS-mediated innate immune responses.
2. AARS1/2 act as lactate sensors and lactyltransferases. They catalyze an ATP-dependent reaction that links lactate to lysine residues on target proteins, leading to substrate-specific lysine lactylation.
3. AARS2 senses the interaction between L-lactate and cGAS. This promotes cGAS lactylation, leading to cGAS inactivation, reduced cGAMP synthesis, and suppression of innate immune signaling.
4. Blocking L-lactate transport restores immune activation. In innate immune cells, AZD-mediated inhibition of monocarboxylate transporter 1 (MCT1) blocks L-lactate transport, reduces cGAS lactylation, and restores immune responses.

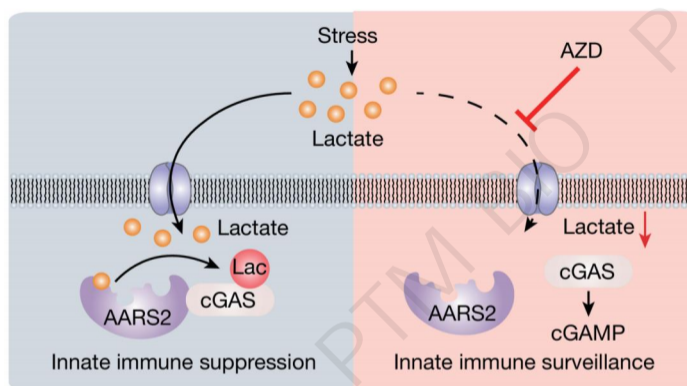
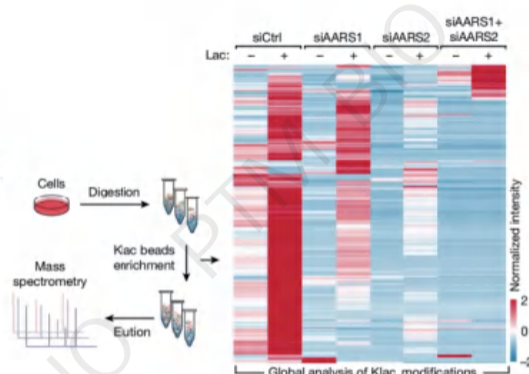
Applied Products:

• Lactylation PTMomics

• PTM Antibodies:

Anti-Pan-Lac PTM-1401

Anti-Pan-Lac PTM-1401RM



Lactylation PTMomics reveals that AARS1/2 regulate global lactylation levels

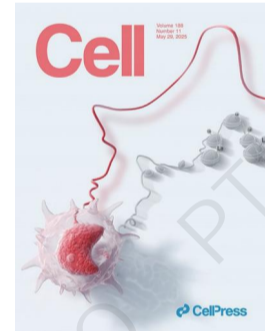
Working Model

Reference ▶▶▶

Li, H., Liu, C., Li, R., *et al.* 2024. AARS1 and AARS2 sense L-lactate to regulate cGAS as global lysine lactyltransferases. *Nature*.

Case Study 2 ►►

Long-term histone lactylation connects metabolic and epigenetic rewiring in innate immune memory



Key Findings

1. Lactate production is linked to trained immunity.

The study revealed a long-term association between lactate generation and trained immune responses, identifying intracellular lactate accumulation as a key metabolic feature of trained immunity.

2. BCG training induces histone H3K18 lactylation.

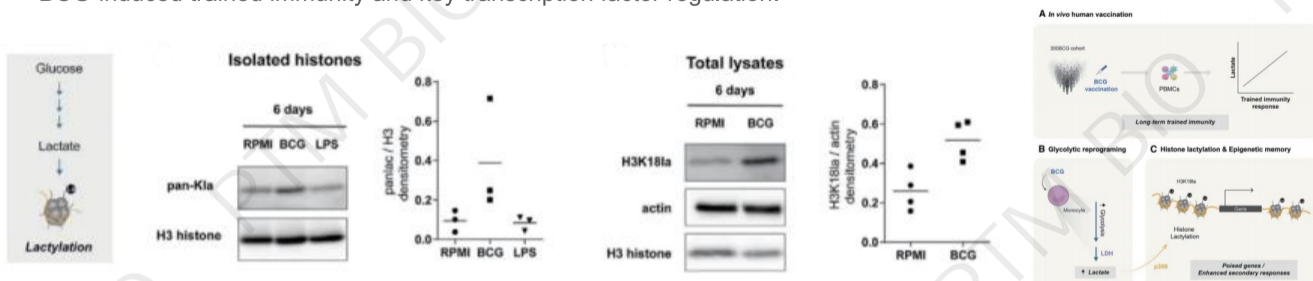
Antibody-based validation showed that BCG-trained macrophages exhibit increased histone H3K18 lactylation, a process regulated by p300/CBP.

3. H3K18la regulates IL1B expression.

Further analysis demonstrated that H3K18la participates in epigenetic regulation of the IL1B gene in BCG-trained cells, contributing to trained immune responses.

4. H3K18la marks trained immunity-associated genomic regions.

The study confirmed that H3K18la acts as a dynamic histone mark associated with genomic regions involved in BCG-induced trained immunity and key transcription factor regulation.



Applied Products:

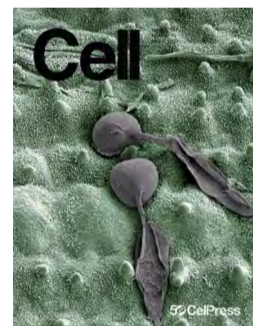
· PTM Antibodies: PTM-1401RM, PTM-1406, PTM-1427RM

Reference ►►

Ziogas A, et al. 2025. Long-term histone lactylation connects metabolic and epigenetic rewiring in innate immune memory. Cell.

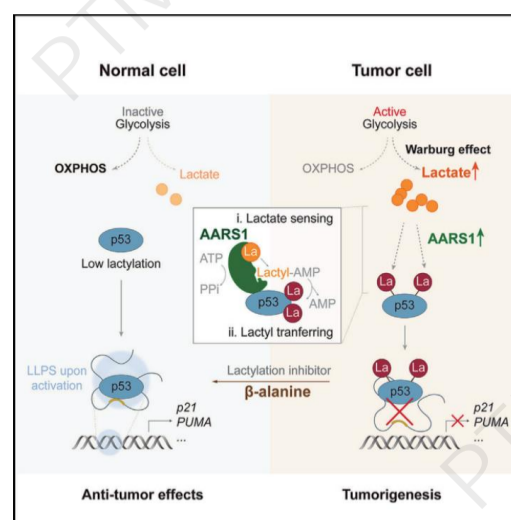
Case Study 3 ▶▶▶

Alanyl-tRNA synthetase, AARS1, is a lactate sensor and lactyltransferase that lactylates p53 and contributes to tumorigenesis



Key Findings

This Cell study identified AARS1 as a lactate sensor and lactyltransferase that catalyzes p53 lactylation. AARS1 directly binds lactate and promotes lactylation of p53 at K120 and K139, leading to reduced DNA binding, impaired transcriptional activation, and weakened tumor-suppressive activity. Inhibition of AARS1-mediated p53 lactylation by β -alanine may help restore p53 function and improve chemotherapy response.



Applied Products:

· PTM Antibodies:

- Anti-L-Lactyl Lysine Rabbit pAb PTM-1401
- Anti-L-Lactyl Lysine Rabbit mAb PTM-1401RM
- Anti-Acetyl-p53 (Lys139) Mouse mAb PTM-185
- Anti-L-lactyllysine antibody conjugated agarose beads PTM-1404

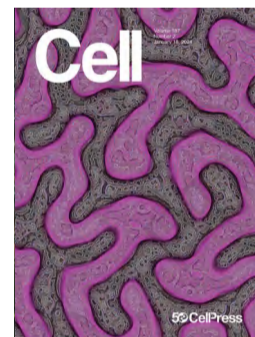
· PTM BIO's lactylation-specific monoclonal antibodies provide **high specificity, strong batch-to-batch consistency, and excellent reproducibility**, helping ensure reliable and high-quality lactylation research data.

Reference ▶▶▶

Zong z, *et al.* 2024. Alanyl-tRNA synthetase, AARS1, is a lactate sensor and lactyltransferase that lactylates p53 and contributes to tumorigenesis. Cell.

Case Study 4 ►►►

Metabolic Regulation of Homologous Recombination Repair by MRE11 Lactylation



Key Findings

This Cell study revealed that cancer cell metabolism can regulate homologous recombination repair through MRE11 lactylation. Lactylation PTMomics identified CBP-mediated MRE11 K673 lactylation, which enhances MRE11 DNA binding, promotes DNA end resection and homologous recombination repair, and contributes to chemotherapy resistance. Targeting MRE11 lactylation may improve tumor sensitivity to DNA-damaging therapies.

Applied Products:

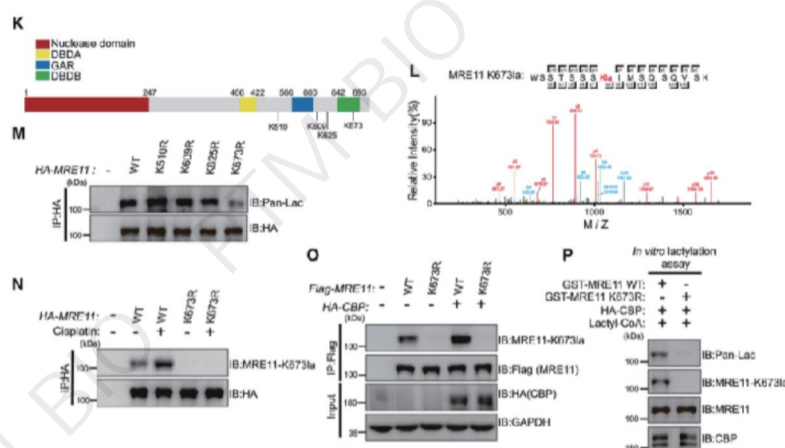
• Lactylation PTMomics

• PTM Antibodies:

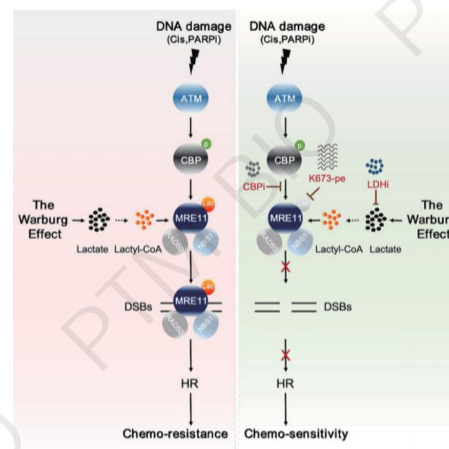
Anti-Pan-Lac PTM-1401RM

Anti-Pan-Ac PTM-101

• Anti-MRE11-K673la Custom Antibody



Lactylation PTMomics identifies CBP-mediated MRE11 K673 lactylation



Working Model

Reference ►►►

Yuping Chen, *et al.* 2024. Metabolic regulation of homologous recombination repair by MRE11 lactylation. *Cell*.

Case Study 5 ▶▶▶

Functional reprogramming of neutrophils within the brain tumor microenvironment by hypoxia-driven histone lactylation



Key Findings

1. Hypoxia drives functional reprogramming of neutrophils in the brain tumor microenvironment.

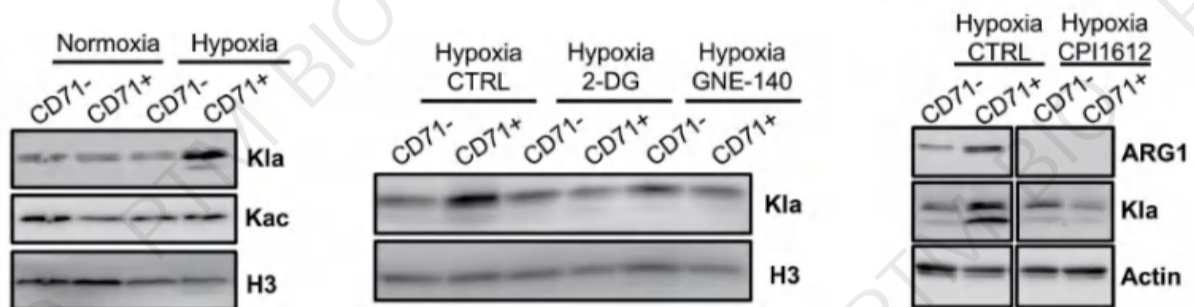
The study found that hypoxic stress promotes tumor growth and resistance to immunotherapy by inducing an immunosuppressive phenotype in CD71+ neutrophils within the brain tumor microenvironment.

2. Lactylation links hypoxia-induced glycolysis to ARG1 expression.

Mechanistic validation using lactylation antibodies showed that hypoxia enhances glycolysis in CD71+ neutrophils, leading to lactate accumulation and increased histone lactylation. This subsequently promotes ARG1 expression, a key factor required for T cell suppression, thereby contributing to tumor progression.

3. Targeting lactate metabolism may reduce neutrophil-mediated immunosuppression.

Further translational exploration showed that inhibiting lactate-related metabolic pathways reduced histone lactylation and ARG1 expression in CD71+ neutrophils, ultimately weakening their immunosuppressive activity.



Histone lactylation regulates ARG1 expression in CD71+ neutrophils

Applied Products

• PTM Antibodies: PTM-1401, PTM-1401RM, PTM-1429, PTM-1701RM, PTM-801, PTM-901, PTM-501.

Reference ▶▶▶

Alessio Ugolini, *et al.* 2025. Functional reprogramming of neutrophils within the brain tumor microenvironment by hypoxia-driven histone lactylation. *Cancer Discov.*

Case Study 6 ▶▶▶

Gut microbiota-derived butyric acid regulates calcific aortic valve disease pathogenesis by modulating GAPDH lactylation and butyrylation



Key Findings

1. Gut microbiota regulates calcific aortic valve disease.

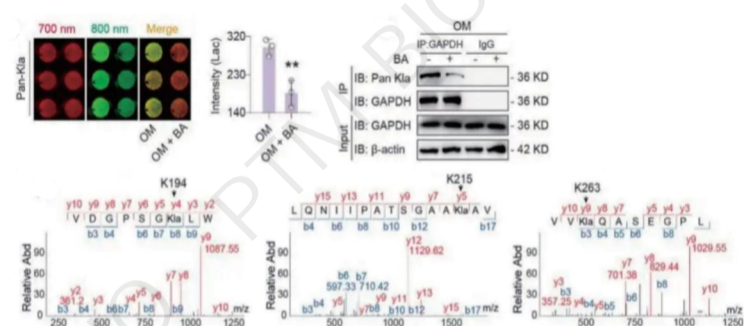
The study found that the gut microbiota contributes to the regulation of **calcific aortic valve disease (CAVD)**, with **Faecalibacterium prausnitzii** identified as a key bacterial species that suppresses valve calcification.

2. Butyrate protects against CAVD through multiple mechanisms.

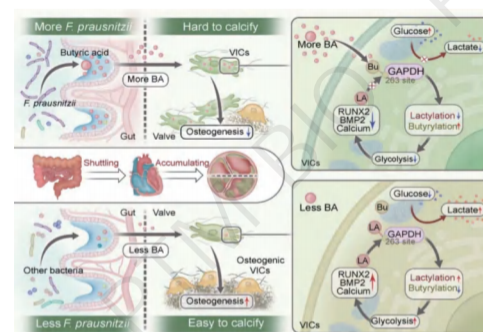
Further analysis showed that butyrate can cross the intestinal barrier and enter circulation, where it protects cardiac tissue by: **downregulating inflammatory signaling molecules such as Runx2 and BMP2, reversing calcification-associated gene expression changes, and restoring glycolytic metabolic balance in human valvular interstitial cells (HVICs).**

3. GAPDH lactylation and butyrylation reveal a new anti-calcification mechanism.

Lactylation PTMomics showed that butyrate exerts an anti-calcification effect by competitively inhibiting **GAPDH K263 lactylation**, thereby suppressing calcium signaling pathway activation.



Multi-omics analysis validates the interplay between GAPDH lactylation and butyrylation



Working Model

Applied Products:

- Lactylation PTMomics
- PTM Antibodies: PTM-1401RM, PTM-301RM
- Anti-GAPDH-K263Bu Custom Antibody, Anti-GAPDH-K263Lac Custom Antibody

Reference ▶▶▶

Wang, Chunli, *et al.* . 2025. Gut Microbiota - Derived Butyric Acid Regulates Calcific Aortic Valve Disease Pathogenesis by Modulating GAPDH Lactylation and Butyrylation. *iMeta*.

►► Collaborative Articles

Title	Journal	Key Words
Metabolic regulation of gene expression by histone lactylation	Nature (IF=48.5)	Discovery of Lactylation, Inflammation and Immunity
AARS1 and AARS2 sense lactate to regulate cGAS as global lysine lactyltransferases	Nature (IF=48.5)	PTM-Regulating Enzymes and Innate Immunity
Long-term histone lactylation connects metabolic and epigenetic rewiring in innate immune memory	Cell (IF=42.5)	Immunity and Epigenetic Regulation
Alanyl-tRNA synthetase, AARS1, is a lactate sensor and lactyltransferase that lactylates p53 and contributes to tumorigenesis	Cell (IF=42.5)	Inflammation and Immunity
Metabolic Regulation of Homologous Recombination Repair by MRE11 Lactylation	Cell (IF=42.5)	Cancer Biology
Erythroid mitochondrial retention triggers myeloid-dependent type I interferon in human SLE	Cell (IF=42.5)	PTM-Regulating Enzymes and Cancer
TRAP1 drives smooth muscle cell senescence and promotes atherosclerosis via HDAC3-primed histone H4 lysine 12 lactylation	European Heart Journal (IF=35.6)	Atherosclerosis
Cyclic immonium ion of lactyllysine reveals widespread lactylation in the human proteome	Nature Methods (IF=20.8)	Method Development
Nonenzymatic lysine D-lactylation induced by glyoxalase II substrate SLG dampens inflammatory immune responses	Cell Research (IF=25.9)	D-lactylation and Inflammatory Immunity
α -myosin heavy chain lactylation maintains sarcomeric structure and function and alleviates the development of heart failure	Cell Research (IF=25.9)	Heart Failure
ACSS2 acts as a lactyl-CoA synthetase and couples KAT2A to function as a lactyltransferase for histone lactylation and tumor immune evasion	Cell Metabolism (IF=30.9)	Lactyltransferases and Tumor Immunity
Nuclear GTPSCS functions as a lactyl-CoA synthetase to promote histone lactylation and gliomagenesis	Cell Metabolism (IF=30.9)	Lactyl-CoA Synthetase and Glioma
Augmentation of scleral glycolysis promotes myopia through histone lactylation	Cell Metabolism (IF=30.9)	Myopic Sclera
Positive feedback regulation of microglial glucose metabolism by histone H4 lysine 12 lactylation in Alzheimer's disease	Cell Metabolism (IF=30.9)	Alzheimer's Disease
Gli1 facilitates induction of pluripotency via an epigenome-metabolome-epigenome signalling cascade	Nature Metabolism (IF=20.8)	Epigenetic Network Regulation
Lactylome analysis suggests lactylation-dependent mechanisms of metabolic adaptation in hepatocellular carcinoma	Nature Metabolism (IF=20.8)	Liver Cancer
Histone Lactylation Boosts Reparative Gene Activation Post Myocardial Infarction	Circulation Research (IF=16.2)	Myocardial Infarction
Lactylation of METTL16 promotes cuproptosis via m ⁶ A-modification on FDX1 mRNA in gastric cancer	Nature Communications (IF=15.7)	
YiaC and CobB regulate lysine lactylation in Escherichia coli	Nature Communications (IF=15.7)	<i>E. Coli</i>
Lysine L-lactylation is the dominant lactylation isomer induced by glycolysis	Nature Chemical Biology (IF=13.7)	D-lactylation
Trash to treasure: lactate and protein lactylation in maize root impacts response to drought	Science China Life Science (IF=9.5)	Plant Drought Stress

Company Introduction

PTM BIO is a leading innovator in proteomics technology development and application in China. Built on the scientific foundation of proteomics and precision medicine, PTM BIO has established an integrated business model covering R&D, production, and scientific services. The company has developed comprehensive technology platforms for proteomics, PTMomics, bioinformatics analysis, PTM-specific antibody development, high-efficiency rabbit monoclonal antibody development, and big-data-driven biological interpretation. PTM BIO is also expanding its capabilities in diagnostic assay development and biomarker discovery platforms.

Platform Highlights

● Comprehensive Coverage

PTM BIO supports 25+ PTM types and provides 400+ PTM-specific antibodies, enabling broad and systematic analysis of protein regulation

● Multi-omics Analysis

Integrated solutions covering proteomics, PTMomics, and multi-omics analysis help researchers connect protein abundance, modification dynamics, and biological mechanisms

● High Sensitivity

Industry-leading high-resolution, high-sensitivity mass spectrometry platforms enable deep and reliable proteomics and PTMomics profiling

● Expert Support

An experienced proteomics research team provides professional project support, from experimental design to after-sales consultation, helping ensure reliable data and meaningful biological insights.

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