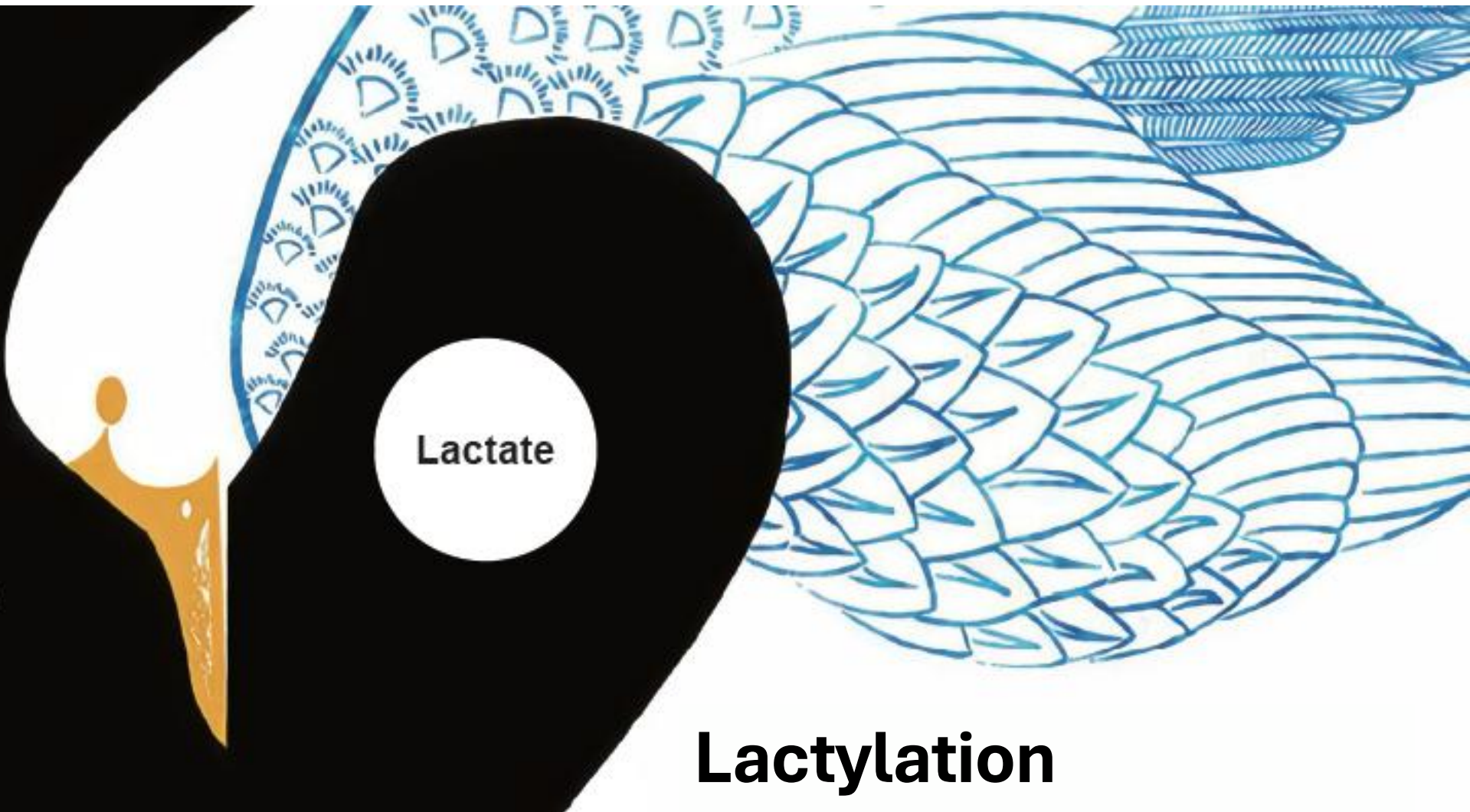


Lactylation

The Epigenetic Impact of Metabolic Reprogramming

Explore its roles in:

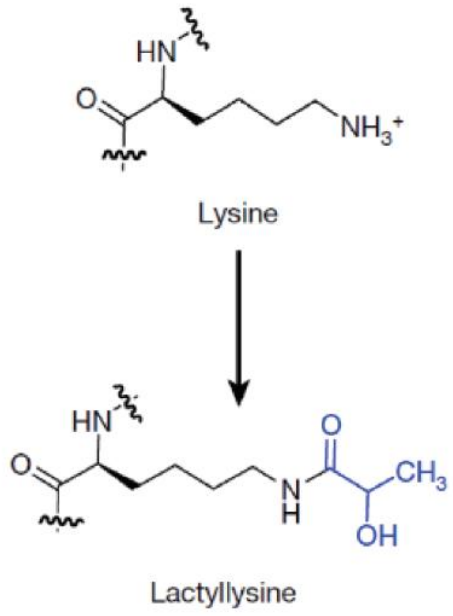
- Tumor Microenvironment
- Inflammation and Immune Regulation
- Cardiovascular Disease
- Neurological Disease

PTM BIO

Pioneer in Proteomics

Lactylation: A Bridge Between Metabolism and Epigenetics

Lactate is a metabolite produced during cellular glycolysis and has long been regarded simply as a cellular energy source or metabolic byproduct. In cancer cells, even under aerobic conditions, energy is preferentially generated through glycolysis, leading to excessive lactate accumulation. This reprogrammed metabolic profile, known as the Warburg effect, was redefined in 2019 by researchers at the University of Chicago in a landmark study published in *Nature*, titled *"Metabolic regulation of gene expression by histone lactylation."* The study revealed that accumulated lactate is not just a waste product, but a critical regulator that serves as a precursor for lysine lactylation (Kla) on histones, fundamentally altering our understanding of metabolism and gene regulation. This groundbreaking discovery expanded the scope of metabolic regulation and ignited widespread interest in lactylation research.



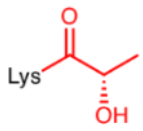
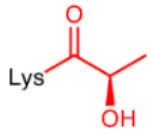
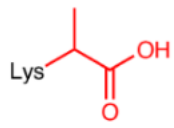
Lysine Lactylation

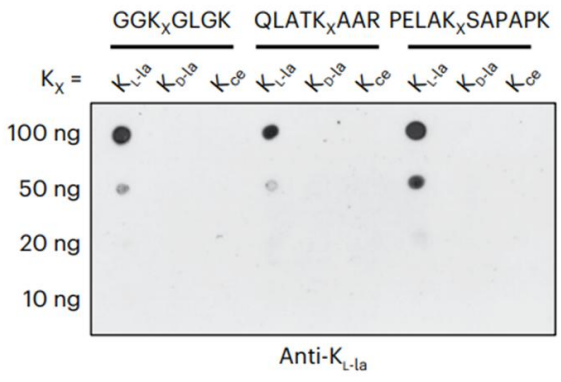
Lactylation involves the covalent addition of a lactyl group derived from Lactyl-CoA to lysine residues on proteins, introducing a novel layer of epigenetic regulation. Initially identified on histone proteins, this modification has since been found on a numerous non-histone proteins. The occurrence and extent of lactylation are tightly linked to both intracellular and extracellular lactate levels, highlighting the direct connection between cellular metabolism and epigenetic regulation.

At the forefront of this field, **PTM BIO** is a pioneer in post-translational modification research and the original supplier of lysine lactylation antibodies that enabled the discovery of lysine L-lactylation ($K_{L\text{-}la}$) in 2019 and D-lactylation ($K_{D\text{-}la}$) in 2024. Despite the identical molecular weight and structural similarity among $K_{L\text{-}la}$, $K_{D\text{-}la}$, and N-ε-carboxyethylation (K_{ce}), PTM BIO successfully developed highly specific monoclonal antibodies for each modification. These antibodies have been rigorously validated through immunoblotting and mass spectrometry. To further empower epigenetics and proteomics research, PTM BIO offers an expansive panel of site-specific histone lactylation antibodies, as well as antibody-conjugated agarose beads for efficient enrichment of lactylated peptides.

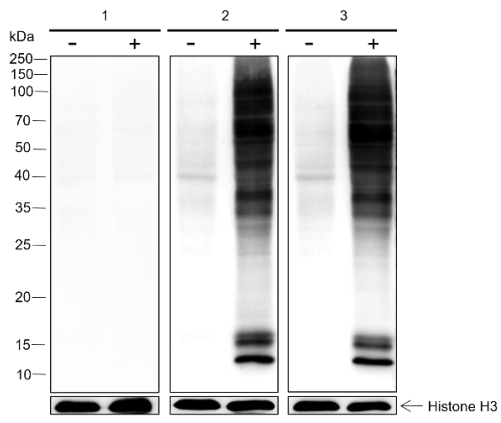
Contents

Isomers of Lysine Lactylation

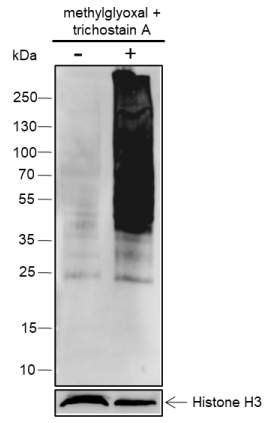
Isomer	L-Lactyllysine ($K_{L\text{-}la}$)	D-Lactyllysine ($K_{D\text{-}la}$)	N-ε-Carboxyethyl-lysine (K_{ce})
Chemical Structure			
Precursor	L-lactate, primary product of glycolysis	D-lactate from glyoxalase (GLO) pathway	Methylglyoxal (MGO), metabolites of glycolysis
Abundance	Dominant isomer	Less abundant	Less abundant
Enzymatic Involvement	Enzymatic Writers: p300/CBP, GCN5, HBO1, MOF, TIP60, AARS1/2; Erasers: HDAC1-3, SIRT2/3	Non-enzymatic between proteins and *S*-D-lactoylglutathione (LGSH)	Non-enzymatic
Potential Roles	Gene regulation (oncogene activation/suppressor silencing), metabolic pathway modulation, immune suppression, drug resistance, implicated in various cancers	Mitochondrial dysfunction and oxidative stress	May have distinct biological functions
Pan-PTM Antibody	Anti-L-Lactyllysine Rabbit mAb (Cat #PTM-1401RM)	Anti-D-Lactyllysine Rabbit mAb (Cat #PTM-1429RM)	Anti-Carboxyethyllysine Rabbit mAb (Cat #PTM-1701RM)
Antibody for PTM Peptides Enrichment	Anti-L-Lactyllysine Antibody Conjugated Agarose Beads (Cat # PTM-1404)	Anti-D-Lactyllysine Antibody Conjugated Agarose Beads (Cat # PTM-1434)	



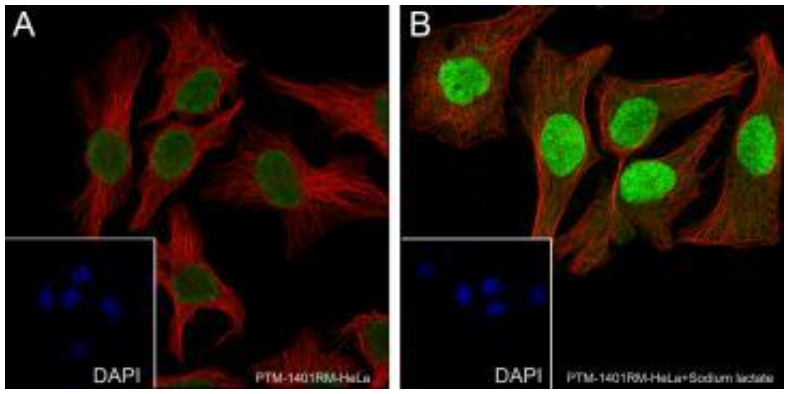
Dot blot analysis demonstrating the specificity of L-Lactyllysine Rabbit mAb (Cat # PTM-1401RM) for $K_{L\text{-}la}$ modified synthetic histone peptides over peptides modified with $K_{D\text{-}la}$ and K_{ce}.



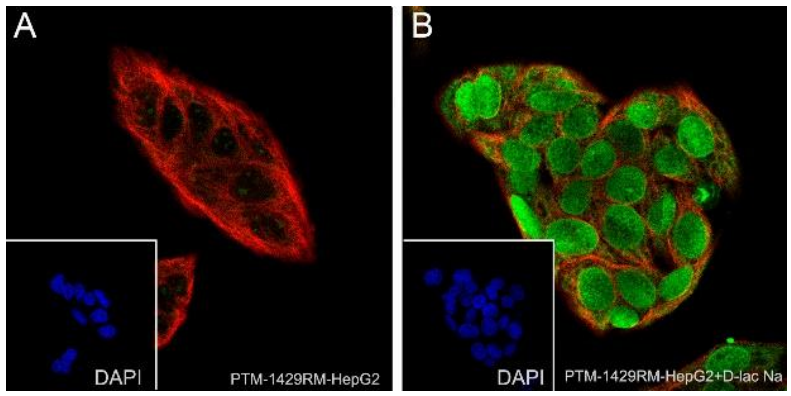
Western blot analysis of extracts from HepG2 cells untreated or treated with 100 mM sodium D-lactate for 18 hrs using D-Lactyllysine Rabit mAb (Cat # PTM-1429RM) pre-adsorbed with 1) 3 µM D-lactylated peptides, 2)unmodified peptides, or 3) no peptide blocking.



Western blot analysis of extracts from HepG2 cells untreated or treated with methylglyoxal (2 mM, 24 hrs) followed by trichostatin A (1 µm, 5 hrs) using Carboxyethyllysine Rabit mAb (Cat # PTM-1701RM)



ICC/IF analysis of HeLa cells, untreated or treated with 100 mM sodium L-lactate for 24 hrs, labeled with L-Lactyllysine Rabit mAb (Cat # PTM-1401RM). Nuclear DNA was stained with DAPI (blue), tubulin with a red fluorescent marker, and L-lactyllysine signals were detected in green.



ICC/IF analysis of HeLa cells, untreated or treated with 100 mM sodium D-lactate for 18 hrs, labeled with D-Lactyllysine Rabit mAb (Cat # PTM-1429RM). Nuclear DNA was stained with DAPI (blue), tubulin with a red fluorescent marker, and D-lactyllysine signals were detected in green.

Expanding the Horizons of Lactylation Research

The discovery of lactylation has opened new avenues for exploring the role of the metabolic byproduct lactate in areas such as cancer and immunology. PTM BIO's products and services can enable your research in the following areas:

- **Mechanistic Studies**

Investigate the enzymes responsible for generating the intermediate metabolite lactyl-CoA;
Elucidate the site-specific functions of histone lactylation;
Identify the "writers," "erasers," and "readers" of histone lactylation.

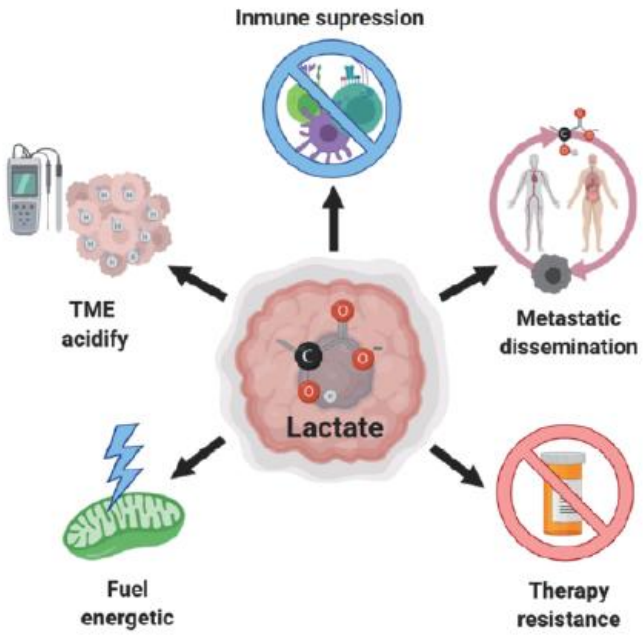
- **Physiological and Pathological Functions**

Many physiological and pathological processes rely heavily on glycolysis and produce high levels of lactate—for example, tumorigenesis and cancer progression, ischemic cardiovascular and cerebrovascular diseases, immune cell activation, and anaerobic metabolism during intense exercise. Understanding the functional roles and regulatory mechanisms of lactate modifications in these contexts is critical for advancing our knowledge of disease pathogenesis and future clinical applications.

Hot Topic 1: Tumor Microenvironment

Lactylation significantly influences the tumor microenvironment (TME) and the immune responses within it. It modulates the polarization, recruitment, and function of various immune cells, including macrophages and T cells, which infiltrate the tumor. Lactylation can promote and immunosuppressive TME by inhibiting the activity of anti-tumor immune cells and fostering the development of pro-tumorigenic immune populations, thus facilitating immune evasion by cancer cells.

Research has elucidated the specific roles of lactylation in a diverse range of cancer types. This highlights the critical need for robust tools to study this modification and to explore its therapeutic potential.



Title	Year	Journal
Targeting lactylation reinforces NK cell cytotoxicity within the tumor microenvironment	2025	Nature Immunology
Alanyl-tRNA synthetase, AARS1, is a lactate sensor and lactyltransferase that lactylates p53 and contributes to tumorigenesis	2024	Cell
NBS1 lactylation is required for efficient DNA repair and chemotherapy resistance	2024	Nature
Metabolic regulation of homologous recombination repair by MRE11 lactylation	2023	Cell
Lactylome analysis suggests lactylation-dependent mechanisms of metabolic adaptation in hepatocellular carcinoma	2023	Nature Metabolism
Lactylation of METTL16 promotes cuproptosis via m^6A-modification on FDX1 mRNA in gastric cancer	2023	Nat Commun
Lactylation-driven METTL3-mediated RNA m^6A modification promotes immunosuppression of tumor-infiltrating myeloid cells	2022	Mol Cell

Hot Topic 2: Inflammation and Immune Regulation

Lactate serves as a key regulator of tumor immunity, antiviral responses, and overall immune homeostasis. Under conditions of hypoxia or enhanced glycolysis, lactate accumulation suppresses inflammatory macrophage activation through multiple mechanisms, thereby maintaining cellular homeostasis. The discovery of protein lactylation reveals that lactate modulates immune responses not only through metabolic signaling but also via epigenetic regulation.

Future research will aim to elucidate how hypoxia-induced signaling integrates with canonical inflammatory pathways, advancing our understanding of the metabolic-epigenetic regulation of immunity and its potential as a therapeutic target in inflammatory diseases.

Title	Year	Journal
Histone lactylation promotes rheumatoid arthritis progression by increasing NFATc2 expression and the production of anti-lactylated histone autoantibodies	2025	Nat Commun
Long-term histone lactylation connects metabolic and epigenetic rewiring in innate immune memory	2025	Cell
AARS1 and AARS2 sense lactate to regulate cGAS as global lysine lactyltransferases	2024	Nature
Histone Lactylation Drives CD8+T Cell Metabolism and Function	2024	Nature Immunology
Hepatocyte HSPA12A inhibits macrophage chemotaxis and activation to attenuate liver ischemia/reperfusion injury via suppressing glycolysis-mediated HMGB1 lactylation and secretion of hepatocytes	2023	Theranostics
Lactate promotes macrophage HMGB1 lactylation, acetylation, and exosomal release in polymicrobial sepsis	2022	Cell Death Differ
Erythroid mitochondrial retention triggers myeloid-dependent type I interferon in human SLE	2021	Cell

Hot Topic 3: Cardiovascular Disease

Lactate in the blood is a product of anaerobic respiration and a marker of insufficient oxidative capacity. Clinical studies have shown that lactate levels are associated with hypertension, and that impaired oxidative capacity or mitochondrial dysfunction may contribute to its development. At the same time, lactate levels can serve as diagnostic and prognostic indicators in acute cardiac conditions, such as acute coronary syndrome, cardiogenic shock, and cardiac surgery. However, whether lactate accumulation contributes to the onset of ischemic heart and brain diseases, and the specific mechanisms involved, remain to be further investigated.

Title	Year	Journal
S100a9 lactylation triggers neutrophil trafficking and cardiac inflammation in myocardial ischemia/reperfusion injury	2025	J Clin Invest
TRAP1 drives smooth muscle cell senescence and promotes atherosclerosis via HDAC3-primed histone H4 lysine 12 lactylation	2024	Eur Heart J
α-myosin heavy chain lactylation maintains sarcomeric structure and function and alleviates the development of heart failure	2023	Cell Research
Lactate promotes endothelial-to-mesenchymal transition via Snail1 lactylation after myocardial infarction	2023	Sci Adv
Histone Lactylation Boosts Reparative Gene Activation Post-Myocardial Infarction	2023	Circ Res
Plasma lactate and incident hypertension in the atherosclerosis risk in communities study	2023	Am J Hypertens

Hot Topic 4: Neurological Disease

Lactate levels are closely associated with a variety of neurological disorders, including Alzheimer's disease, Parkinson's disease, and stroke. When the brain is affected by disease, energy metabolism is often disrupted, and imbalances in lactate production and utilization may impair normal neuronal function. At the same time, lactate levels have emerged as a potential biomarker for the diagnosis and prognosis of neurological conditions. For example, measuring lactate in blood or cerebrospinal fluid during an acute stroke can help clinicians assess disease severity and predict patient recovery. A deeper understanding of the role of lactylation in neurological diseases could provide new therapeutic targets for neuroprotection and repair.

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
Positive feedback regulation of microglial glucosemetabolism by histone H4 lysine 12 lactylation inAlzheimer's disease	2022	Cell Metab

Hot Topic 5: D-Lactylation

As a newly reported type of modification, D-lactylation has vast potential for further exploration. Clinical research has found that abnormal D-lactate metabolism is closely associated with the onset and progression of various diseases:

- **Intestinal diseases:** Patients with short bowel syndrome show significantly elevated levels of D-lactate in their urine (*New England Journal of Medicine*, 1979; 301(5):249–252); D-lactate derived from the gut microbiota can enter the liver via the portal vein, altering the morphology and size of Kupffer cells, enhancing their ability to capture and kill pathogens (*Cell Host & Microbe*, 2020; 28(5):660–668.e4).
- **Neurological diseases**: Accumulation of D-lactate can cause acute neuronal injury (*The Lancet*, 2001; 358(9295):1814).
- **Tumor immunity**: D-lactate regulates M2 tumor-associated macrophages and reshapes the immunosuppressive tumor microenvironment in hepatocellular carcinoma (*Science Advances*, 2023; 9(29):eadg2697).

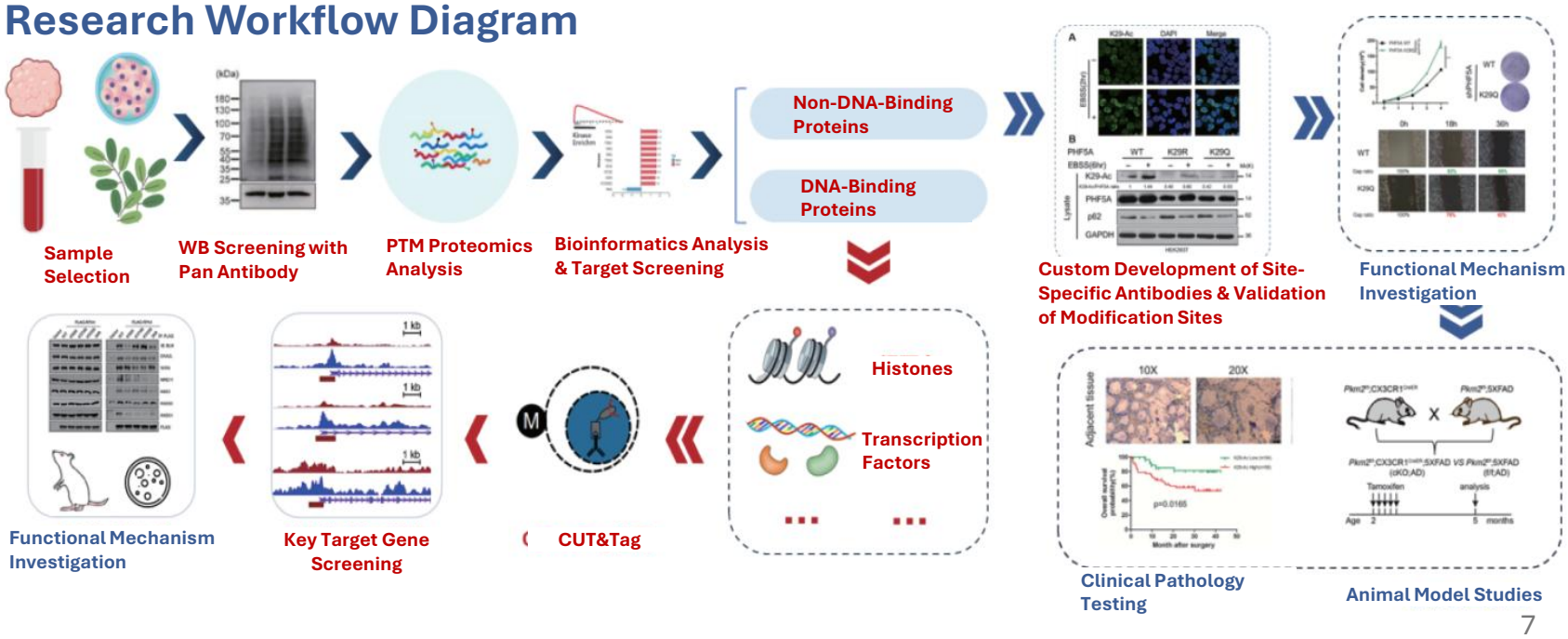
These findings suggest that D-lactylation may play a significant role in intestinal diseases, neurological disorders, and cancers. In addition, whether D-lactylation and L-lactylation crosstalk during the progression of these diseases remains to be further investigated.

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	2024	Cell Res

PTM BIO: Your Partner in Lactylation Research

PTM BIO offers a comprehensive suite of high-quality antibodies and cutting-edge proteomics services designed to empower your research into the role of lactylation in cancer. As the original supplier of lysine lactylation antibodies, we provide reliable and validated tools to help you unlock the secrets of this crucial post-translational modification.

Research Workflow Diagram



Upstream: Preliminary screening using pan anti-lactylation antibodies by Western blot (WB), followed by WB-based screening of histone lactylation sites to validate modification patterns.
Midstream: Proteomics analysis of lactylation modifications and CUT&Tag services to identify key research targets and specific modification sites.
Downstream: Custom development of target-/site-specific lactylation antibodies to support subsequent mechanistic studies.

PTM BIO Lactylation Antibody Portfolio

Pan-Lactyllysine Antibodies: Developed for the global detection of lactylated proteins, these antibodies recognize proteins bearing L- or D-lactylated lysine residues, regardless of the surrounding amino acid sequence. They are rigorously validated for a variety of applications, including WB, immunohistochemistry (IHC-P), immunocytochemistry/immunofluorescence (ICC/IF), flow cytometry (FC), immunoprecipitation (IP), and chromatin immunoprecipitation (ChIP), and are predicted to react across all species.

Antibody Name	Cat #	Target	Reactivity	Applications	Citations
Anti-L-Lactyllysine Rabbit mAb	PTM-1401RM	$K_{L\text{-}la}$	All	WB, IHC-P, ICC/IF, FC, IP, ChIP	209
Anti-D-Lactyllysine Rabbit mAb	PTM-1429RM	$K_{D\text{-}la}$	H	WB, ICC/IF, IP	4

Site-Specific Lactyl-Histone Antibodies: Targeting specific lysine residues on histones to understand epigenetic regulation.

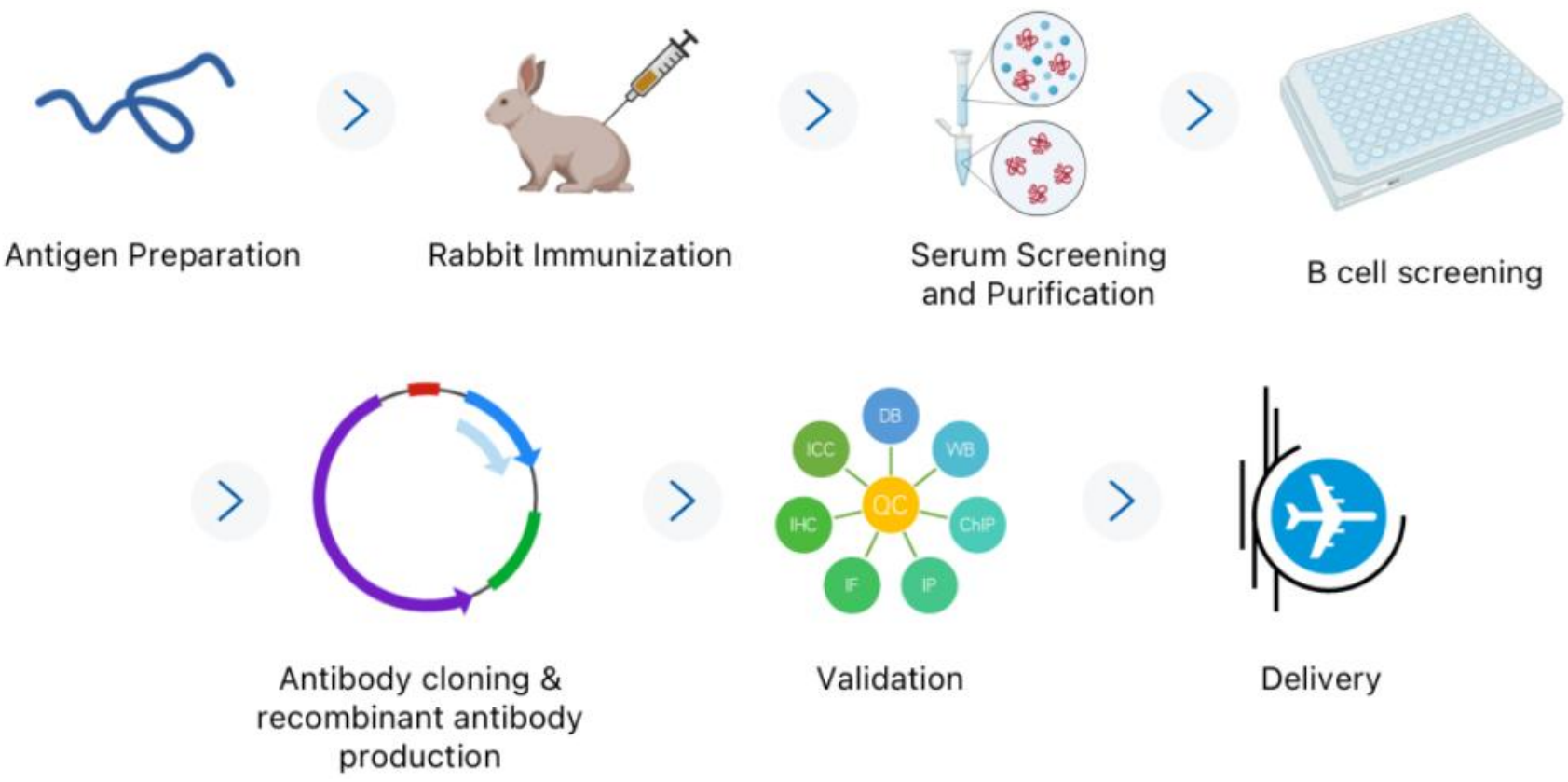
Antibody Name	Cat #	Reactivity	Applications	Citations
L-Lactyl-Histone H2A.Z (Lys11) Rabbit mAb	PTM-1422RM	H, M, R	WB, IHC-P, ICC/IF, ChIP	3
L-Lactyl-Histone H2B (Lys15) Rabbit mAb	PTM-1426RM	H, M,	WB, ChIP	1
L-Lactyl-Histone H2B (Lys16) Rabbit mAb	PTM-1424RM	H, M, R	WB	6
L-Lactyl-Histone H2B (Lys120) Rabbit pAb	PTM-1423	H, M, R	WB	1
L-Lactyl-Histone H3 (Lys9) Rabbit mAb	PTM-1419RM	H, M, R	WB, IHC-P, ChIP	55
L-Lactyl-Histone H3 (Lys14) Rabbit mAb	PTM-1414RM	H, M, R	WB, ICC/IF, ChIP	33
L-Lactyl-Histone H3 (Lys18) Rabbit mAb	PTM-1406RM	H, M, R	WB, IHC-P, ICC/IF, IP	103
L-Lactyl-Histone H3 (Lys18) Rabbit mAb (ChIP Grade)	PTM-1427RM	H, M	WB, ChIP, CUT&Tag	61
L-Lactyl-Histone H3 (Lys23) Rabbit mAb	PTM-1413RM	H, M, R	WB, IHC-P, ChIP	12
L-Lactyl-Histone H3 (Lys27) Rabbit mAb	PTM-1428	H, M	WB, ChIP	8
L-Lactyl-Histone H3 (Lys56) Rabbit mAb	PTM-1421RM	H	WB, FC	11
L-Lactyl-Histone H4 (Lys5) Mouse mAb	PTM-1409	H, M, R	WB, FC	8
L-Lactyl-Histone H4 (Lys5) Rabbit mAb	PTM-1407RM	H, M, R	WB, ICC/IF, FC, IP, CUT&Tag	29
L-Lactyl-Histone H4 (Lys8) Rabbit mAb	PTM-1415RM	H, M, R	WB, ChIP, CUT&Tag	28
L-Lactyl-Histone H4 (Lys12) Rabbit mAb	PTM-1411RM	H, M, R	WB, IHC-P, IP, ChIP	47
L-Lactyl-Histone H4 (Lys16) Rabbit mAb	PTM-1417RM	H, M, R	WB, IHC-P, ICC/IF, ChIP	18

Antibody Conjugated Agarose Beads: Designed for PTM peptide immunoaffinity enrichment prior to LC-MS/MS, these beads feature a mixture of highly specific immobilized antibodies. The dynamic range and recognition capability of the antibody conjugated agarose beads are optimized for selective peptide capture.

Antibody Name	Cat #	Target	Reactivity	Applications	Citations
Anti-L-Lactyllysine Antibody Conjugated Agarose Beads	PTM-1404	$K_{L\text{-}la}$	All	IAP	52
Anti-D-Lactyllysine Antibody Conjugated Agarose Beads	PTM-1434	$K_{D\text{-}la}$	All	IAP	0

PTMab® Custom Antibody Services

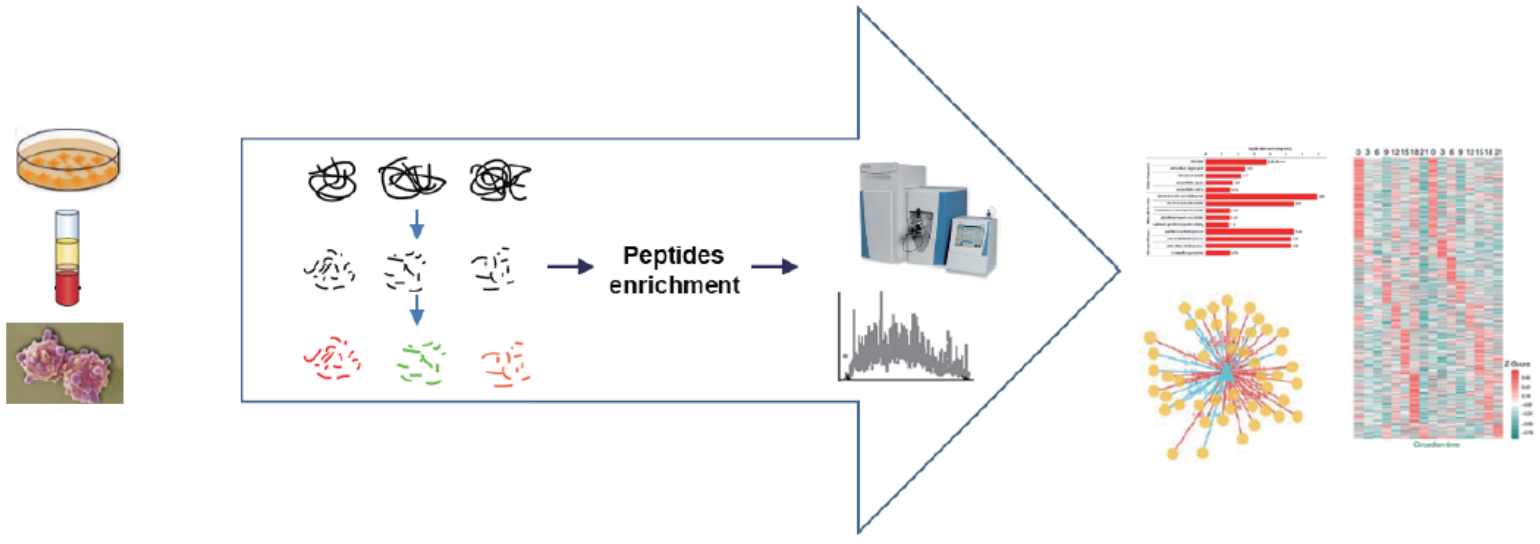
- Proprietary Rabbit mAb development platform with full validation across key applications
- Unique antigen design software ensuring exceptional antibody development success rates
- Custom development of antibodies targeting novel acylation modifications of 25+ PTM types
- Established development workflow & flexible service options to meet diverse customer needs
- Professional technical & project management teams ensuring smooth and efficient project completion



L-/D-Lactylation Proteomics Services

Relying on the exclusive L-/D-Lactylation pan-antibodies developed by PTM BIO, combined with industry-leading mass spectrometry clusters (Orbitrap Astral, timsTOF HT, timsTOF Pro/Pro2, Exploris 480, Q Exactive HF-X, Orbitrap Fusion Lumos), and leveraging advanced mass spectrometry analysis technologies (such as 10X Proteomics, 4D PTM Proteomics, etc.), we can conduct high-quality L-/D-Lactylation modification proteomics analysis to assist researchers in various scientific fields.

- **L-/D-Lactylation modification site identification**
- **L-/D-Lactylation modification quantitative analysis**
- **L-/D-Lactylation protein modification profile analysis**



Sample Collection

Trypsin Digestion

LC-MS/MS for Protein and PTMs Profiling

Bioinformatics Analysis

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