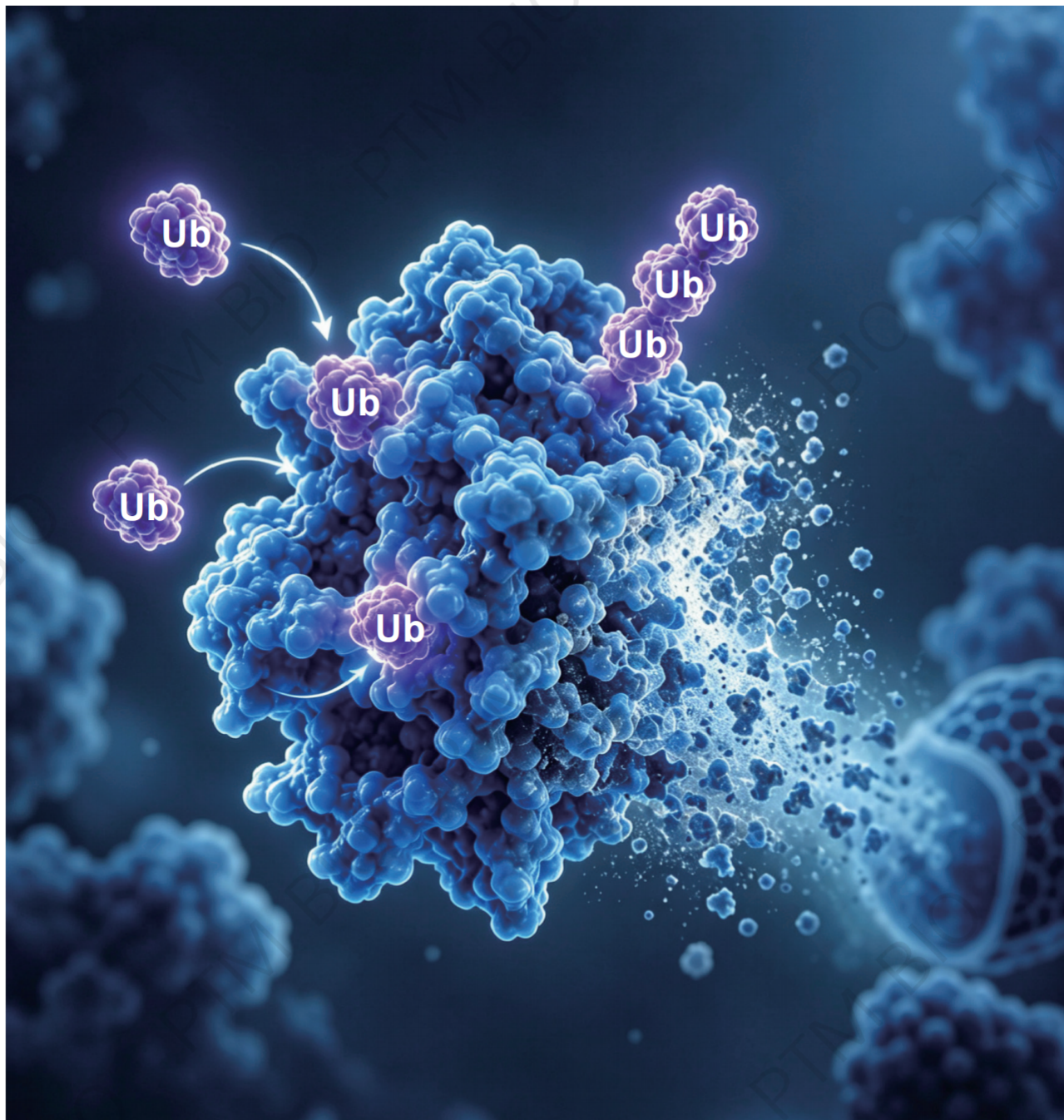


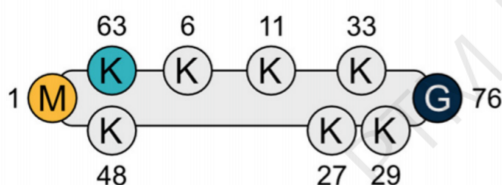


Ubiquitinomics Solutions

Decoding Ubiquitination in Protein Fate and Function

Ubiquitination: A Central Regulator of Protein Fate

Ubiquitin (Ub):



- Ubiquitin is a small protein composed of 76 amino acids, with a molecular weight of approximately 8.5 kDa.
- Depending on how ubiquitin molecules are linked, ubiquitin chains can be classified as homotypic or heterotypic.
- Ubiquitin is highly conserved and widely expressed in eukaryotic cells. It contains seven lysine residues, an N-terminal methionine residue (M1), and a C-terminal glycine residue (G76).
- Ubiquitin chains may be homotypic or heterotypic and can be unbranched or branched.

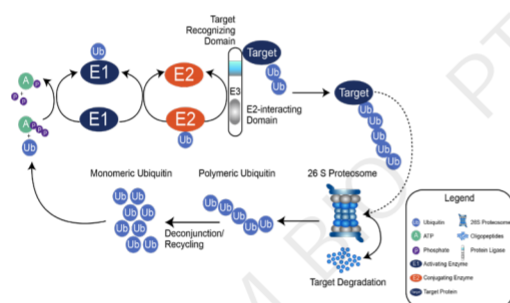
Ubiquitination

Ubiquitination is an enzymatic post-translational modification (PTM) in which ubiquitin is covalently attached to a target protein through the sequential action of an E1 ubiquitin-activating enzyme, an E2 ubiquitin-conjugating enzyme, and an E3 ubiquitin ligase.

Enzymes Regulating Ubiquitination

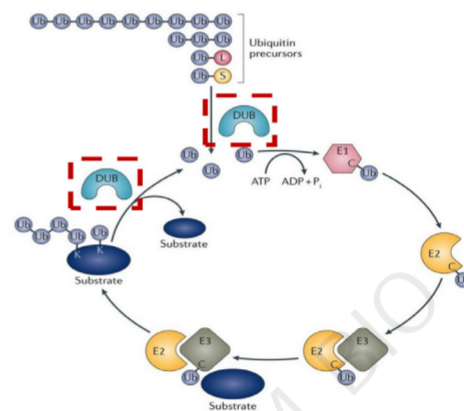
Ubiquitination Enzymes

1. In an ATP-dependent reaction, an E1 ubiquitin-activating enzyme activates ubiquitin.
2. The E1 enzyme transfers the activated ubiquitin to an E2 ubiquitin-conjugating enzyme.
3. An E3 ubiquitin ligase facilitates the transfer of ubiquitin from the E2 enzyme to the target protein.

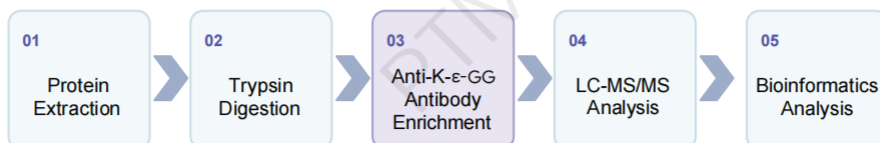
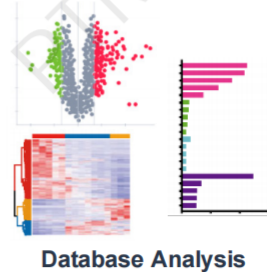
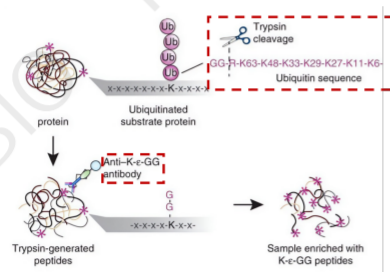


Deubiquitinating Enzymes

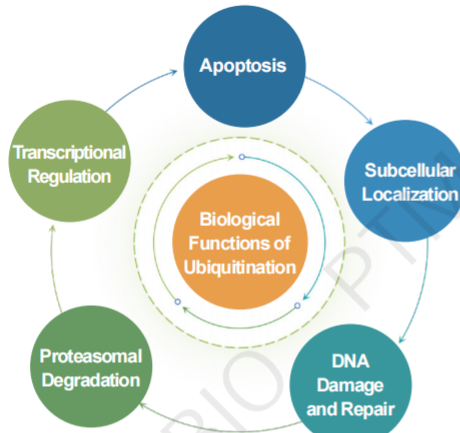
Deubiquitinating enzymes (DUBs) hydrolyze ester, peptide, or isopeptide bonds involving the C terminus of ubiquitin. Through this activity, DUBs selectively remove ubiquitin from ubiquitinated proteins or ubiquitin precursor proteins, thereby reversing ubiquitination.



PTM BIO Ubiquitinomics Workflow



Applications of Ubiquitinomics



Aging

Cancer

Immunity and Inflammation

Neurodegenerative Diseases

Stress Responses

Plant Stress Responses

nature
Rewiring of the ubiquitinated proteome determines ageing in *C. elegans*

CANCER DISCOVERY
A Ubiquitination Cascade Regulating the Integrated Stress Response and Survival in Carcinomas

nature
Multilevel proteomics reveals host perturbations by SARS-CoV-2 and SARS-CoV

Science Advances
Trisomy 21-induced dysregulation of microglial homeostasis in Alzheimer's brains is mediated by USP25

Science
Ubiquitination is essential for recovery of cellular activities after heat shock

The Plant Cell
The TGN/EE SNARE protein SYP61 and the ubiquitin ligase ATL31 cooperatively regulate plant responses to carbon/nitrogen conditions in Arabidopsis

Representative Studies

Integrated Ubiquitinomics Characterization of Hepatocellular Carcinomas

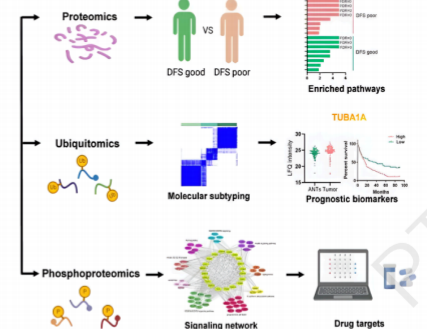
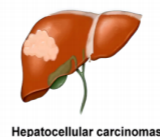
Integrated proteome, phosphoproteome, and ubiquitinome profiling identified candidate prognostic biomarkers and a potentially actionable AKT–USP14–TUBA1A axis in hepatocellular carcinoma.

Study Objective: To characterize the HCC ubiquitinome and identify biomarkers and therapeutic targets for aggressive disease.

Samples: 85 HCC tumor tissues and 18 adjacent non-tumor tissues (ANTs).

Key Findings:

1. Multi-omics analysis revealed crosstalk among ubiquitination, metabolism, and metastasis in HCC.
2. Ubiquitinome-based signatures defined HCC subtypes with distinct clinical outcomes and identified candidate high-risk biomarkers.
3. AKT-mediated activation of USP14 promoted deubiquitination of TUBA1A at K370 in aggressive HCC.
4. Targeting the AKT–USP14–TUBA1A axis promoted TUBA1A degradation and suppressed tumorigenesis in vivo.



Targeting E3 Ubiquitin Ligase Hrd1 Prevents Myocardial Ischemia-Reperfusion Injury Through Enhancing ALDH2 Enzymatic Activity

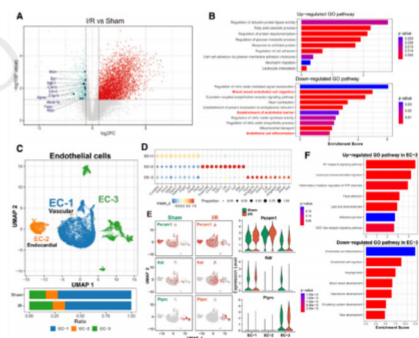
Integrated ubiquitinomics identifies endothelial Hrd1 as a key regulator and potential therapeutic target in myocardial ischemia-reperfusion injury.

Study Objective: To characterize ubiquitination in myocardial ischemia-reperfusion (I/R) injury and identify key therapeutic regulators.

Samples/Models: Mouse hearts following sham or I/R surgery, human and mouse I/R specimens, and Hrd1 knockout and overexpression mouse models.

Key Findings:

1. Multi-omics analysis identified increased Hrd1 expression in CD45+ endothelial cells after I/R injury.
2. Hrd1 catalyzed K33-linked polyubiquitination of ALDH2, impairing ALDH2 activity and endothelial function.
3. Hrd1 deletion reduced myocardial injury, endothelial dysfunction, and inflammatory-cell infiltration.
4. Pharmacologic Hrd1 inhibition alleviated myocardial I/R injury, supporting Hrd1 as a candidate therapeutic target.



+ Selected Publications Featuring PTM BIO Products and Services

Title	Journal
Metabolic regulation of gene expression by histone lactylation	<i>Nature</i> (IF=48.5)
Alanyl-tRNA synthetase, AARS1, is a lactate sensor and lactyltransferase that lactylates p53 and contributes to tumorigenesis	<i>Cell</i> (IF=42.5)
Metabolic regulation of homologous recombination repair by MRE11 lactylation	<i>Cell</i> (IF=42.5)
Increased glucose metabolism in TAMs fuels O-GlcNAcylation of lysosomal Cathepsin B to promote cancer metastasis and chemoresistance	<i>Cancer Cell</i> (IF=44.5)
Branched-chain amino acid catabolism promotes thrombosis risk by enhancing tropomodulin-3 propionylation in platelets	<i>Circulation</i> (IF=38.6)
Sex-determining region Y gene promotes liver fibrosis and accounts for sexual dimorphism in its pathophysiology	<i>Journal of Hepatology</i> (IF=33.0)
An integrated multi-omics analysis reveals osteokines involved in global regulation	<i>Cell Metabolism</i> (IF=30.9)
Senescent immune cells release grancalcin to promote skeletal aging	<i>Cell Metabolism</i> (IF=30.9)
Proteogenomic insights into early-onset endometrioid endometrial carcinoma: predictors for fertility-sparing therapy response	<i>Nature Genetics</i> (IF=29.0)
Multimic analysis of cervical squamous cell carcinoma identifies cellular ecosystems with biological and clinical relevance	<i>Nature Genetics</i> (IF=29.0)
Global profiling of crotonylation on non-histone proteins	<i>Cell Research</i> (IF=25.9)
Lysine 2-hydroxyisobutyrylation of NAT10 promotes cancer metastasis in an ac4C-dependent manner	<i>Cell Research</i> (IF=25.9)
Targeting UBE2T potentiates gemcitabine efficacy in pancreatic cancer by regulating pyrimidine metabolism and replication stress	<i>Gastroenterology</i> (IF=25.1)



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