

Ubiquitins and PROTAC®: A New Frontier in Targeted Therapy

Background

Ubiquitins are essential proteins that regulate cellular functions by marking other proteins for degradation, thereby maintaining homeostasis. Targeted Protein Degradation (TPD) leverages this principle through Proteolysis Targeting Chimera (PROTAC®) technology, which selectively degrades pathological proteins by linking them to E3 ubiquitin ligases. The major advantage of PROTACs is the ability to overcome drug resistance and degrade “undruggable” target proteins, making them a novel tool for targeted therapy. SignalChem Biotech supports research into new PROTAC®-based therapies by offering a diverse array of ubiquitin enzymes and validated E3 ligases, which are crucial for the development of innovative therapeutics.

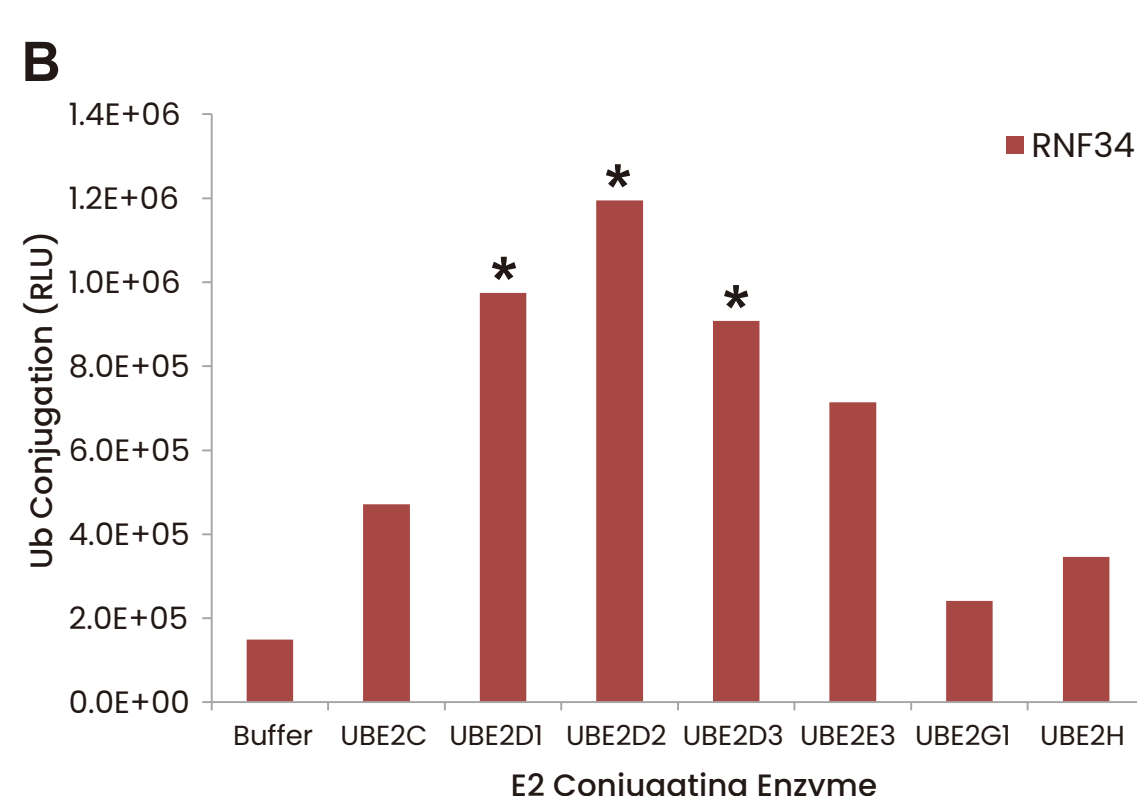
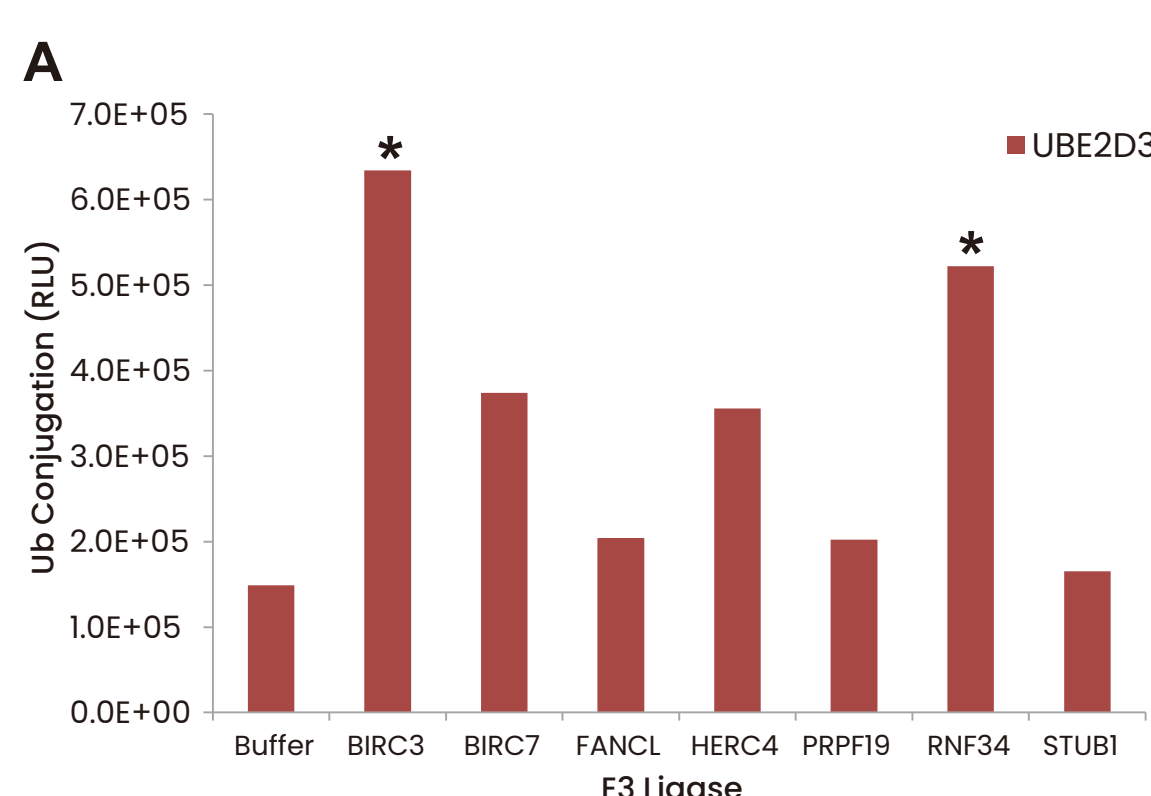
Bench to Beside

PROTAC® drugs represent a significant advancement in targeted protein degradation. Table below provides an overview of the leading PROTAC® drugs currently in clinical trials aimed at treating cancers and other complex diseases.

| Target(s) | PROTAC Drugs | Target Disease(s) |
|--------------------|---|---|
| ERα | Vepdegestrant UM-ERD-4001 SNIPER (ER)-113 and other 136 drugs | Breast Cancer |
| BTK | BGB-16673 NX-5948 HZ-Q1070 and other 65 drugs | Chronic Lymphocytic Leukemia, B-Cell Malignant Neoplasm |
| BRD4 | XH2 XH1 (University of California) NJH-05-143 and other 80 drugs | Autoimmune Diseases, Prostatic Cancer |
| BRD4 | HRS-5041 GT-20029 HP-518 and other 40 drugs | Prostate Cancer |
| JAK1 x JAK2 | Quinoxaline series PROTACs 5 Pyrimidine series PROTACs 11 Quinoxaline series PROTACs 1 and other 21 drugs | - |
| BRD2 x BRD3 x BRD4 | MZ-1 PHOTAC-1-11 macroPROTAC-1 and other 19 drugs | Leukemia |
| Bcr-Abl | SIAISI78 BT2 (University of California) BT1 and other 35 drugs | Leukemia |
| HMG-CoA reductase | L17A L16AR P13A1 and other 37 drugs | Cardiovascular Diseases |
| HDAC6 | WH221 YZ167 WH629 and other 35 drugs | Multiple Myeloma |
| CDK4 x CDK6 | MS-140 pal-pom BSJ-03-204 and other 33 drugs | Acute Lymphoblastic Leukemia, Mantle-Cell Lymphoma |

Application of Ubiquitins in Research

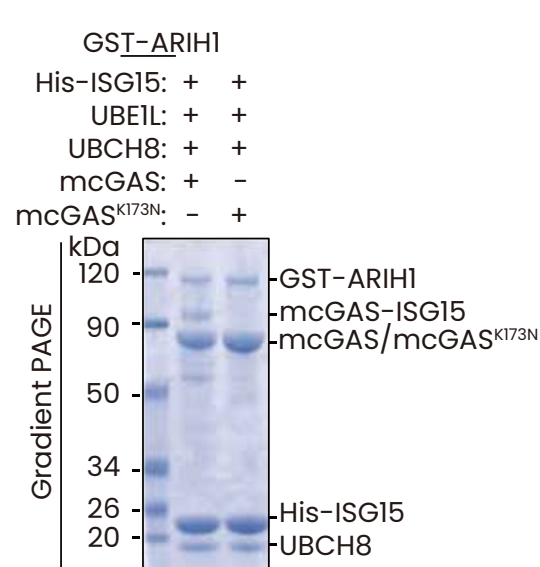
Identified various functional combinations of ubiquitin enzyme components by SignalChem Biotech



Ubiquitin conjugation catalyzed by various combinations of ubiquitinating enzymes. (A) AMP-Glo™ assay was performed with ATP, Ub, UBA1 (E1) and indicated E3s in presence of UBE2D3 as E2. (B) AMP-Glo™ assay was performed with ATP, Ub, UBA1 (E1) and indicated E2s in presence of RNF34 as E3.

Utilized UBE1L to demonstrate that ARIH1 directly catalyzes the mono-ISGylation of cGAS

Cited Product: Human Ubiquitin Activating Enzyme E1/UBA1 Protein (Cat#: 11990-H20B, Sino Biological)

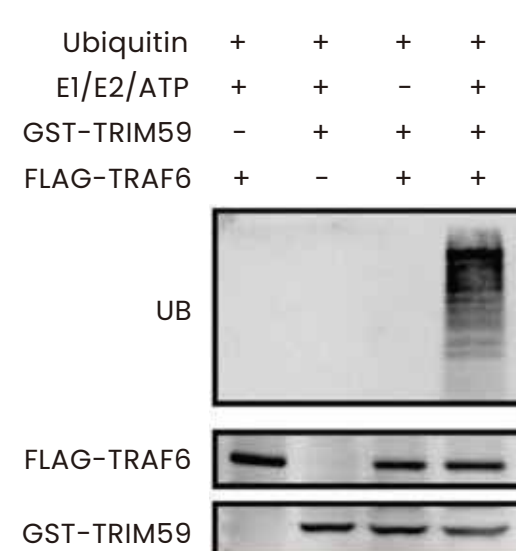


mcGAS or mcGASK173N was incubated for 2 hours with UBE1L, UBCH8, His-ISG15, and GST-ARIH1 in the reaction buffer, followed by gradient SDS-PAGE and staining with Coomassie brilliant blue.

DOI: 10.1038/s41467-022-33671-5

Employed UBE2D1 to reveal that TRIM59 directly ubiquitinates TRAF6

Cited Product: Human Ubch5/UBE2D1 Protein (Cat#: 11432-H07E, Sino Biological)



The purified GST-TRIM59 was incubated with ubiquitin, UBA1/UBE1, UBE2D1 (Cat#: 11432-H07E), ATP and TRIM59.

DOI: 10.1080/15548627.2018.1491493

Featured Active Ubiquitin Enzymes

Wide Reaching Impact

Remarkable Specificity

Quality, Support, Trust, and Speed

Extensive Range of Ubiquitin Enzymes

| Products | Name | Cat# | Species | Tag | Expression | Sequence |
|-----------------------|------------------------|-----------|---------|-----|---------------|-------------|
| Ubiquitin Enzymes -E1 | UBA1 (UBE1), Active | U201-380G | Human | GST | Sf9 Cells | Full Length |
| | UBA6, Active | U206-380G | Human | GST | Sf9 Cells | Full Length |
| | UBA7(UBE1L), Active | U207-380G | Human | GST | Sf9 Cells | Full Length |
| Ubiquitin Enzymes -E2 | UBE2A, Active | U210-380H | Human | HIS | <i>E.coli</i> | Full Length |
| | UBE2C, Active | U212-380H | Human | HIS | <i>E.coli</i> | Full Length |
| | UBE2E1 (UBCH6), Active | U217-380H | Human | HIS | <i>E.coli</i> | 2-end |
| Ubiquitin Enzymes -E3 | BIRC3, Active | B280-380G | Human | GST | Sf9 Cells | Full Length |
| | BIRC7, Active | B281-380G | Human | GST | Sf9 Cells | Full Length |
| | HERC4, Active | H265-381G | Human | GST | Sf9 Cells | 642-end |