Revision 1

Store at -20C

#72032

CRL4/CRBN Targeted Protein Degradation Complex Antibody Sampler Kit

1 Kit (6 x 20 microliters)

Cell Signaling TECHNOLOGY®

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Product Includes	Product #	Quantity	Mol. Wt	Isotype/Source
CRBN (D8H3S) Rabbit mAb	71810	20 µl	55 kDa	Rabbit IgG
CUL4A Antibody	2699	20 µl	80, 82 kDa	Rabbit
DDB-1 (D4C8) Rabbit mAb	6998	20 µl	127 kDa	Rabbit IgG
RBX1 (D3J5I) Rabbit mAb	11922	20 µl	13 kDa	Rabbit IgG
NEDD8 (19E3) Rabbit mAb	2754	20 µl	9 kDa	Rabbit IgG
Ubiquitin (E4I2J) Rabbit mAb	43124	20 µl		Rabbit IgG
Anti-rabbit IgG, HRP-linked Antibody	7074	100 µl		Goat

Please visit cellsignal.com for individual component applications, species cross-reactivity, dilutions, protocols, and additional product information.

Description

The CRL4/CRBN Targeted Protein Degradation Complex Antibody Sampler Kit provides an economical means of detecting the individual components of a CRL4/CRBN E3 ubiquitin ligase complex, including free and conjugated forms of both NEDD8 and ubiquitin. The kit includes enough antibodies to perform two western blot experiments with each primary antibody.

Storage

Supplied in 10 mM sodium HEPES (pH 7.5), 150 mM NaCl, 100 µg/mL BSA, 50% glycerol and less than 0.02% sodium azide. Store at –20°C. *Do not aliquot the antibodies.*

Background

Targeted protein degradation is an experimental method of drug-based protein targeting that leverages endogenous proteolysis machinery, such as the the ubiquitin proteasome system (UPS), to selectively degrade proteins of interest (POIs). It is being actively explored as a therapeutic strategy to target and degrade POIs that contribute to disease progression (1). This approach differs from traditional small-molecule therapeutics that seek to suppress disease proteins (e.g., kinases) by sterically blocking catalytic domains. Proteolysis-targeting chimeras (PROTACs) and "molecular glue" degraders are the two primary degrader modalities used in UPS-mediated targeted protein degradation. PROTACs are bivalent, chemically-linked ligands that induce proximity between a POI and an E3 ubiquitin ligase, resulting in ubiquitination of the target protein, and its subsequent degradation by the UPS (2,3). Molecular glues are molecules that chemically generate novel interaction surfaces between two proteins, which can used to induce proximity between a POI and an E3 ligase. Cereblon (CRBN) is the substrate-recognition component of a Cullin-RING-ubiquitin (E3) ligase complex (CRL4/CRBN) that was among the first to be recognized for its therapeutic potential via targeted protein degradation (4). The CRL4/CRBN complex is comprised of CRBN, DDB-1, RBX1, and the scaffold protein CUL4A; its ligase activity is dynamically regulated via the covalent modification (neddylation) of CUL4A by NEDD8 (5). In unrelated mechanistic studies of multiple myeloma drugs, it was revealed that phthalimides (e.g., thalidomide, lenalidomide) promoted CRBN-dependent recruitment, ubiquitination, and proteasomal degradation of the transcription factors Ikaros (IKZF1) and Aiolos (IKZF3) (6). The discovery that phthalimides were functioning as molecular glue degraders that could selective degrade what were previously considered "undruggable" targets, led to a rapid acceleration and expansion of research into targeted protein degradation, with the promise of novel therapies for diseases deemed largely intractable using conventional small-molecule therapies (7-9).

Background References

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4. Krönke, J. et al. (2014) *Science* 343, 301-5.
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6. Lu, G. et al. (2014) *Science* 343, 305-9.
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8. Alabi, S.B. and Crews, C.M. (2021) *J Biol Chem* 296, 100647.
9. Alabi, S. et al. (2021) *Nat Commun* 12, 920.

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