Recombinant Human CRBN-midi His-tag

Catalog Number: 11724-CB

DESCRIPTION

Source *E. coli*-derived human CRBN protein

6-His tag	Sumo-tag	Human CRBN-midi (Ala41-Glu187/GSG/Asp249-Ile426, with mutations) Accession # Q96SW2.1

N-terminus C-terminus

N-terminal Sequence Analysis	Met
Predicted Molecular Mass	49 kDa

SPECIFICATIONS

SDS-PAGE	52-57, 38-46 kDa, under reducing conditions
Endotoxin Level	<0.10 EU per 1 µg of the protein by the LAL method.
Purity	>80%, by SDS-PAGE visualized with Silver Staining and quantitative densitometry by Coomassie® Blue Staining.
Formulation	Supplied as a 0.2 µm filtered solution in HEPES, NaCl, TCEP and Glycerol. See Certificate of Analysis for details.

PREPARATION AND STORAGE

Shipping	The product is shipped with dry ice or equivalent. Upon receipt, store it immediately at the temperature recommended below.
Stability & Storage	**Use a manual defrost freezer and avoid repeated freeze-thaw cycles.** • 6 months from date of receipt, -20 to -70 °C as supplied. • 3 months, -20 to -70 °C under sterile conditions after opening.

BACKGROUND

Protein cereblon (CRBN) is a ubiquitously expressed cytosolic substrate receptor component of the Cullin4 E3 ligase complex CUL4-RBX1-DDB1 (1,2). As the substrate receptor subunit component of an E3 ligase complex, CRBN recruits specific targets such as the transcriptional regulator MEIS2 (2) and large-conductance calcium activated potassium channel KCNMA1 (3) to its E3 ligase complex to induce protein ubiquitination and subsequent degradation. CRBN was identified as the target of the infamous drug thalidomide and related immunomodulatory drugs such as lenalidomide that are approved for the treatment of multiple myeloma and other haematological malignancies (4,5). CRBN consists of an unstructured N-terminal region and three folded domains: the Lon protease-like domain (Lon), the helical bundle (HB) that binds the adaptor protein DDB1, and the thalidomide binding domain (TBD) with a conserved zinc binding site (2,6). Thalidomide and lenalidomide bind non-covalently to CRBN and mimic the C-terminal cyclic imide degron of CRBN substrates (2,6). Utilizing the capability of CRBN and other E3 receptor components for specific substrate recognition, development of small-molecule degraders targeted to these receptor components allows for targeted protein degradation (TPD) to strategically address medical therapeutic needs that are currently impossible using conventional drugs (4,5,7,8). Most of the current clinical degrader candidates reported to date in the literature in TPD models have targeted CRBN. Due to challenges in producing a suitable soluble recombinant CRBN protein (2,6), CRBN-based degraders have had limited structure-guided drug design as there has been an inadequate number of published high-resolution ternary complex (CRBN:degrader:target) drug designs (6,9,10) and also limited in vitro biophysical characterization (11,12). A truncated CRBN construct, resulting in a protein version called CRBNmidi, was created, tested, and validated for use in a range of biophysical techniques (6). CRBNmidi enabled determination of high-resolution crystal structures of binary and ternary complexes with various ligands and degraders and their neo-substrate targets and thus CRBNmidi can be an effective tool to enable high-throughput structure-guided drug design of CRBN-based ligands and degraders (6). Recombinant Human CRBN-midi His-tag protein is a Sumo tag-cleavable version of the CRBN-midi construct.

References:

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