USP19 -TM(1-1290) [GST-tagged]

Deconjugating enzyme: Deubiquitylase

Alternate Names: Zinc finger MYND domain containing protein 9, ZMYND9

Cat. No.	**64-0022-050**	Quantity:	50 µg
Lot. No.	**30062**	Storage:	-70˚C

FOR RESEARCH USE ONLY NOT FOR USE IN HUMANS

Background

Deconjugating enzymes (DCEs) are proteases that process ubiquitin or ubiquitin-like gene products, reverse the modification of proteins by a single ubiquitin or ubiquitin-like protein (UBL) and remodel polyubiquitin (or poly-UBL) chains on target proteins (Reyes-Turcu *et al.*, 2009). The deubiquitylating – or deubiquitinating – enzymes (DUBs) represent the largest family of DCEs and regulate ubiquitin dependent signaling pathways. The activities of the DUBs include the generation of free ubiquitin from precursor molecules, the recycling of ubiquitin following substrate degradation to maintain cellular ubiquitin homeostasis and the removal of ubiquitin or ubiquitin-like proteins (UBL) modifications through chain editing to rescue proteins from proteasomal degradation or to influence cell signalling events (Komander *et al.*, 2009). There are two main classes of DUB; cysteine proteases and metalloproteases. Ubiquitin specific protease 19 (USP19) is a member of the cysteine protease enzyme family and cloning of the human gene was first described by Nagase *et al.* (1998). USP19 is a ubiquitin-specific protease anchored via its C-terminal to the endoplasmic-reticulum. USP19 rescues the endoplasmic-reticulum-associated degradation (ERAD) substrates: cystic fibrosis transmembrane conductance regulator (CFTR) and T-cell receptor-α (TCRα) from proteasomal degradation. It also deubiquitylates and prevents proteasomal degradation of RNF123 which in turn stimulates CDKN1B ubiquitin-dependent degradation thereby playing a role in cell proliferation (Hassink *et al.*, 2009). USP19 modulates transcription of major myofibrillar proteins

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Physical Characteristics

Species: human

Source: *E. coli*

Quantity: 50 µg

Concentration: 0.5 mg/ml

Formulation: 50 mM HEPES pH 7.5, 150 mM sodium chloride, 2 mM dithiothreitol, 10% glycerol

Molecular Weight: ~170 kDa

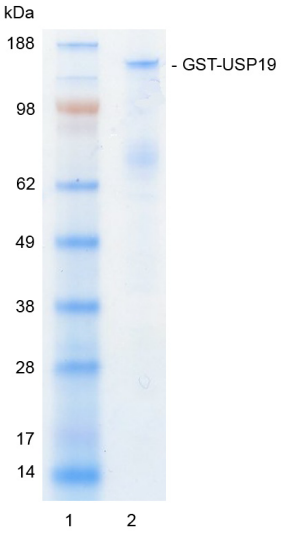
Purity: >79% by InstantBlue™ SDS-PAGE

Stability/Storage: 12 months at -70˚C; aliquot as required

Protein Sequence: Please see page 2

Quality Assurance

Purity:
4-12% gradient SDS-PAGE
InstantBlue™ staining
lane 1: MW markers
lane 2: 1 µg GST-USP19



Protein Identification:
Confirmed by mass spectrometry.

Deubiquitylase Enzyme Assay:
The activity of GST-USP19 was validated by determining the increase in fluorescence measured as a result of the enzyme catalysed cleavage of the fluorogenic substrate Ubiquitin-Rhodamine110-Glycine generating Ubiquitin and Rhodamine110-Glycine. Incubation of the substrate in the presence or absence of GST-USP19 was compared confirming the deubiquitylating activity of GST-USP19.

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Lot-specific COA version tracker: v1.0.0

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Background

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and is involved in decreased protein synthesis in atrophying skeletal muscle. Inhibition of USP19 could be a novel therapeutic mechanism for the prevention and treatment of muscle protein catabolism (Sundaram *et al.*, 2009). During the cell cycle, USP19 regulates p27 levels by deubiquitylating and stabilizing RNF123, an E3 ubiquitin ligase that ubiquitylates p27 and targets it for proteasomal degradation at the G1 phase. Enhanced degradation of p27 in G1 phase is associated with several cancers, and thus USP19 could be a possible target for oncology research (Lu *et al.*, 2009). Cellular inhibitors of apoptosis (c-IAPs) are stabilised by USP19 in a deubiquitylase-independent mechanism, by inhibiting the self-ubiquitin ligase activity of c-IAPs (Mei *et al.*, 2011).

References:

Hassink GC, Zhao B, Sompallae R, Altun M, Gastaldello S, Zinin NV, Masucci MG, Lindsten K (2009) The ER-resident ubiquitin-specific protease 19 participates in the UPR and rescues ERAD substrates. *EMBO Rep* **10**, 755-761.

Komander D, Clague MJ, Urbe S (2009) Breaking the chains: structure and function of the deubiquitinases. *Nat Rev Mol Cell Biol* **10**, 550-563.

Lu Y, Adegoke OA, Nepveu A, Nakayama KI, Bedard N, Cheng D, Peng J, Wing SS (2009) USP19 deubiquitinating enzyme supports cell proliferation by stabilizing KPC1, a ubiquitin ligase for p27Kip1. *Mol Cell Biol* **29**, 547-558.

Mei Y, Hahn AA, Hu S, Yang X (2011) The USP19 deubiquitinase regulates the stability of c-IAP1 and c-IAP2. *J Biol Chem* **286**, 35380-35387.

Nagase T, Ishikawa K, Suyama M, Kikuno R, Miyajima N, Tanaka A, Kotani H, Nomura N, Ohara O (1998) Prediction of the coding sequences of unidentified human genes. XI. The complete sequences of 100 new cDNA clones from brain which code for large proteins *in vitro*. *DNA Res* **5**, 277-286.

Reyes-Turcu FE, Ventii KH, Wilkinson KD (2009) Regulation and cellular roles of ubiquitin-specific deubiquitinating enzymes. *Ann Rev Biochem* **78**, 363-397.

Sundaram P, Pang Z, Miao M, Yu L, Wing SS (2009) USP19-deubiquitinating enzyme regulates levels of major myofibrillar proteins in L6 muscle cells. *Am J Physiol Endocrinol Metab* **297**, E1283-1290.

Physical Characteristics

Continued from page 1

Protein Sequence:

MSPILGYWKIKGLVQPTRLLLEYLEEKYEEHLYER
DEGDKWRNKKFELGLEFPNLPYYIDGDVKLTQSMAI
IRYIADKHNMLGGCPKERAEISMLEGAVLDIRYGVS
RIAYSKDFETLKVDFLSKLPEMLKMFEDRLCHK
TYLNGDHVTHPDFMLYDALDVVLYMDPMCLDAF
PKLVCFKKRIEAIPQIDKYLKSSKYIAWPLQG
WQATFGGGDHPPKSDLEVLFQGPLGSPNSRVD***M***SG
GASATGPRRGPPGLEDTTSKKKQKDRANQESKDGD
PRKETGSRYVAQAGLEPLASGDPSASASHAAGITG
SRHRTRLFFPSSSGSASTPQEEQTKEGACEDPHDL
LATPTPELLLDWRQSAEEVIVKLRVGVGPLQLED
VDAAFTDTDCVVRFAGGQQWGGVFYAEIKSS
CAKVQTRKGSLLHLTLPKKVPMLTWPSLLVEAD
EQLCIPPLNSQTCLLGSEENLAPLAGEKAVPPGND
PVSPAMVRSRNPGKDDCAKEEMAVAADAATLVDE
PESMVNLAFVKNDSYEKGPDSVVVHVYVKE
ICRDTSRVLFREQDFTLIFQTRDGNFLRLHPGCG
PHTTFRWQVKLRNLIEPEQCTFCFTASRIDICL
RKRQSQRWGGLEAPAARVGGAKVAVPTGPTPLD
STPPGGAPHPLTGQEEEARAVEKDKSKARSEDT
GLDSVATRTPMEHVTPKPETHLASPKPTCMVPP
MPHSPVSGDSVEEEEEEEKKVCLPGFTGLVNL
GNTCFMNSVIQSLSNTRELRDFFHDRSFEAEINYN
NPLGTGGRLAIGFAVLLRALWKGTHHAFQP
SKLKAIVASKASQFTGYAQHDAQEFMAFLLDGL
HEDLNRIQNKPYTETVDSDGRPDEVVAEEAWQRH
KMRNDSFIVDLFQGQYKSKLVCPVCAKVSITFDP
FLYLPVPLPQKQKVLPVFYFAREPHSKPIKFLVS
VSKENSTASEVLDSLSQSVHVKPENLRLAEVIKN
RFHRVFLPSHSLDTVSPSDTLLCFELLSSELAKERV
VVLEVQQRPQVPSVPISKCAACQRKQQSEDEKLKRC
TRCYRVGYCNQLCQKTHWPDHKGLCRPENIGYP
FLVSVPASRLTYARLAQLLEGYARYSVSVFQP
PFQPGRMALESQSPGCTTLLSTGSLEAGDSERD
PIQPPELQLVTPMAEGDTGLPRVWAAPDRG
PVPSTSGISSEMLASGPIEVGSLPAGERVSR
PEAAVPGYQHPSEAMNAHTPQFFIYKIDSSN
REQRLEDKGDTPLELGDDCSLALVWRNNERLQEFV
LVASKELECAEDPGSAGEAARAGHFTLDQCLN
LFTRPEVLAPEEAWYCPQCKQHREASKQLLLWR
LPNVLIVQLKRFSFRSFIWRDKINDLVEFPVRN
LDLSKFCIGQKEEQLPSYDLYAVINHYGGMIG
GHYTACARLPNDRSSQRSDVGWRLFDDSTVTT
VDESQVVTRYAYVLFYRRRNSPVERPPRAGHSE
HHPDLGPAAEAAASQASRIWQELEAEEEPVPEGS
GPLGPWGPQDWVGPLPRGPTTPDEGCLR

Tag (**bold text**): N-terminal GST
Protease cleavage site: PreScission™ (LEVLFQ▼GP)
USP19 (regular text): Start ***bold italics*** (amino acid residues 1-1290)
Accession number: NP_006668

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Lot-specific COA version tracker: v1.0.0