SignalSilence® MetAP2 siRNA I

#12149 Store at -20°C

☑ 10 µM in 300 µl (3 nmol)

Cell Signaling TECHNOLOGY®

Orders ■ 877-616-CELL (2355) orders@cellsignal.com
Support ■ 877-678-TECH (8324) info@cellsignal.com
Web ■ www.cellsignal.com

rev. 05/16/16

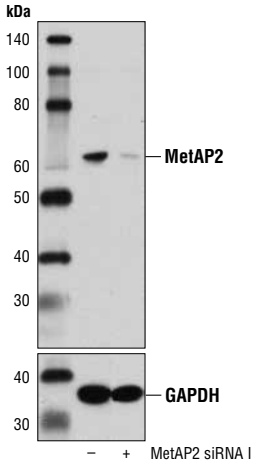
For Research Use Only. Not For Use In Diagnostic Procedures.

Species Cross-Reactivity: H, (Mk)

Description: SignalSilence® MetAP2 siRNA I from Cell Signaling Technology (CST) allows the researcher to specifically inhibit MetAP2 expression using RNA interference, a method whereby gene expression can be selectively silenced through the delivery of double stranded RNA molecules into the cell. All SignalSilence® siRNA products from CST are rigorously tested in-house and have been shown to reduce target protein expression by western analysis.

Background: Eukaryotic initiation factor 2 (eIF2)-associated glycoprotein, p67/methionine aminopeptidase 2 (MetAP2) is one of the three known MetAPs responsible for the co-translational processing of the N-terminal initiator methionine from nascent proteins in cells. MetAP2 regulates the rates of global protein synthesis by controlling the levels of eIF2α phosphorylation (1). MetAP2 has also been shown to bind Erk1/2 to inhibit their activation and activity, thus connecting the protein synthesis machinery with the cell signaling pathway mediated by Erk1/2 MAP kinases (2-4). Although MetAP2 is characterized as having aminopeptidase activity that removes the N-terminal methionine from nascent peptides *in vitro*, mounting evidence suggests that MetAP2 has no methionine aminopeptidase activity. Rather, MetAP2 possesses auto-proteolytic activity that can be inhibited by several small molecule inhibitors including anti-angiogenic drugs, fumagilin and its derivatives (5). It has also been demonstrated that O-GlcNAcylation of MetAP2 plays a major role in its stability, eIF2α binding, and maintenance of the level of eIF2α phosphorylation (6).

MetAP2 knockout mice show embryonic lethality, suggesting its role in embryonic development and survival at the initiation of gastrulation (7). It is likely that lowering the levels of MetAP2 from mammalian cells leads to apoptosis due to the high levels of eIF2α phosphorylation that inhibits global protein synthesis and causes cell growth inhibition (8). During pathological or various stress conditions, MetAP2 dissociates from eIF2 subunits possibly due to its deglycosylation-induced autoproteolytic cleavage. As a result, eIF2α becomes hyperphosphorylated and global protein synthesis is inhibited. MetAP2 that is dissociated from the eIF2 complex also displays a higher affinity toward Erk1/2, which results in blockade of Erk1/2 activity. Thus, MetAP2 mediates cooperation between cell signaling and protein synthesis machinery to regulate cell growth and proliferation during physiological and pathological conditions (9). Indeed, research studies have shown higher expression of MetAP2 in human cancers, supporting the contention that MetAP2 plays a role in oncogenesis. For example, investigators have reported high MetAP2 expression in follicular lymphomas, large B-cell lymphomas, and Burkitt's lymphomas (10). Elevated expression of MetAP2 has also been reported in human colorectal adenocarcinomas (11).



Western blot analysis of extracts from 293T cells, transfected with 100 nM SignalSilence® Control siRNA (Unconjugated) #6568 (-) or SignalSilence® MetAP2 siRNA I (+), using MetAP2 Antibody #11833 (upper) or GAPDH (D16H11) XP® Rabbit mAb #5174 (lower). The MetAP2 Antibody confirms silencing of MetAP2 expression, while the GAPDH (D16H11) XP® Rabbit mAb is used as a loading control.

Source/Purification: SignalSilence® MetAP2 siRNA I inhibits human and monkey MetAP2 expression.

Directions for Use: CST recommends transfection with 100 nM SignalSilence® MetAP2 siRNA I 48 to 72 hours prior to cell lysis. For transfection procedure, follow protocol provided by the transfection reagent manufacturer. Please feel free to contact CST with any questions on use.

Each vial contains the equivalent of 100 transfections, which corresponds to a final siRNA concentration of 100 nM per transfection in a 24-well plate with a total volume of 300 µl per well.

Quality Control: Oligonucleotide synthesis is monitored base by base through trityl analysis to ensure appropriate coupling efficiency. The oligo is subsequently purified by affinity-solid phase extraction. The annealed RNA duplex is further analyzed by mass spectrometry to verify the exact composition of the duplex. Each lot is compared to the previous lot by mass spectrometry to ensure maximum lot-to-lot consistency.

Entrez-Gene ID #10988
Swiss-Prot Acc. #P50579

Storage: MetAP2 siRNA I is supplied in RNAse-free water. *Aliquot and store at -20°C.*

Please visit www.cellsignal.com for a complete listing of recommended companion products.

Background References:

(1) Datta, B. (2000) *Biochimie* 82, 95-107.
(2) Datta, B. et al. (2004) *Arch Biochem Biophys* 427, 68-78.
(3) Datta, B. et al. (2004) *Biochemistry* 43, 14821-31.
(4) Datta, B. et al. (2005) *Exp Cell Res* 303, 174-82.
(5) Bradshaw, R.A. and Yi, E. (2002) *Essays Biochem* 38, 65-78.
(6) Datta, B. et al. (1999) *Exp Cell Res* 250, 223-30.
(7) Yeh, J.R. et al. (2006) *Proc Natl Acad Sci USA* 103, 10379-84.
(8) Datta, B. and Datta, R. (1999) *Exp Cell Res* 246, 376-83.
(9) Ghosh, A. et al. (2006) *Exp Cell Res* 312, 3184-203.
(10) Kanno, T. et al. (2002) *Lab Invest* 82, 893-901.
(11) Selvakumar, P. et al. (2004) *Clin Cancer Res* 10, 2771-5.

Applications Key: **W**—Western **IP**—Immunoprecipitation **IHC**—Immunohistochemistry **ChIP**—Chromatin Immunoprecipitation **IF**—Immunofluorescence **F**—Flow cytometry **E-P**—ELISA-Peptide
Species Cross-Reactivity Key: **H**—human **M**—mouse **R**—rat **Hm**—hamster **Mk**—monkey **Mi**—mink **C**—chicken **Dm**—D. melanogaster **X**—Xenopus **Z**—zebrafish **B**—bovine **Dg**—dog **Pg**—pig **Sc**—S. cerevisiae **Ce**—C. elegans **Hr**—Horse **All**—all species expected Species enclosed in parentheses are predicted to react based on 100% homology.