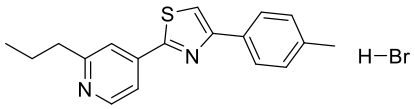
Product data sheet

MedKoo Cat#: 330177 Name: Fatostatin HBr CAS#: 298197-04-3 (HBr) Chemical Formula: $C_{18}H_{19}BrN_2S$ Molecular Weight: 375.328	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Fatostatin, also known as 125B11 or Fatostatin A, is an inhibitor of SREBP activation, preventing SCAP-mediated escort of either SREBP-1 or SREBP-2 to the Golgi (IC50 = 5.6 μM).

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	9.62	25.63
DMF	1.0	2.66
Ethanol	0.11	0.29

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.66 mL	13.32 mL	26.64 mL
5 mM	0.53 mL	2.66 mL	5.33 mL
10 mM	0.27 mL	1.33 mL	2.66 mL
50 mM	0.05 mL	0.27 mL	0.53 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Brovkovych V, Izhar Y, Danes JM, Dubrovskyi O, Sakallioglu IT, Morrow LM, Atilla-Gokcumen GE, Frasor J. Fatostatin induces pro- and anti-apoptotic lipid accumulation in breast cancer. Oncogenesis. 2018 Aug 24;7(8):66. doi: 10.1038/s41389-018-0076-0. PMID: 30140005; PMCID: PMC6107643.
2. Li J, Yan H, Zhao L, Jia W, Yang H, Liu L, Zhou X, Miao P, Sun X, Song S, Zhao X, Liu J, Huang G. Inhibition of SREBP increases gefitinib sensitivity in non-small cell lung cancer cells. Oncotarget. 2016 Aug 9;7(32):52392-52403. doi: 10.18632/oncotarget.10721. PMID: 27447558; PMCID: PMC5239560.

In vivo study

1. Jie Z, Xie Z, Xu W, Zhao X, Jin G, Sun X, Huang B, Tang P, Wang G, Shen S, Qin A, Fan S. SREBP-2 aggravates breast cancer associated osteolysis by promoting osteoclastogenesis and breast cancer metastasis. Biochim Biophys Acta Mol Basis Dis. 2019 Jan;1865(1):115-125. doi: 10.1016/j.bbadis.2018.10.026. Epub 2018 Oct 28. PMID: 30394316.
2. Chen M, Zhang J, Sampieri K, Clohessy JG, Mendez L, Gonzalez-Billalabeitia E, Liu XS, Lee YR, Fung J, Katon JM, Menon AV, Webster KA, Ng C, Palumbieri MD, Diolombi MS, Breitkopf SB, Teruya-Feldstein J, Signoretti S, Bronson RT, Asara JM, Castillo-Martin M, Cordon-Cardo C, Pandolfi PP. An aberrant SREBP-dependent lipogenic program promotes metastatic prostate cancer. Nat Genet. 2018 Feb;50(2):206-218. doi: 10.1038/s41588-017-0027-2. Epub 2018 Jan 15. PMID: 29335545; PMCID: PMC6714980.

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7. Bioactivity

Biological target:

Fatostatin hydrobromide (125B11 hydrobromide), a specific inhibitor of SREBP activation, impairs the activation of SREBP-1 and SREBP-2.

In vitro activity

Together, findings suggest that FS (fatostatin) acts to inhibit growth and induce apoptosis in ER (estrogen receptor)+ breast cancer cells and tumors. The mechanism of FS action in lipid-sufficient conditions involves activation of EnRS (endoplasmic reticulum stress) and the accumulation of lipid species (Fig. 7). The source of lipids for this lipid accumulation is unclear but de novo lipogenesis genes, such as FASN (fatty acid synthase) and ACC (acetyl-CoA carboxylase), are not regulated (either up or down) by FS in lipid-containing FBS suggesting other lipogenesis regulators, such as ChREBP or LXRα, are not involved. SCAP/SREBP inhibition does not appear to be involved in FS action in these conditions as SREBP target genes were not regulated and lipid levels were not reduced. However, SCAP/SREBP inhibition has been linked to induction of EnRS18, making this pathway a potential contributor to the findings observed. Both pro-apoptotic and anti-apoptotic lipid species accumulated in response to FS. On one hand, ceramide synthesis was elevated, which contributed to the apoptotic effects of FS, while on the other, FS activated DGATs (diacylglycerol acyltransferases) and promoted accumulation of PUFA-TAGs (poly unsaturated fatty acids-triacylglycerides), which appeared to play a protective role and limit apoptosis. Overall, global changes in the lipidome in response to FS tended to favor cell death but this could be further enhanced by blocking PUFA-TAG production.

Reference: Oncogenesis. 2018 Aug; 7(8): 66. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6107643/

In vivo activity

To further corroborate the crucial role of SREBP-dependent lipogenesis in PML-loss-driven CaP growth and metastasis, this study carried out in vivo preclinical studies of fatostatin targeting SREBP in Ptenpc−/−; Pmlpc−/− mice. Fatostatin is a recently discovered SREBP chemical inhibitor that directly binds SREBP cleavage-activating protein and blocks the endoplasmic reticulum–Golgi transport and the subsequent activation of SREBP. Treatment with fatostatin for two months in Ptenpc−/−; Pmlpc−/− mice inhibited both prostate tumor growth (Fig. 6c, d) and distant lymph node metastasis (Fig. 6e and Supplementary Fig. 5c). This potent antitumor and antimetastatic activity of fatostatin is presumably due to the suppression of SREBP pathway, because fatostatin-treated Ptenpc−/−; Pmlpc−/− tumors displayed markedly lower expression of SREBP-regulated enzymes for synthesis of FA and cholesterol (Fig. 6f, g). In agreement with the crucial role of lipid metabolism in various aspects of cancer development, fatostatin-treated Ptenpc−/−; Pmlpc−/− tumors, compared with vehicle-treated tumors, displayed a drastic decrease in the frequency of mitotic cells positive for Ki-67 staining, along with a concomitant induction of apoptosis, as indicated by higher expression of cleaved Parp and cleaved caspase 3 (Fig. 6f, g). These functional data suggested that SREBP-mediated lipogenesis is a key downstream effector of PML-loss-driven CaP growth and metastasis.

Reference: Nat Genet. 2018 Feb; 50(2): 206–218. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6714980/