

Product Data Sheet

Product Name: iFSP1
Cat. No.: GC45928

Chemical Properties

Cas. No. 150651-39-1

Chemical Name 1-amino-3-(4-methylphenyl)-pyrido[1,2-a]benzimidazole-2,4-dicarbonitrile

SMILES NC1=C(C#N)C(C2=CC=C(C)C=C2)=C(C#N)C3=NC4=CC=CC=C4N31

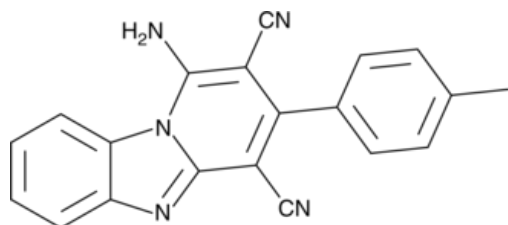
Formula $C_{20}H_{13}N_5$ M.Wt 323.4

Solubility 1mg/mL in ethanol, 25mg/mL in DMSO, 30mg/mL in DMF Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines 4-hydroxytamoxifen (TAM)-inducible *Gpx4*^{-/-} murine immortalized fibroblasts (Pfa1)

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These cells harbor two loxP-flanked *Gpx4* alleles and stably express TAM inducible Cre recombinase allowing the genetic deletion of *Gpx4* at will. For all experiments using *Gpx4*^{-/-} the well were treated with 4-hydroxitamoxifen (TAM) 1μM. All cells were cultured with were cultured in DMEM-high glucose (4.5g glucose/L) with 10% fetal bovine serum (FBS) , Glutamax , and 1% penicillin/ streptomycin at 37°C with 5% CO₂ and verified to be negative for mycoplasma. The cells were treated with 3μM iFSP1 within 3h .

Reaction
Conditions 3μM , 3h

Applications iFSP1 is a potent inhibitor of FSP1.

Animal experiment [2]:

Animal models Male C57BL/6N mice

Preparation Method For hydrodynamic tail vein injection (HDTV_i) model , fatty livers were induced by replacing standard diets with HFD 24 hours prior to HDTV_i and for the duration of the experiment. FSP1 was inhibited in vivo by daily intraperitoneal injections of 10 mg/kg iFSP1 . To study the effect of iFSP1 on tumor immune infiltrates, HDTV_i-induced tumors were harvested 4 weeks post HDTV_i for dissociation and histological analysis.

Dosage form 10mg/kg ; 4 weeks ; intraperitoneal injection.

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Applications iFSP1 potently induced ferroptosis , which promoted innate and adaptive antitumor immune responses and effectively suppressed Hepatocellular carcinoma (HCC) tumor growth.

References:

- [1] XAVIER DA SILVA T N, SCHULTE C, ALVES A N, et al. Molecular characterization of AIFM2/FSP1 inhibition by iFSP1-like molecules [J]. Cell Death Dis, 2023, 14(4): 281.
- [2] CHEU J W, LEE D, LI Q, et al. Ferroptosis Suppressor Protein 1 Inhibition Promotes Tumor Ferroptosis and Anti-tumor Immune Responses in Liver Cancer [J]. Cell Mol Gastroenterol Hepatol, 2023, 16(1): 133-59.

Background

iFSP1 is a potent glutathione-independent ferroptosis suppressor protein 1 (FSP1) inhibitor , which has an EC₅₀ value of 103nM^[1]. iFSP1 inhibits ferroptosis by catalyzing the production of antioxidant CoQH₂ ^[2].

iFSP1 (6μM , 24h) will restore cancer cell sensitivity to ferroptosis ^[3] . iFSP1 (3μM , 3h) only exerts its function on hFSP1 but not mFSP1^[4]. iFSP1 (3μM , 24h) combined with CD36 overexpression induces the increasing synthesis of ferroptosis marker ACSL4 in Transformed C3H Mouse Kidney-1 (TCMK-1) cells upon the treatment of cisplatin^[5].

iFSP1 (10mg/kg/day ; 4 weeks ; intraperitoneal injection) potently induced ferroptosis, which promoted innate and adaptive antitumor immune responses and effectively suppressed Hepatocellular carcinoma (HCC) tumor growth^[6]. iFSP1 (2mg/kg/day ; 2 weeks ; intraperitoneal injection) and olaparib combined treatment strongly inhibited tumour proliferation in breast cancer susceptibility gene (BRCA)-proficient ovarian cancer cell lines , patient-derived organoids (PDOs) and xenograft mouse models^[7].

References:

- [1] DOLL S, FREITAS F P, SHAH R, et al. FSP1 is a glutathione-independent ferroptosis suppressor

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- [J]. Nature, 2019, 575(7784): 693-8.
- [2] TAO H, DAR H Y, TIAN C, et al. Differences in hepatocellular iron metabolism underlie sexual dimorphism in hepatocyte ferroptosis [J]. Redox Biol, 2023, 67(102892).
- [3] PANCZYSZYN E, SAVERIO V, MONZANI R, et al. FSP1 is a predictive biomarker of osteosarcoma cells' susceptibility to ferroptotic cell death and a potential therapeutic target [J]. Cell Death Discov, 2024, 10(1): 87.
- [4] XAVIER DA SILVA T N, SCHULTE C, ALVES A N, et al. Molecular characterization of AIFM2/FSP1 inhibition by iFSP1-like molecules [J]. Cell Death Dis, 2023, 14(4): 281.
- [5] MA Y, HUANG L, ZHANG Z, et al. CD36 promotes tubular ferroptosis by regulating the ubiquitination of FSP1 in acute kidney injury [J]. Genes Dis, 2024, 11(1): 449-63.
- [6] CHEU J W, LEE D, LI Q, et al. Ferroptosis Suppressor Protein 1 Inhibition Promotes Tumor Ferroptosis and Anti-tumor Immune Responses in Liver Cancer [J]. Cell Mol Gastroenterol Hepatol, 2023, 16(1): 133-59.
- [7] MIAO H, MENG H, ZHANG Y, et al. FSP1 inhibition enhances olaparib sensitivity in BRCA-proficient ovarian cancer patients via a nonferroptosis mechanism [J]. Cell Death Differ, 2024, 31(4): 497-510.

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