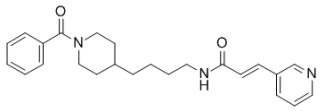
Data Sheet

Product Name:	FK866
Cat. No.:	HY-50876
CAS No.:	658084-64-1
Molecular Formula:	$C_{24}H_{29}N_3O_2$
Molecular Weight:	391.51
Target:	Autophagy; Nampt
Pathway:	Autophagy; Metabolic Enzyme/Protease
Solubility:	10 mM in DMSO



BIOLOGICAL ACTIVITY:

FK866 is an effective inhibitor of nicotinamide phosphoribosyltransferase (**NMPRTase**) with **IC_{50}** of 0.09 nM.
IC50 & Target: IC50: 0.09 nM (NMPRTase)
In Vitro: Nampt inhibition with FK866 induces significant NAD^+ intracellular reduction and selectively kills MM cells. FK866–induced cell death is associated with inhibition of Nampt activity, rather than protein expression, and higher NAD^+ baseline levels in MM cells than normal PBMCs confer FK866 sensitivity. FK866 abrogates the survival advantage conferred by the bone marrow microenvironment[1]. FK866 prevents the $[Ca^{2+}]i$ increase induced by different mitogens and reduces the Ca^{2+} content of TG–responsive Ca^{2+} stores in Jurkat and in activated PBLs. FK866 reduces the Ca^{2+} content of TG–responsive Ca^{2+} stores in Jurkat cells but not in Bcl2–Jurkat cells[2]. Inhibition of NAMPT by FK866, or inhibition of SIRT by nicotinamide decreases proliferation and triggered death of 293T cells involving the p53 acetylation pathway[3].
In Vivo: FK866 (30 mg/kg, i.p.) decreases the tumor burden in CB17–SCID mice, and the tumor tissue demonstrates a significant decrease in ERK phosphorylation and proteolytic cleavage of LC3[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]MM1S cells (2×10^4 cells/well) are cultured for 72 and 96 hours in BMSC–coated 96–well plates in the presence or absence of drug. DNA synthesis is measured by (^3H)–thymidine uptake, with (^3H)–thymidine added (0.5 μCi/well) during the last 8 hours of cultures.
Animal Administration: [1]CB17–SCID mice (28–35 days old) are irradiated (200 cGy), and then inoculated subcutaneously in the right flank with 3×10^6 MM1S cells in 100 μL RPMI 1640. After detection of tumor (2 weeks after the injection), 7 mice are treated intraperitoneally with either vehicle or FK866 (30 mg/kg body weight) twice a day for 4 days, repeated weekly over 3 weeks. Caliper measurements of the longest perpendicular tumor diameters are performed twice a week to estimate the tumor volume using the following formula: length×$width^2$×0.5. Tumor growth inhibition (TGI) is calculated. Animals are killed when tumors reach 2 cm^3 or the mice appear moribund. Survival is evaluated from the first day of treatment until death.

References:

[1]. Cea M, et al. Targeting NAD+ salvage pathway induces autophagy in multiple myeloma cells via mTORC1 and extracellular signal–regulated kinase (ERK1/2) inhibition. Blood. 2012 Oct 25;120(17):3519–29.
[2]. Magnone M, et al. NAD+ levels control Ca2+ store replenishment and mitogen–induced increase of cytosolic Ca2+ by Cyclic ADP–ribose–dependent TRPM2 channel gating in human T lymphocytes. J Biol Chem. 2012 Jun 15;287(25):21067–81.
[3]. Thakur BK, et al. Inhibition of NAMPT pathway by FK866 activates the function of p53 in HEK293T cells. Biochem Biophys Res Commun. 2012 Aug 3;

424(3):371–7.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA