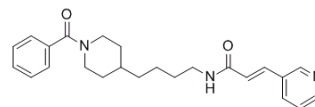


Data Sheet

Product Name:	FK866
Cat. No.:	HY-50876
CAS No.:	658084-64-1
Molecular Formula:	C ₂₄ H ₂₉ N ₃ O 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 **IC₅₀** 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 [Ca²⁺]_i increase induced by different mitogens and reduces the Ca²⁺ content of TG-responsive Ca²⁺ stores in Jurkat and in activated PBLs. FK866 reduces the Ca²⁺ content of TG-responsive Ca²⁺ 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 (2×10⁴ 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 3×10⁶ 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×width²×0.5. Tumor growth inhibition (TGI) is calculated. Animals are killed when tumors reach 2 cm³ 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;

Caution: Product has not been fully validated for medical applications. For research use only.

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