FM-381

Cat. No.: HY-102046

CAS No.: 2226521-65-7

Molecular Formula: $C_{24}H_{24}N_6O_2$

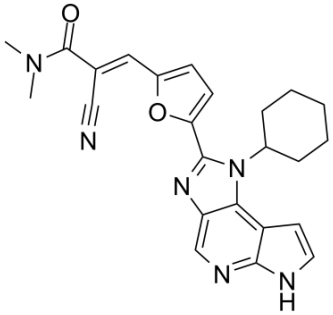
Molecular Weight: 428.49

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 8.33 mg/mL (19.44 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3338 mL	11.6689 mL	23.3378 mL
5 mM	0.4668 mL	2.3338 mL	4.6676 mL
10 mM	0.2334 mL	1.1669 mL	2.3338 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

FM-381 is a potent covalent reversible inhibitor of JAK3 targeting the unique Cys909. FM-381 has an IC_{50} of 127 pM for JAK3, with 410, 2700 and 3600-fold selectivity over JAK1, JAK2 and TYK2, respectively.

IC_{50} & Target

JAK3
127 pM (IC_{50})

In Vitro

FM-381 is screened against a panel of 410 kinases at concentrations of 100 nM and 500 nM. FM-381 has no relevant effect on the activity of any tested kinases except JAK3 at a concentration of 100 nM. At 500 nM, FM-381 moderately inhibits 11 other kinases besides JAK3 with residual activities below 50%. FM-381 is found to be inactive in a selectivity panel of frequently hit BRDs (BRD4, BRPF, CECR, FALZ, TAF1, BRD9). FM-381 selectively inhibits JAK3 signaling in human $CD4^+$ T Cells. FM-381 shows an apparent EC_{50} of 100 nM in a dose dependent BRET assay and blocks IL2 stimulated (JAK3/JAK1 dependent) STAT5 phosphorylation at 100 nM, but not JAK3 independent IL6 (JAK1/2/TYK dependent) stimulated STAT3 signalling in human $CD4^+$ T cells up to 1 μM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]

$CD4^+$ T Cell cytokine stimulation assay is performed. T cells are purified from peripheral blood mononuclear cells from human donors. Equal numbers of cells are incubated for 1 hr with JAK inhibitors (FM-381) (0, 10, 50, 100, 300 nM) or DMSO control and stimulated with cytokines for 30 min. The cells are lysed, and the proteins are separated via PAGE and transferred to a polyvinylidene fluoride membrane. The proteins of interest are blotted with specific antibodies and visualized with an infrared imaging system[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Forster M, et al. Selective JAK3 Inhibitors with a Covalent Reversible Binding Mode Targeting a New Induced Fit Binding Pocket. Cell Chem Biol. 2016 Nov 17;23(11):1335-1340.

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