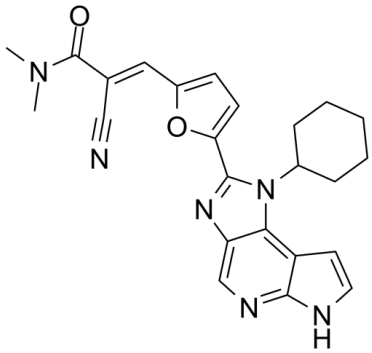
Data Sheet

Product Name:	FM381
Cat. No.:	CS-0022839
CAS No.:	2226521-65-7
Molecular Formula:	C24H24N6O2
Molecular Weight:	428.49
Target:	JAK
Pathway:	Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt
Solubility:	DMSO : 12.8 mg/mL (29.87 mM; Need ultrasonic and warming)



BIOLOGICAL ACTIVITY:

FM381 is a potent covalent reversible inhibitor of **JAK3** targeting the unique Cys909 at the gatekeeper position +7 in JAK3. FM-381 has an **IC_{50}** of 127 pM for JAK3, with 410, 2700 and 3600-fold selectivity over JAK1, JAK2 and TYK2, respectively. IC50 & Target: IC50: 127 pM (JAK3)[1] **In Vitro:** FM381 is screened against a panel of 410 kinases at concentrations of 100 nM and 500 nM. FM381 has no relevant effect on the activity of any tested kinases except JAK3 at a concentration of 100 nM. At 500 nM, FM381 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). Strongest hits is 500 nM for TAF1@2. FM381 selectively Inhibit JAK3 Signaling in Human CD4+ T Cells. FM-381 shows an apparent EC50 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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: FM381 is prepared in DMSO[1].[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 **(FM381) (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].

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.

CAIndexNames:

(E)-2-cyano-3-(5-(1-cyclohexyl-1,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridin-2-yl)furan-2-yl)-N,N-dimethylacrylamide

SMILES:

CN(C(/C(C#N)=C/C1=CC=C(C2=NC3=CN=C(NC=C4)C4=C3N2C5CCCCC5)O1)=O)C

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

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