Tanzisertib

Cat. No.: HY-15495

CAS No.: 899805-25-5

Molecular Formula: $C_{21}H_{23}F_3N_6O_2$

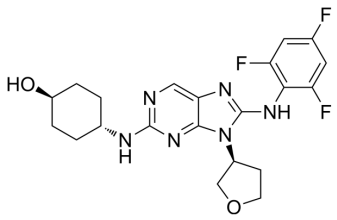
Molecular Weight: 448.44

Target: JNK

Pathway: MAPK/ERK Pathway

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

1M HCl : 100 mg/mL (223.00 mM; ultrasonic and adjust pH to 1 with HCl)

DMSO : ≥ 33 mg/mL (73.59 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2300 mL	11.1498 mL	22.2995 mL
5 mM	0.4460 mL	2.2300 mL	4.4599 mL
10 mM	0.2230 mL	1.1150 mL	2.2300 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.57 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.57 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.57 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tanzisertib (CC-930) is a potent JNK1/2/3 inhibitor with IC_{50}s of 61/7/6 nM, respectively.

IC_{50} & Target

JNK3	JNK2	JNK1
6 nM (IC_{50})	7 nM (IC_{50})	61 nM (IC_{50})

In Vitro	Tanzisertib (CC-930) inhibits the formation of phospho-cJun in human PBMC stimulated by phorbol-12-myristate-13-acetate and phytohemeagglutinin (IC_{50}=1 μM)[1]. Tanzisertib (CC-930) (1-2 μM) substantially reduces hepatocyte apoptosis and necrosis, abrogates apoptosis and necrosis in FC-loaded WT hepatocytes[2]. Tanzisertib (CC-930) blocks the JNK pathway that is activated by pro-fibrotic cytokines in systemic sclerosis[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tanzisertib (CC-930) (10 and 30 mg/kg, p.o.) inhibits the production of TNFa by 23% and 77% in the acute rat LPS-induced TNFa production PK-PD model[1]. Tanzisertib (CC-930) (150 mg/kg) prevents the development of fibrosis in different models, but can also induce the regression of pre-existing fibrosis[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	Systemic sclerosis (SSc) fibroblasts are incubated with 1 μM Tanzisertib (CC-930) in 96-well plates for 20 h. Then MTT is added at a final concentration of 1 mg/mL, and the cells are further incubated at 37°C for 4 h. Mock-treated fibroblasts are used as controls, and all other results are normalised to untreated cells. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	To evaluate the regression of fibrosis on inhibition of JNK, a modified model of bleomycin-induced dermal fibrosis is used. In this model, treatment is initiated 3 weeks after the beginning of the challenge with bleomycin, when significant dermal fibrosis is already established. The outcome of six different groups with a total number of 40 mice is analysed. The first group of mice receive subcutaneous injections of NaCl for 6 weeks. The second group is injected for 3 weeks with bleomycin followed by injections of NaCl for another 3 weeks to analyse the degree of fibrosis before treatment, and to control the spontaneous regression of fibrosis. The third group of mice is killed after 6 weeks of injections with bleomycin. The fourth and the fifth group are treated with Tanzisertib (CC-930) at doses of 50 mg/kg and 150 mg/kg for the last 3 weeks of continuous challenge with bleomycin for 6 weeks. The sixth group is a positive control group consisting of mice challenged with bleomycin for 6 weeks and treated in parallel with imatinib at doses of 50 mg/kg for the last 3 weeks. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Science. 2017 Dec 1;358(6367):eaan4368.
- Nat Cell Biol. 2017 Jun;19(6):698-710.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Nat Commun. 2020 Jan 3;11(1):71.
- Cell Death Differ. 2020 May;27(5):1569-1587.

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REFERENCES

[1]. Lay T Gan, et al. Hepatocyte free cholesterol lipotoxicity results from JNK1-mediated mitochondrial injury and is HMGB1 and TLR4-dependent. J Hepatol. 2014 Dec;61(6):1376-84.

[2]. Nicole Reich, et al. Jun N-terminal kinase as a potential molecular target for prevention and treatment of dermal fibrosis. Ann Rheum Dis. 2012 May;71(5):737-45.

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

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