PI4KIII beta inhibitor 3

Cat. No.: HY-15679

CAS No.: 1245319-54-3

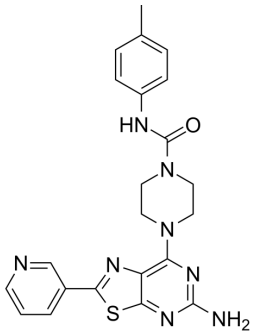
Molecular Formula: $C_{22}H_{22}N_8OS$

Molecular Weight: 446.53

Target: PI4K

Pathway: PI3K/Akt/mTOR

Storage: 4°C, protect from light
* In solvent : -80°C, 2 years; -20°C, 1 year (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (44.79 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	2.2395 mL	11.1975 mL	22.3949 mL
	5 mM	0.4479 mL	2.2395 mL	4.4790 mL
	10 mM	0.2239 mL	1.1197 mL	2.2395 mL

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

BIOLOGICAL ACTIVITY

Description

PI4KIII beta inhibitor 3 is a novel and high effective PI4KIIIβ inhibitor with IC_{50} of 5.7 nM.

IC_{50} & Target

PI4KIIIβ
5.7 nM (IC_{50})

In Vitro

PI4KIII beta inhibitor 3 is a PI4KIII inhibitor extracted from patent WO/2013034738 A1, the compound of formula 3, has an IC_{50} of 5.7 nM. PI4KIII beta inhibitor 3 exerts significant immunosuppressive activity, with IC_{50} value of 3 nM in the mixed lymphocyte reaction (MLR) assay. PI4KIII beta inhibitor 3 inhibits IL2 and IFNy secretion with IC_{50} values of less than InM in each case. Thus, PI4KIII beta inhibitor 3 is shown to be as effective at inhibiting IL2 and IFNy secretion as conventional immunosuppressants such as cyclosporine A. IC_{50} on IFNy and IL-2 release of Cyclosporine A are 2nM and less than 1 nM respectively[1].

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

In Vivo

PI4KIII beta inhibitor 3 (40 mg/kg per day, n=12) is able to delay the onset of arthritic symptoms and also to decrease symptom severity in a preventive model of arthritis compared to a vehicle control (MC 1%, n=12). PI4KIII beta inhibitor 3 reduces the anti-CII IgG titre and histological scores in the collagen-induced arthritis mouse model. Oral administration of PI4KIII beta inhibitor 3 results in prolonged graft survival in 3 out of 6 grafts in each group at day 30. Several grafts continued

beating after withdrawal of the treatment (up to 60 days), indicating the induction of a certain type of graft tolerance. To evaluate the operational tolerance phenotype, animals with functional graft at day 60 are challenged with a second graft from the same donor strain or from a third party. No treatment is applied. The second grafts from the third party are rejected at day 8 (n=2) whereas second grafts from the same donor strain are functional for more than 90 days (n=2)[1].

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PROTOCOL

Animal Administration [1]

Mice[1]

DBA1 male mice, 8-10 weeks old, are distributed in 2 groups according to the treatment. Twelve animals received daily treatment with vehicle (1% methylcellulose), twelve others receive PI4KIII beta inhibitor 3 at 40 mg/kg/d in 1% methylcellulose. The treatment initiation started the day before the intradermal injection at the base of the tail of 100 µg of emulsified chicken collagen II in presence of complete Freund adjuvant and added heat-killed Mycobacterium butyricum. Daily inspection of the mice is performed to weight animals and quantify disease score according to the following scale (score 0: normal; score 1 : redness and/or swelling in one joint; score 2: redness and/or swelling in more than one joint; score 3: redness and/or swelling in the entire paw; score 4: deformity and/or ankylosis). On the day of sacrifice (day 42) serum are collected and anti-collagen II antibody titers are determined by ELISA. Joints are harvested, fixed in 6% paraformaldehyde, decalcified in formic acid 6% for 48 h, sliced and stained by hematoxylin and eosin staining. Hyperplasia of the synovium, infiltration of mono and polymorphonuclear cells and pannus formation parameters are scored blindly.

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

CUSTOMER VALIDATION

- bioRxiv. 2023 Feb 23.
- Patent. US20220273624A1.

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REFERENCES

[1]. Jean Herman, et al. Autoimmune and inflammatory disorder therapy. From PCT Int. Appl. (2013), WO 2013034738 A1

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