YKL-05-099

Cat. No.: HY-101147

CAS No.: 1936529-65-5

Molecular Formula: $C_{32}H_{34}ClN_7O_3$

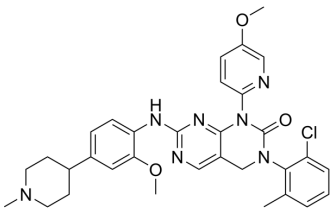
Molecular Weight: 600.11

Target: Salt-inducible Kinase (SIK)

Pathway: Immunology/Inflammation

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 75 mg/mL (124.98 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6664 mL	8.3318 mL	16.6636 mL
5 mM	0.3333 mL	1.6664 mL	3.3327 mL
10 mM	0.1666 mL	0.8332 mL	1.6664 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 (4.17 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.17 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.17 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

YKL-05-099 is a salt-inducible kinase (SIK) inhibitor. YKL-05-099 binds to SIK1 and SIK3 with IC_{50}s of ~10 and ~30 nM, respectively. YKL-05-099 has slightly less potent SIK2-inhibitory (IC_{50}=40 nM)[1].

IC_{50} & Target	SIK1	SIK3

In Vitro

YKL-05-099 has slightly less potent SIK2-inhibitory (IC_{50}=40 nM) and IL-10-enhancing activities (EC_{50}=460 nM). YKL-05-099

	binds to SIK1 and SIK3 with IC_{50}s of 10 and 30 nM, respectively, in a competitive binding assay. Preincubating bone marrow-derived macrophages with YKL-05-099 reduces LPS stimulated phosphorylation of HDAC5 at the SIK-specific phosphorylation site Ser259. YKL-05-099 suppresses production of the inflammatory cytokines TNFα, IL-6 and IL-12p40, and only modestly enhances IL-1β release in BMDCs stimulated with the yeast cell wall extract Zymosan A[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	YKL-05-099 is non-toxic at concentrations less than 10 μM and stable in mouse liver microsomes for more than 2 hours. YKL-05-099 is highly soluble (PBS solubility=428 μM) and present in an unbound state at appreciable levels in mouse plasma. YKL-05-099 dose dependently decreases phosphorylation of HDAC5 at the SIK-regulated site Ser259; reduced phosphorylation is observed at the lowest dose (5 mg/Kg) and is below the limit of detection by immunoblotting beginning at the 20 mg/Kg dose. YKL-05-099 dose-dependently reduces abundance of TNFα in serum beginning at 5 mg/Kg, and increases IL-10 levels at the 20 mg/Kg dose by more than 2-fold[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice: YKL-05-099 is diluted in 5% N-methyl-2-pyrrolidinone, 5% Solutol HS15 and 90% normal saline and administered IP to male 8–10 week-old C57BL/6 mice. Serum and tissue samples are collected after euthanizing mice by CO_2 inhalation overdose followed by cervical dislocation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- JCI Insight. 2022 May 10;e150363.
- Patent. US20200246435A1.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Sundberg TB, et al. Development of Chemical Probes for Investigation of Salt-Inducible Kinase Function in Vivo. ACS Chem Biol. 2016 Aug 19;11(8):2105-11.

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