GNF4877

Cat. No.: HY-129492

CAS No.: 2041073-22-5

Molecular Formula: $C_{25}H_{27}FN_6O_4$

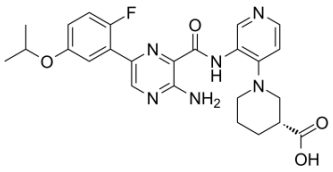
Molecular Weight: 494.52

Target: DYRK; GSK-3

Pathway: Protein Tyrosine Kinase/RTK; PI3K/Akt/mTOR; 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 : 4.17 mg/mL (8.43 mM; Need ultrasonic and warming)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0222 mL	10.1108 mL	20.2216 mL
5 mM	0.4044 mL	2.0222 mL	4.0443 mL
10 mM	---	---	---

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

BIOLOGICAL ACTIVITY

Description

GNF4877 is a potent DYRK1A and GSK3β inhibitor with IC_{50}s of 6 nM and 16 nM, respectively, which leads to blockade of nuclear factor of activated T-cells (NFATc) nuclear export and increased β-cell proliferation (EC_{50} of 0.66 μM for mouse β (R7T1) cells)[1].

IC_{50} & Target

GSK3β	DYRK1A
16 nM (IC_{50})	6 nM (IC_{50})

In Vitro

High glucose concentrations and glucokinase activators (GKAs) increase Ca^{2+} signalling in β-cells, and increase intracellular Ca^{2+} leads to activation of calcineurin and nuclear translocation of NFATc proteins. Indeed, concentrations of GNF4877 ((0.1 μM, 0.3 μM) well below the EC_{50} for β-cell proliferation are able to induce proliferation in the presence of high glucose or pharmacological activators of glucokinase. Finally, increasing intracellular Ca^{2+} with glibenclamide (a sulfonylurea receptor 1 inhibitor) or Bay K8644 (an L-type Ca^{2+} channel activator) show additive activity with GNF4877[1].

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

In Vivo

GNF4877 (50 mg/kg; oral gavage; twice a day; for 15 days; double transgenic RIP-DTA male mice) treatment induces β-cell

proliferation, increases β-cell mass and insulin content, and improves glycaemic control[1].

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

Animal Model:	Double transgenic RIP-DTA male mice (Tg (Ins 2-rtTA) 2 Efr Tg (teto-DTA) 1 Gfi/J) with Doxycycline (28.8±2.4 g; 82±2 days)[1]
Dosage:	50 mg/kg
Administration:	Oral gavage; twice a day; for 15 days
Result:	Induced β-cell proliferation, increased β-cell mass and insulin content, and improved glycaemic control.

REFERENCES

[1]. Shen W, et al. Inhibition of DYRK1A and GSK3β induces human β-cell proliferation. Nat Commun. 2015 Oct 26;6:8372.

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