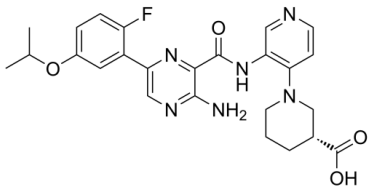
Data Sheet

Product Name:	GNF4877
Cat. No.:	CS-0105879
CAS No.:	2041073-22-5
Molecular Formula:	$C_{25}H_{27}FN_6O_4$
Molecular Weight:	494.52
Target:	DYRK; GSK-3
Pathway:	PI3K/Akt/mTOR; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt
Solubility:	DMSO : 4.17 mg/mL (8.43 mM; Need ultrasonic and warming)



BIOLOGICAL ACTIVITY:

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]. ***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]. ***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].

References:

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

CAIndexNames:

3-Piperidinecarboxylic acid, 1-[3-[[[3-amino-6-[2-fluoro-5-(1-methylethoxy)phenyl]-2-pyrazinyl]carbonyl]amino]-4-pyridinyl]-, (3R)-

SMILES:

O=C([C@H]1CN(C2=C(NC(C3=NC(C4=CC(OC(C)C)=CC=C4F)=CN=C3N)=O)C=NC=C2)CCC1)O

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

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