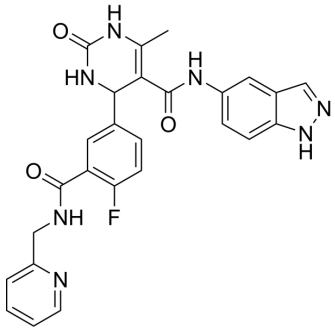
CCG215022

Cat. No.:	HY-18991
CAS No.:	1813527-81-9
Molecular Formula:	$C_{26}H_{22}FN_7O_3$
Molecular Weight:	499.5
Target:	PKA
Pathway:	Stem Cell/Wnt; TGF-beta/Smad
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 : ≥ 28 mg/mL (56.06 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0020 mL	10.0100 mL	20.0200 mL
5 mM	0.4004 mL	2.0020 mL	4.0040 mL
10 mM	0.2002 mL	1.0010 mL	2.0020 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 (5.01 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.01 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

CCG215022 is a G protein-coupled receptor kinases (GRKs) inhibitor with IC_{50}s of 0.15±0.07 μM, 0.38±0.06 μM and 3.9±1 μM for GRK2, GRK5 and GRK1, respectively.

IC_{50} & Target

IC50 & Target: 3.9±1.0 μM (GRK1), 0.15±0.07 μM (GRK2), 0.38±0.06 μM (GRK5), 120±40 μM (PKA)[1]

In Vitro

CCG215022 has nanomolar potency against both GRK2 and GRK5 and is at least 20-fold more potent than Paroxetine. In the course of a GRK2 structure-based drug design campaign, CCG215022 exhibits nanomolar IC_{50} values against both GRK2 and GRK5 and good selectivity against other closely related kinases such as GRK1 and PKA. Treatment of murine cardiomyocytes with CCG215022 results in significantly increases contractility at 20-fold lower concentrations than Paroxetine, an inhibitor

with more modest selectivity for GRK2[1].

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

PROTOCOL

Kinase Assay [1]

GRK5 and urea-washed bovine rod outer segments (ROS) are mixed in the dark in buffer containing 20 mM HEPES, pH 7.5, 4 mM $MgCl_2$, and 2 mM EDTA and incubated for 35 min at room temperature. The reaction mixtures are exposed to ambient fluorescent light for 1 min prior to initiation of the reaction by addition of ATP (with [γ-^{32}P]ATP) to a final concentration of 1 mM. Final concentration of GRK5 is 100 nM and ROS is between 0.75 and 24 μM. Reactions are initiated at room temperature, and samples are taken at 2-5 min and then quenched with SDS-PAGE loading dye. Proteins are separated using SDS-PAGE, gel is dried, and the incorporation of γ-^{32}P is detected using a phosphor storage screen. Rates at 0 min are plotted against the ROS concentration, and Vmax and Kmvalues are determined using the Michaelis-Menten equation. Vmax of each curve is normalized to the Vmax of GRK5561 run in parallel. Melting point determinations in response to 200 μM CCG215022 are performed in 20 mM HEPES, pH 7.0, 5 mM $MgCl_2$, 2 mM DTT, 1 mM CHAPS at a final GRK5 concentration of 0.2 mg/mL and 100 μM anilinonaphthalene-8-sulfonic acid using a ThermoFluor plate reader. Melting points of GRK5 variants are assayed in a buffer containing 20 mM HEPES, pH 8.0, 200 mM NaCl, 2 mM DTT, 2.5 mM $MgCl_2$, and 0.1 mM anilinonaphthalene-8-sulfonic acid with or without 5 mM ATP. Final GRK5 concentration for these assays is 0.1 mg/mL[1].

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

CUSTOMER VALIDATION

- Nat Metab. 2023 Mar 6.
- Am J Hum Genet. 2020 Aug 6;107(2):211-221.
- Commun Biol. 2020 Jan 15;3(1):27.

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REFERENCES

[1]. Homan KT, et al. Crystal Structure of G Protein-coupled Receptor Kinase 5 in Complex with a Rationally DesignedInhibitor. J Biol Chem. 2015 Aug 21;290(34):20649-59.

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