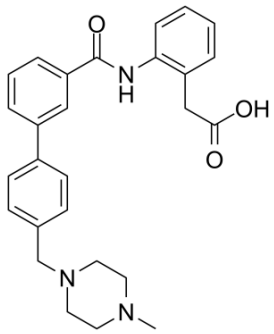
NF-56-EJ40



Cat. No.:	HY-130246		
CAS No.:	2380230-73-7		
Molecular Formula:	$C_{27}H_{29}N_3O_3$		
Molecular Weight:	443.54		
Target:	Others		
Pathway:	Others		
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 : 5 mg/mL (11.27 mM; Need ultrasonic)

H_2O : 4.55 mg/mL (10.26 mM; ultrasonic and adjust pH to 9 with NaOH)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2546 mL	11.2729 mL	22.5459 mL
5 mM	0.4509 mL	2.2546 mL	4.5092 mL
10 mM	0.2255 mL	1.1273 mL	2.2546 mL

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

BIOLOGICAL ACTIVITY

Description

NF-56-EJ40 is a potent, high-affinity, and highly selective human SUCNR1 (GPR91) antagonist with an IC_{50} of 25 nM and a K_i of 33 nM, and shows almost no activity towards rat SUCNR1. NF-56-EJ40 has high affinity for humanized rat SUCNR1 with a K_i value of 17.4 nM[1].

IC_{50} & Target

SUCNR1 (GPR91)[1]

In Vitro

NF-56-EJ40 is bound deep inside the hydrophobic pocket, with the acid group coordinated by the hydroxyl groups of the conserved residues $Y83^{2.64}$ and $Y30^{1.39}$ on one side, and $R281^{7.39}$ on the other side. The conserved $E18^{1.27}$ is predicted to form an additional hydrogen bond to the piperazine ring of NF-56-EJ40. $E22^{1.31}$ and $N274^{7.32}$ in human SUCNR1 are replaced by K181.31 and $K269^{7.32}$ in rat SUCNR1. These two amino acid exchanges could prevent the binding of NF-56-EJ40 to rat SUCNR1 owing to steric hindrance. Radioligand-binding studies with human SUCNR1 showed partial agreement with our homology model: the $Y30^{1.39}$F mutant of human SUCNR1, shows reduced binding of NF-56-EJ40. Similar effects are observed with the $E18^{1.27}$K and $E18^{1.27}$R mutants, probably owing to steric clashes of the Lys and Arg residues with NF-56-EJ40 and the loss of a hydrogen bond to its piperazine ring[1].

Human SUCNR1 residues are introduced into rat SUCNR1 to form the double mutant K18$^{1.31}$E/K269$^{7.32}$N (hereafter denoted humanized rat SUCNR1) (K_i of 17.4 nM and 33.5 nM for human and humanized rat SUCNR1, respectively). NF-56-EJ40 increases the thermal stability of both humanized rat SUCNR1 and human SUCNR1, but not that of rat SUCNR1[1].

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

REFERENCES

[1]. Haffke M, et al. Structural basis of species-selective antagonist binding to the succinate receptor. Nature. 2019 Oct;574(7779):581-585.

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