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DATASHEET

JHU37152 (DREADD ligand)

Product overview

Name	JHU37152 (DREADD ligand)
Cat No	HB6252
Alternative names	J52
Purity	>98%
Description	Novel DREADD agonist with high affinity and potency for hM3Dq and hM4Di. Active in vivo. Freebase.

Images

Biological Data

Biological description

Overview

JHU37152 is reported to be a novel DREADD agonist with high in vivo DREADD potency for CNS applications.

It has high affinity in vitro for hM3Dq and hM4Di (K_i values are 1.8 nM (hM3Dq) and 8.7 nM (hM4Di).

It selectively displaces [^{3}H]clozapine from DREADDs and not from other clozapine-binding sites at concentrations up to 10 nM when tested for in situ [3H]clozapine displacement in brain tissue from WT and D_1-DREADD mice.

JHU37152 activates hM3Dq and hM4Di with high potency and efficacy in fluorescent and BRET-based assays in HEK-293 cells (EC_{50} values are 5 and 0.5 nM at hM3Dq and hM4Di respectively.

Occupancy

JHU37152 exhibits high in vivo DREADD occupancy and was not reported to be a P-gp substrate.

In vivo application

JHU37152 is reported to be a potent in vivo DREADD agonist, which selectively inhibits locomotor activity in D_1-hM3Dq and D_1-hM4Di mice without any significant locomotor effects observed in wild type (WT) mice (at doses ranging 0.01 - 1 mg/kg).

It also produces robust and selective increases in hM3Dq-stimulated locomotion in rats expressing hM3Dq in tyrosine hydroxylase expressing neurons (at doses ranging 0.01 – 0.3 mg/kg).

While its selectivity is not ideal (i.e. comparable to clozapine), its high in vivo potency allows for dose adjustments with minimal off-target effects. The compound exhibits promising characteristics for DREADD use in monkeys.

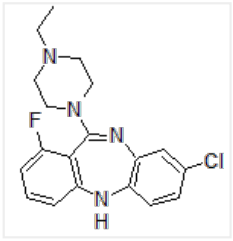
Water soluble version also available.

Sold under license from the NIH, US patent pending 62/627,527

Solubility & Handling

Storage instructions	Room temperature
Solubility overview	Soluble in DMSO (100 mM)
Important	This product is for RESEARCH USE ONLY and is not intended for therapeutic or diagnostic use. Not for human or veterinary use

Chemical Data

Chemical name	8-chloro-11-(4-ethylpiperazin-1-yl)-1-fluoro-5H-dibenzo[b,e][1,4]diazepine
Molecular Weight	358.84
Chemical structure	
Molecular Formula	$C_{19}H_{20}ClFN_4$
CAS Number	2369979-67-7
PubChem identifier	0
SMILES	CCN1CCN(CC1)C2=Nc4cc(Cl)ccc4Nc3cccc(F)c23
Source	Synthetic
InChi	InChI=1S/C19H20ClFN4/c1-2-24-8-10-25(11-9-24)19-18-14(21)4-3-5-16(18)22-15-7-6-13(20)12-17(15)23-19/h3-7,12,22H,2,8-11H2,1H3
InChiKey	NZMZJNNWMSYDNX-UHFFFAOYSA-N
Appearance	Yellow solid
Licensing details	Sold under license from the NIH, US patent pending 62/627,527

References

Chemogenetic ligands for translational neurotheranostics

Bonaventura et al (2018) bioRxiv doi: https://doi.org/10.1101/487

High-potency ligands for DREADD imaging and activation in rodents and monkeys.

Bonaventura et al (2019) Nat Commun. 10(1)
PubMedID 31604917

0067 Humanized Chemogenetic Approach to Treat Sleep Apnea

Curado et al (2019) Sleep (42)

OP-01-02 Graft-host synaptic connectivity can be chemogenetically inhibited with clinically relevant activators to eliminate graft-induced dyskinesias (GID) without loosing anti-parkinsonian benefits of dopaminergic grafts

Subramanian et al (2019) World Congress On Parkinson's Disease And Related Disorders 2019 Poster abstract

DREADDs: The Power of the Lock, the Weakness of the Key. Favoring the Pursuit of Specific Conditions Rather than Specific Ligands.

Goutaudier et al (2019) eNeuro 6
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