JNJ-54082730: A Chemical Probe for PDE2A

Version 1.0 (18th June 2024)

Web link for more details: https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/JNJ-54082730

Overview

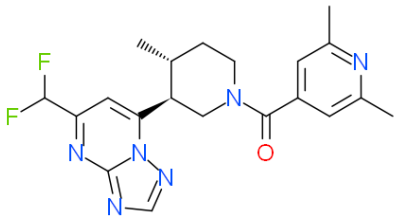
PDE2A is a dual cGMP/cAMP phosphodiesterase that is predominantly expressed in brain. Inhibition increases cellular cGMP/cAMP concentrations that leads to the activation of CREB-mediated gene transcription (e.g. BDNF). It plays a role in synaptic plasticity to restore cognitive function in Alzheimer disease.

Summary

Chemical Probe Name	JNJ-54082730
Negative control compound	JNJ-54103985
Target(s) (synonyms)	PDE2A (Phosphodiesterase 2A)
Recommended *in vitro* assay concentration	Use with control for best interpretation of data
Suitability for *in* vivo use and recommended dose	Tested in dogs (dose: 0.5 – 1 mg/kg) and rats. Binds to PDE2 in rat brain with the occupancy correlating with exposure (dose: 0.6 to 40 mg/kg, PO, 1 h). Enhances cGMP in primary rat hippocampal cultures; Functional cGMP increase in dog CSF (cerebrospinal fluid).
Publications	None at time of publication
In vitro assay(s) used to characterise	Scintillation proximity assay (SPA)
Cellular assay(s) for target-engagement	Target occupancy Striatum

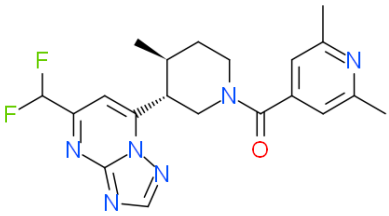
Chemical Probe & Negative Control Structures and Use

JNJ-54082730 Chemical Probe



SMILES: Cc1cc(cc(C)n1)C(N1CC[C@@H](C)[C@@H](C1)c1cc(C(F)F)nc2ncnn12)=O
InChiKey: OKZITNMVZCTKEZ-IAQYHMDHSA-N
Molecular weight: 400.18 g/mol
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C. DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use
Dissolution: Soluble in DMSO up to 10 mM; use only 1 freeze/thaw cycle per aliquot

JNJ-54103985 Negative Control



SMILES: Cc1cc(cc(C)n1)C(N1CC[C@H](C)[C@H](C1)c1cc(C(F)F)nc2ncnn12)=O

InChiKey: OKZITNMVZCTKEZ-NHYWBVRUSA-N
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Chemical Probe Profile

In vitro Potency & Selectivity:

JNJ-54082730 is a potent PDE2A inhibitor with IC_{50} = 0.9 nM (n=93, SPA). The PDE panel (SPA) is clean with the closest hits hPDE10A2 (IC_{50} = 99 nM) and hPDE3 (IC_{50} = 6.64 µM). The Eurofins Cerep panel and the DiscoverX KinaseScreen are clean.

Potency in Cells and Cellular Target Engagement:

The target occupancy for the Striatum is ED_{50} = 5.3 mg/kg (p.o. 1 h).