

JNJ-6204: Dual Chemical Probe for CSNK1D, CSNK1E

Version 1.0 (25th July 2022)



Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/JNJ-6204>

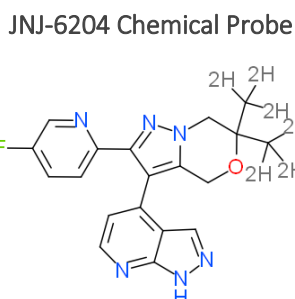
Overview

[CSNK1D](#) and [CSNK1E](#) are essential serine/threonine-protein kinases which regulate many cellular growth and survival processes including DNA repair and circadian rhythms. CSNK1D can phosphorylate a large number of proteins such as Tau, α -synuclein, TDP-43 and PER2. CSNK1E has been shown to interact with PER1 and AXIN1. Pathologies associated with increased CSNK1D expression/activity are oncology, metabolic, neurodegenerative and mood/psychiatric disorders.

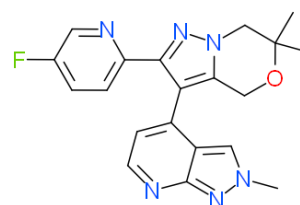
Summary

Chemical Probe Name	JNJ-6204
Negative control compound	JNJ-0293
Target(s) (synonyms)	CSNK1D (Casein Kinase 1 Delta, CK1D), CSNK1E (Casein Kinase 1 Epsilon, CK1E)
Recommended <i>in vitro</i> assay concentration	Use at concentration up to 1 μ M for JNJ-6204 and JNJ-0293; use with control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Tested in mice with 5 mg/kg po, 1 mg/kg iv dosage; shows good brain exposure in mice.
Publications	WO2022058920A1
<i>In vitro</i> assay(s) used to characterise	ADP-Glo with purified enzyme
Cellular assay(s) for target-engagement	BRET whole cell binding assay and PER2 translocation whole cell functional assay

Chemical Probe & Negative Control Structures and Use



JNJ-0293 Negative Control



SMILES: [2H]C1([2H])Cn2c(CO1)c(c1ccnc3c1cn[nH]3)c(c1ccc(cn1)F)n2

InChiKey: UAPTUVNFZRAYXQI-UHFFFAOYSA-N

Molecular weight: 338.11 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

SMILES: CC1(C)Cn2c(CO1)c(c1ccnc3c1cn(C)n3)c(c1ccc(cn1)F)n2

InChiKey: MNCAUYFDXJSKPL-UHFFFAOYSA-N

Molecular weight: 378.16 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

Chemical Probe Profile

In vitro Potency & Selectivity:

JNJ-6204 shows potent activity on human CSNK1D (IC_{50} = 2.3 nM) and CSNK1E (IC_{50} = 137 nM) (ADP-Glo assay). Closest hits in a panel of 370 kinases at 1 μ M are the related kinase CSNK1A1 (IC_{50} = 419 nM) and TNIK (IC_{50} = 1.6 μ M).

Potency in Cells and Cellular Target Engagement:

For CSNK1D the IC_{50} was 72 nM in the BRET whole cell binding assay and 542 nM in the PER2 translocation whole cell functional assay.