

JNJ-79883960: A Chemical Probe for NLRP3

Version 1.0 (9th April 2025)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/JNJ-79883960>

Overview

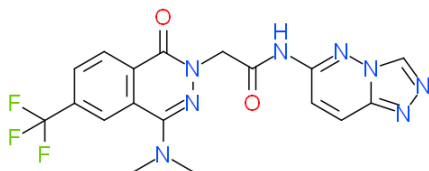
NLRP3 builds together with the adaptor apoptosis speck (ASC) protein, pro-caspase-1 and other proteins the NLRP3 inflammasome which is a prion like complex. The activated NLRP3 inflammasome results in an immune response with release of IL-1 β and IL-18 - a key pro-inflammatory cytokine. Pre-clinically NLRP3 has been shown to be linked to over 50 potential pathologies, driven by inflammation.

Summary

Chemical Probe Name	JNJ-79883960
Negative control compound	JNJ-78832000
Target(s) (synonyms)	NLRP3 (NLR family pyrin domain containing 3)
Recommended <i>in vitro</i> assay concentration	Use at concentration up to 10 μ M for JNJ-79883960 and JNJ-78832000; use with control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Tested in mouse with 5mpk PO and 1 mpk IV, no brain penetration.
Publications	PMID: 39653810 (Compound: A)
<i>In vitro</i> assay(s) used to characterise	Target engagement checked with: Nano-DSF, HDx –Hydrogen/Deuterium exchange, ATPase activity, Cryo-EM
Cellular assay(s) for target-engagement	NLRP-3 cell assay

Chemical Probe & Negative Control Structures and Use

JNJ-79883960 Chemical Probe



SMILES: CN(C)C1c2cc(ccc2C(N(CC(Nc2ccc3nncn3n2)=O)N=1)=O)C(F)(F)F

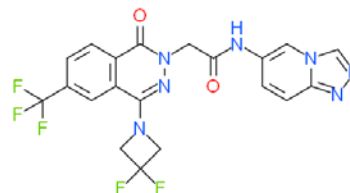
InChiKey: DYDFSGCLYZSAQ-UHFFFAOYSA-N

Molecular weight: 432.13 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-78832000 Negative Control



SMILES: C(C(Nc1ccc2nncn2c1)=O)N1C(c2ccc(cc2C(=N1)N1CC(C1)(F)F)C(F)(F)F)=O

InChiKey: QYHROBCDRVECQE-UHFFFAOYSA-N

Molecular weight: 479.11 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

Chemical Probe Profile

In vitro Potency & Selectivity:

The target engagement was tested with Nano-DSF, HDx –Hydrogen/Deuterium exchange, ATPase activity and generated Cryo-EM (<3Å).

Potency in Cells and Cellular Target Engagement:

JNJ-79883960 shows a high potency for NLRP3 in the NLRP-3 cell assay with IL1- β inhibition in PBMC cells (IC₅₀ = 27.6 nM), but not with IL-6 or TNF inhibition (IC₅₀ > 20 μ M) in the same assay.