

JNJ-9350: A Chemical Probe for SMOX

Version 1.0 (6th September 2022)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!/specificprobeoverview/JNJ-9350>

Overview

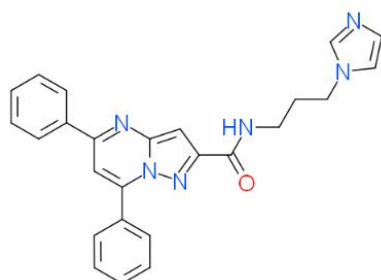
SMOX is a polyamine catabolic enzyme that is induced by inflammatory stimuli resulting in increased reactive oxygen species (ROS) and DNA damage. It catalyzes the conversion of spermine in the presence of oxygen to spermidine, 3-aminopropanol and hydrogen peroxide. SMOX plays an important oncogenic role in human and has been found in several epithelial cancers such as colorectal cancer, gastric cancer, prostate cancer, hepatocellular carcinoma.

Summary

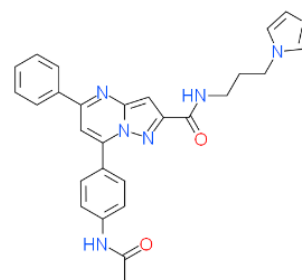
Chemical Probe Name	JNJ-9350
Negative control compound	JNJ-4545
Target(s) (synonyms)	SMOX (spermine oxidase)
Recommended <i>in vitro</i> assay concentration	Use at concentration up to 10 μ M for JNJ-9350 and JNJ-4545; use with control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Tested in mice with oral (10 mg/kg) and intravenous (2 mg/kg) administration.
Publications	None at time of writing
<i>In vitro</i> assay(s) used to characterise	HyperBlue enzymatic assay
Cellular assay(s) for target-engagement	SMOX CETSA

Chemical Probe & Negative Control Structures and Use

JNJ-9350 Chemical Probe



JNJ-4545 Negative Control



SMILES: C(CNC(c1cc2nc(cc3ccccc3)n2n1)c1ccccc1)=O)Cn1ccnc1

InChiKey: RIGHCDSORZCRDE-UHFFFAOYSA-N

Molecular weight: 422.19 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: CC(Nc1ccc(cc1)c1cc(c2ccccc2)nc2cc(C(NCCCn3ccnc3)=O)nn12)=O

InChiKey: LUURZPBLEVSXGP-UHFFFAOYSA-N

Molecular weight: 479.21 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-9350 is a potent SMOX inhibitor with IC_{50} = 10 nM (HyperBlue assay) and K_i = 9.9 nM in a Horseradish Peroxidase Fluorescence Assay. It shows a good selectivity vs PAOX (IC_{50} = 790 nM, 79-fold) and KDM1A (IC_{50} > 60 μ M) (HyperBlue assay). Closest off-targets in the CEREP panel at 10 μ M (% inhibition) are ADORA1 (98.93), ADORA2A (74.96) and ADORA3 (75.06).

Potency in Cells and Cellular Target Engagement:

JNJ-9350 shows 91 - 108 % recovery of SMOX at 54 °C in a SMOX CETSA assay with IC_{50} = 1.2. μ M.