

MSC-4381: A Chemical Probe for SLC16A3

Version 1.0 (20th October 2021)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!/specificprobeoverview/MSC-4381>

Overview

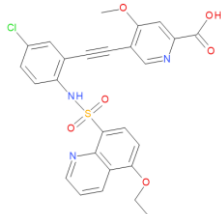
[SLC16A3](#) is a member of the proton-linked monocarboxylate transporter (MCT) family and is highly expressed in tissues with increased glycolysis. The transporter plays a key physiological role in the export of lactate out of the cell and is upregulated through hypoxia. SLC16A3 is one of the most relevant isoforms in tumour pathology. Increased SLC16A3 expression leads to increased extracellular lactate, resulting in tumour growth, metastasis formation and immune suppression.

Summary

Chemical Probe Name	MSC-4381
Negative control compound	MSC-0516
Target(s) (synonyms)	SLC16A3 (MCT4, monocarboxylate transporter 4, solute carrier family 16 member 3)
Recommended <i>in vitro</i> assay concentration	Use at concentration up to 10 μ M for MSC-4381 and MSC-0516; use with control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Tested in non-tumour-bearing C57Bl/6 mice with an oral administration of up to 30 mg/kg QD for 10 days. It was well tolerated without body weight loss or side effects.
Publications	PMID: 34382802
Orthogonal chemical probes	
<i>In vitro</i> assay(s) used to characterise	Fluorescence Cross Correlation Spectroscopy (FCCS)
Cellular assay(s) for target-engagement	MDA-MB-231 (MCT4+/1-) cells lactate efflux inhibition assay

Chemical Probe & Negative Control Structures and Use

MSC-4381 Chemical Probe



SMILES: CCOC1ccc(c2c1cccn2)S(Nc1ccc(cc1C#Cc1cnc(cc1OC)C(O)=O)[Cl])(=O)=O

InChiKey: FNBUZGRPJLEIMO-UHFFFAOYSA-N

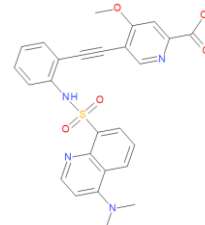
Molecular weight: 537.08 g/mol

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

MSC-0516 Negative Control



SMILES: CN(C)c1ccn2c(cccc12)S(Nc1ccccc1C#Cc1cnc(cc1OC)C(O)=O)(=O)=O

InChiKey: MMSNEMMBFRAGPO-UHFFFAOYSA-N

Molecular weight: 502.13 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

Chemical Probe Profile

In vitro Potency & Selectivity:

MSC-4381 shows potent activity on human SLC16A3 ($K_i = 11$ nM; $IC_{50} = 77$ nM) (FCCS) and is selective against other monocarboxylate transporters: SLC16A1 (MCT1): SNU-398 (MCT1+/4-) cells ($IC_{50} > 4$ μ M), SLC16A7 (MCT2) and SLC16A8 (MCT3): RT4 (MCT2+/3+) cells ($IC_{50} = 638$ nM) (600 fold). Closest hits in the CEREP panel (58 at 10 μ M) are hHTR6 ($IC_{50} = 4.6$ μ M), hAVPR1A ($IC_{50} = 7.1$ μ M). No inhibition of PTGER1 or PTGER2 (both $IC_{50} > 30$ μ M) was observed.

Potency in Cells and Cellular Target Engagement:

MSC-4381 is active in the lactate efflux inhibition assay using MDA-MB-231 (MCT4+/1-) cells ($IC_{50} = 1$ nM).