

PFI-653: A Chemical Probe for VNN1

Version 1.0 (20th October 2021)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/PFI-653>

Overview

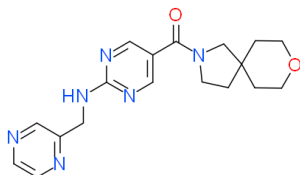
VNN1 is a member of the nitrilase superfamily and biotinidase branch. The enzyme breaks down pantetheine in cysteamine and pantothenic acid, a precursor of coenzyme A and has a role in metabolism, oxidative stress and inflammation, e.g. inflammatory bowel disease.

Summary

Chemical Probe Name	PFI-653
Negative control compound	PFI-653-N
Target(s) (synonyms)	VNN1 (Vanin-1, vascular non-inflammatory molecule-1, Pantetheine hydrolase, Tiff66)
Recommended <i>in vitro</i> assay concentration	Use at concentration up to 1 μ M for PFI-653 and PFI-653-N; use with control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Tested in rat with 2 mg/kg i.v. dose and 10 mg/kg p.o. dose.
Publications	None at time of writing
Orthogonal chemical probes	Human recombinant vanin-1 assay
<i>In vitro</i> assay(s) used to characterise	Human plasma vanin-1 assay
Cellular assay(s) for target-engagement	

Chemical Probe & Negative Control Structures and Use

PFI-653 Chemical Probe



SMILES: C1CN(CC12CCOCC2)C(c1cnc(NCc2cnccn2)nc1)=O

InChiKey: VGR LXWFXGZ RMS-UHFFFAOYSA-N

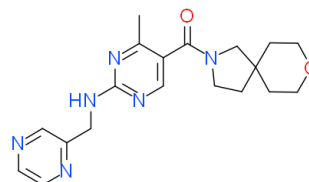
Molecular weight: 354.18 g/mol

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

PFI-653-N Negative Control



SMILES: Cc1c(cnc(NCc2cnccn2)n1)C(N1CCC2(CCOCC2)C1)=O

InChiKey: ZNKDYARBMJGNQA-UHFFFAOYSA-N

Molecular weight: 368.2 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:

PFI-653 shows potent activity on human VNN1 (IC_{50} = 6.85 nM), but not for BTD (Biotinidase) (IC_{50} > 50 μ M, >7000 fold). There are no significant off-targets in the following selectivity screens: Reaction Biology protease panel (63 at 1 μ M; all < 10 % inhibition), Invitrogen kinase panel (483 at 1 μ M and Km ATP; all < 30 % inhibition), CEREP panel (66 enzymes, receptors, and ion channels at 10 μ M; all < 25 % inhibition) and PDE panel (all IC_{50} >30 μ M).

Potency in Cells and Cellular Target Engagement:

PFI-653 is active in the human plasma VNN1 assay using 8 nM VNN1 (IC_{50} = 9.0 nM).