

TP-051: A Chemical Probe for FFAR1

Version 1.0 (29th June 2022)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/TP-051>

Overview

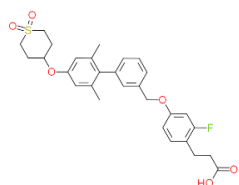
FFAR1 is a Gq-coupled GPCR strongly expressed in the pancreas with a weaker expression in brain. Activation of FFAR1 through medium to long chain saturated and unsaturated fatty acids (C12-C20) leads to an increase of intracellular Ca²⁺ concentrations via the IP3 pathway and stimulates the insulin release in the presence of glucose. It might be a target for Type 2 diabetes.

Summary

Chemical Probe Name	TP-051
Negative control compound	TP-051n
Target(s) (synonyms)	FFAR1 (free fatty acid receptor 1), GPR40
Recommended <i>in vitro</i> assay concentration	Use with control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Tested in rats with 1 mg/kg oral dose; shows a significant plasma glucose-lowering effect and insulinotropic action during an oral glucose tolerance test in rats with impaired glucose tolerance at 0.3 mg/kg.
Publications	PMID: 22428944 (Compound 31)
Orthogonal chemical probes	BI-2081
<i>In vitro</i> assay(s) used to characterise	FFAR1 binding assay
Cellular assay(s) for target-engagement	FLIPR functional assay (Ca influx activity of CHO cells expressing human FFAR1)

Chemical Probe & Negative Control Structures and Use

TP-051 Chemical Probe



SMILES:

Cc1cc(cc(C)c1c1cccc(COc2ccc(CCC(O)=O)c(c2)F)c1)OC1CCS(CC1)(=O)=O

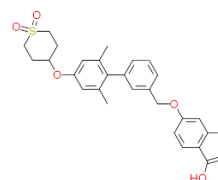
InChIKey: RPAHCZZXEGWBDL-UHFFFAOYSA-N

Molecular weight: 526.18 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

TP-051n Negative Control



SMILES: Cc1cc(cc(C)c1c1cccc(COc2ccc(C(O)=O)c(c2)F)c1)OC1CCS(CC1)(=O)=O

InChIKey: OLF CZVFPNDHIW-UHFFFAOYSA-N

Molecular weight: 498.15 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:

TP-051 shows potent activity on FFAR1 (K_i = 16 nM). From 118 targets of a Eurofins Panlabs panel (at 10 μM) 113 targets are > 10 μM. The closest off-targets are [% inh.] ALOX5 (85), TBXAS1 (64), EGFR (61), MAPK14 (60) and TBXA2R (60).

Potency in Cells and Cellular Target Engagement:

The EC₅₀ was 25 nM in a FLIPR functional assay.