

BIBO3304: A Chemical Probe for NPY1R

Version 1.0 (10th January 2024)

Web link for more details: <https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/BIBO3304>

Overview

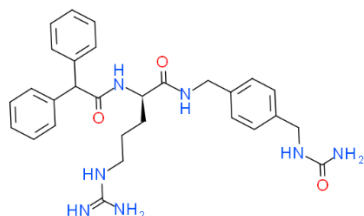
[NPY1R](#) belongs to the G-protein-coupled receptor superfamily. The encoded transmembrane protein mediates the function of neuropeptide Y (NPY), a neurotransmitter, and peptide YY (PYY), a gastrointestinal hormone. The encoded receptor undergoes fast agonist-induced internalization through clathrin-coated pits and is subsequently recycled back to the cell membrane. Activation of NPY1R may result in mobilization of intracellular calcium and inhibition of adenylate cyclase activity.

Summary

Chemical Probe Name	BIBO3304
Negative control compound	BIBO3457
Target(s) (synonyms)	NPY1R (Neuropeptide Y Receptor Y1)
Recommended <i>in vitro</i> assay concentration	Use at concentration of 100 nM for BIBO3304 and BIBO3457; use with negative control for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	Tested in rat with 15 -60 µg injected into the paraventricular nucleus.
Publications	PMID: 9806339
<i>In vitro</i> assay(s) used to characterise	none
Cellular assay(s) for target-engagement	Radioligand binding assay with NPY1R expressed in BHK cells and SK-N-MC cells

Chemical Probe & Negative Control Structures and Use

BIBO3304 Chemical Probe



SMILES:

C(C[C@H](C(NC1ccc(CNC(N)=O)cc1)=O)NC(C1CCCC1)C1CCCC1)=O)CNC(N)=N

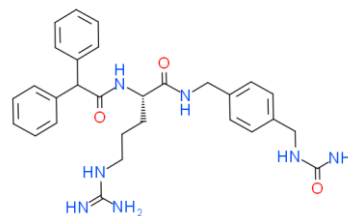
InChiKey: TVMJSGGZULFVCZ-XMMPXPASA-N

Molecular weight: 529.28 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

BIBO3457 Negative Control



SMILES:

C(C[C@H](C(NC1ccc(CNC(N)=O)cc1)=O)NC(C1CCCC1)C1CCCC1)=O)CNC(N)=N

InChiKey: TVMJSGGZULFVCZ-DEOSSOPVSA-N

Molecular weight: 529.28 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:

BIBO3304 is a potent NPY1R antagonist. There are no off-targets within the target family: Human NPY2R: IC₅₀ > 10 µM (SMS-KAN cells), > 1 µM (BHK cells); Human NPY4R: IC₅₀ = 12.3 µM (CHO cells); Human NPY5R: IC₅₀ > 10 µM (HEK293 cells). Closest off-targets in the Eurofins SafteyScreen (146 targets) at 10 µM [% ctrl] are AVPR1A (29), OPRK1 (30), DRD2 (40).

Potency in Cells and Cellular Target Engagement:

IC₅₀ = 0.69 ± 0.16 nM in a assay with hNPY1R expressed in BHK cells and IC₅₀ = 0.38 ± 0.06 nM for a radioligand binding assay with endogenous NPY1R from SK-N-MC cells.