ME43: A Chemical Probe for NR4A

Version 1.0 (25th October 2025)

Web link for more details: https://www.thesgc.org/chemical-probes/me43

Overview

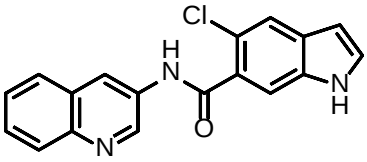
The nuclear NR4A receptors (nerve growth factor IB-like receptor family) are ligand-activated transcription factors with (neuro)protective properties as part of the immediate early response and have emerged as promising therapeutic targets in various pathologies including neurodegeneration. Nurr1 (NR4A2) plays a critical role in the development, function, and maintenance of dopaminergic neurons. Reduced expression of Nurr1 has been observed in both Alzheimer's disease (AD) and Parkinson's disease (PD) patients, as well as in corresponding rodent models, suggesting its potential involvement in the pathogenesis and progression of these disorders.

Summary

Chemical Probe Name	ME43
Negative control compound	ME113
Target(s) (synonyms)	Nur77 (NR4A1), Nurr1 (NR4A2), NOR1 (NR4A3)
Recommended *in vitro* assay concentration	Use at concentration up to 1 µM for ME43 and ME113; use with control for best interpretation of data
Suitability for *in* vivo use and recommended dose	Not tested *in vivo*
Publications	https://doi.org/10.1021/acs.jmedchem.4c03104
In vitro assay(s) used to characterise	ITC
Cellular assay(s) for target-engagement	Gal4-NR4A hybrid reporter assays, activation of response elements NBRE, NurRE and DR5 (full-length Nurr1), gene expression in N27 neuronal cells (qPCR)

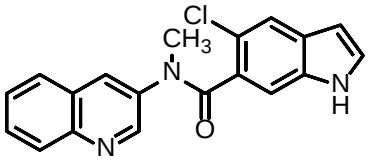
Chemical Probe & Negative Control Structures and Use

ME43 Chemical Probe



SMILES: ClC1=C(C(NC2=CC(C=CC=C3)=C3N=C2)=O)C=C(NC=C4)C4=C1
InChiKey: ZJPUSKBFLQMYJU-UHFFFAOYSA-N
Molecular weight: 321.76 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

ME113 Negative Control



SMILES: ClC1=C(C(N(C)C2=CC(C=CC=C3)=C3N=C2)=O)C=C(NC=C4)C4=C1
InChiKey: AUSKEAIAMTVFBX-UHFFFAOYSA-N
Molecular weight: 335,79 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

Selectivity:

In a panel of 18 nuclear hormone receptors ME43 shows a moderate PXR activation as only off-target outside the NR4A family at 3 µM (EC_{50} = 1.5 ± 0.6 µM), corresponding to at least 25-fold selectivity.

Potency in Cells and Cellular Target Engagement:

The EC50 was determined in Gal4-NR4A hybrid reporter assays yielding the following data: EC_{50} (Nur77) = 0.04±0.01 µM (eff. 2.0 ± 0.1-fold); EC_{50} (Nurr1) = 0.06 ± 0.02 µM (eff. 1.9 ± 0.1-fold); EC_{50} (NOR1) = 0.07±0.03 µM (eff. 2.0 ± 0.2-fold). ME43 activated full-length human Nurr1 on the response elements for the monomer (NBRE, EC_{50} = 0.07 ± 0.02 µM), homodimer (NurRE, EC_{50} = 0.027 ± 0.008 µM) and RXR heterodimer (DR5, EC_{50} = 0.014 ± 0.006 µM) with consistently low nanomolar potency. ME43 induced neuroprotective gene expression (mRNA) in N27 cells at 1 µM.

No toxicity for ME43 was observed at 10 µM in HEK293 and COS-7 cells.