BAY-6096: A Chemical Probe for ADRA2B

Version 1.0 (9th January 2024)

Web link for more details: https://www.sgc-ffm.uni-frankfurt.de/#!specificprobeoverview/BAY-6096

Overview

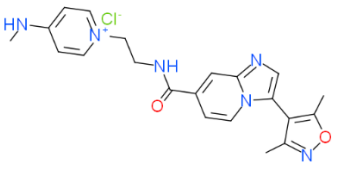
ADRA2B is a member of a subfamily of G protein-coupled receptors that regulate neurotransmitter release from sympathetic nerves and from adrenergic neurons in the central nervous system. ADRA2B receptors have been hypothesized to be involved in the process of inducing reperfusion injury while the blood flow to the ischemic myocardium after acute myocardial infarction is being restored.

Summary

Chemical Probe Name	BAY-6096
Negative control compound	BAY-726
Target(s) (synonyms)	ADRA2B (Adrenoceptor Alpha 2B)
Recommended *in vitro* assay concentration	Use at concentration of 100 nM for BAY-6096 and BAY-726; use with negative control for best interpretation of data
Suitability for *in* vivo use and recommended dose	Tested in rat with up to 0.3 mg/kg IV
Publications	PMID: 36932954 (Compound 24)
In vitro assay(s) used to characterise	Radiometric ADRA2B binding assay (Eurofins #203710)
Cellular assay(s) for target-engagement	Adrenoceptor Reporter Cell Assay (ADRA2B)

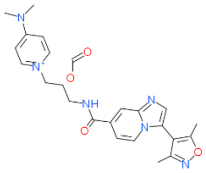
Chemical Probe & Negative Control Structures and Use

BAY-6096 Chemical Probe



SMILES: Cc1c(c2cnc3cc(ccn23)C(NCC[n+]2ccc(cc2)NC)=O)c(C)on1.[Cl-]
InChiKey: HVVLGXULBVAFRZ-UHFFFAOYSA-N
Molecular weight: 426.16 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

BAY-726 Negative Control



SMILES: Cc1c(c2cnc3cc(ccn23)C(NCCC[n+]2ccc(cc2)N(C)C)=O)c(C)on1.C([O-])=O
InChiKey: VEUJAJNSIGBGGZ-UHFFFAOYSA-N
Molecular weight: 464.22 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:

BAY-6096 is a potent antagonist for ADRA2B with a Ki = 21 nM in a Eurofins binding assay. The adrenergic receptor panel is clean with (IC_{50}): ADRA1A (5.516 µM; 394- fold), ADRA1B, ADRA1D, ADRA2A, ADRA2C, ADRB1, ADRB2, ADRB3 all > 10 µM. A Eurofins Panlabs panel with 67 targets at 10 µM is clean. The in-house kinase panel with 22 kinases is clean except for DDR2 with IC_{50} = 1.4 µM.

Potency in Cells and Cellular Target Engagement:

In a cell-based ADRA2B assay IC_{50} = 14 nM for human, 13 nM for rat and 25 nM for dog.