CS640: A Chemical Probe for CAMK1D

Version 1.0 (12th Januray 2023)

Web link for more details: https://www.thesgc.org/chemical-probes/CS640

Overview

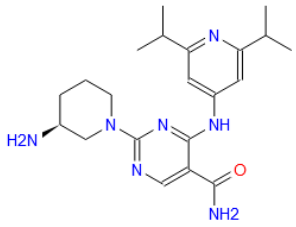
CAMK1D (calcium/calmodulin-dependent protein kinase ID) is a member of the CAMK family of protein kinases. These enzymes play a crucial role in intracellular signaling pathways, and are activated by the binding of calcium ions and calmodulin. CAMK1D is activated has been shown to phosphorylate a variety of substrates, including other kinases and transcription factors.
CAMK1D is widely expressed, and recent studies have suggested that CAMK1D may play a role in the development of triple negative breast cancer is also involved in regulation of insulin release and glucose homeostasis.
Overall, CAMK1D is a multifunctional protein kinase that is involved in a wide range of cellular processes and pathways, making it a potential target for the development of therapeutic drugs for a variety of disease conditions.

Summary

Chemical Probe Name	CS640
Negative control compound	CS640n
Target(s) (synonyms)	CAMK1D
Recommended cell assay concentration	Use at concentration of 1 µM (and < 10 µM) for CS640 and CS640s.
Suitability for *in* vivo use and recommended dose	CS640 was tested in Diet-Induced Obesity *in vivo* mouse Model up 40 mg/mL
Publications	PMID: **32433887**
Orthogonal chemical probes	
***In vitro* assay(s) used to characterise**	DSF, ADP-Glow, pCAMK1D phosphorylation. assay
Cellular assay(s) for target-engagement	NanoBRET™

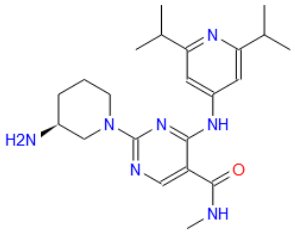
Chemical Probe & Negative Control Structures and Use

CS640 Chemical Probe



SMILES: CC(C)c1cc(Nc2nc(N3CCC[C@H](N)C3)ncc2C(N)=O)cc(C(C)C)n1
InChiKey: InChI=1/C21H31N7O/c1-12(2)17-8-15(9-18(26-17)13(3)4)25-20-16(19(23)29)10-24-21(27-20)28-7-5-6-14(22)11-28/h8-10,12-14H,5-7,11,22H2,1-4H3,(H2,23,29)(H,24,25,26,27)/t14-/m0/s1/f/h25H,23H2
Molecular weight: 397.527
Storage Stable as solid in the dark at -20°C. NB making aliquots rather than freeze-thawing is recommended
Dissolution: Soluble in DMSO up to 10-50 mM

CS640s Negative Control



SMILES: CNC(=O)c1cnc(N2CCC[C@H](N)C2)nc1Nc1cc(C(C)C)nc(C(C)C)c1
InChiKey: InChI=1/C22H33N7O/c1-13(2)18-9-16(10-19(27-18)14(3)4)26-20-17(21(30)24-5)11-25-22(28-20)29-8-6-7-15(23)12-29/h9-11,13-15H,6-8,12,23H2,1-5H3,(H,24,30)(H,25,26,27,28)/t15-/m0/s1/f/h24,26H
Molecular weight: 411.554
Storage: Stable as solid in the dark at -20°C. NB making aliquots rather than freeze-thawing is recommended
Dissolution: Soluble in DMSO up to 10-50 mM

Chemical Probe Profile

In vitro Potency & Selectivity:

CS640 shows potent activity on CAMK1D IC_{50} of 8 nM (ADP-Glow assay) and 11 nM (pCAMK1D phosphorylation assay). CS640 shows excellent selectivity in a Eurofins DiscoverX screen (468 Kinases). The negative control CS640s was not active in an *in-house* kinase panel of about 100 kinases.

Potency in Cells and Cellular Target Engagement:

In NanoBRET assay CS640 binds all kinase from the CAMK1 subfamily: CAMK1A IC_{50} = 23 nM, CAMK1B IC_{50} = 8.2 nM, CAMK1D IC_{50} = 29 nM, CAMK1G IC_{50} = 55 nM. In the Cerep-Panlabs Saftey Screens panel CS60 showed no significant activity.