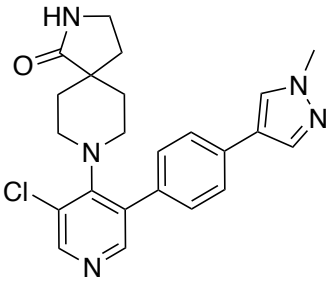
CDK19



CCT251545

Chemical Name: 8-[3-chloro-5-[4-(1-methyl-1H-pyrazol-4-yl)phenyl]-4-pyridinyl]-2,8-diazaspiro[4.5]decan-1-one

CHEBI:143114

Smile String:

O=C(NCC1)C1(CC2)CCN2C3=C(C4=CC=C(C5=CN(C)N=C5)C=C4)C=NC=C3Cl

Chemical Formula: $C_{23}H_{24}ClN_5O$

Molecular Weight: 421.93

cLogP: 1.751

Solubility: aqueous kinetic: 94 µM, aqueous thermodynamic: 0.006 mg/mL

Intrinsic Metabolic Clearance (µL/min/mg): mouse: 141, rat: 54, human: 84

Source: Med Chem Express, Cayman Chemical

References:

Mallinger, A.; *et al*. "Discovery of potent, orally bioavailable, small-molecule inhibitors of WNT signaling from a cell-based pathway screen" *J Med Chem.* **2015**, 58, 1717–1735.

Dale, T.; *et al*. "A selective chemical probe for exploring the role of CDK8 and CDK19 in human disease" *Nat Chem Biol*. **2015**, *11*, 973–980.

Biochemical profiling

Millipore (291 human kinases)

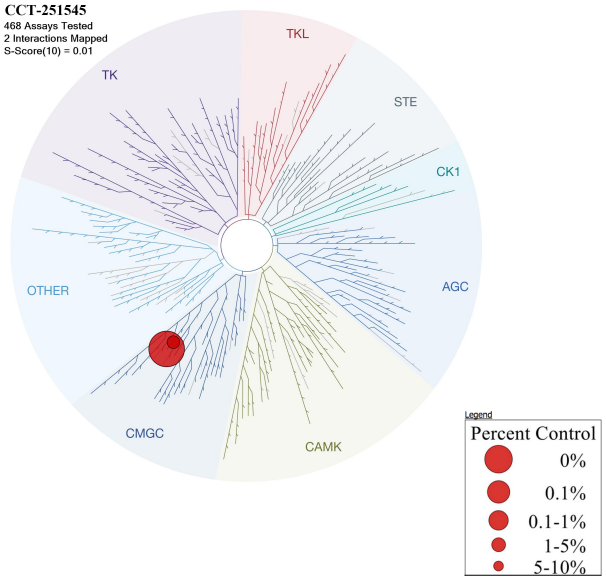
DiscoverX (403 wild-type human kinases)

S_{10} (1µM): 0.007 (3 kinases < 10% control)

CDK19 K_d (DiscoverX) = 74 nM

Kinase	% Control @ 1uM
CDK19	0
PIK3C2G	4.2
CDK8	7.7

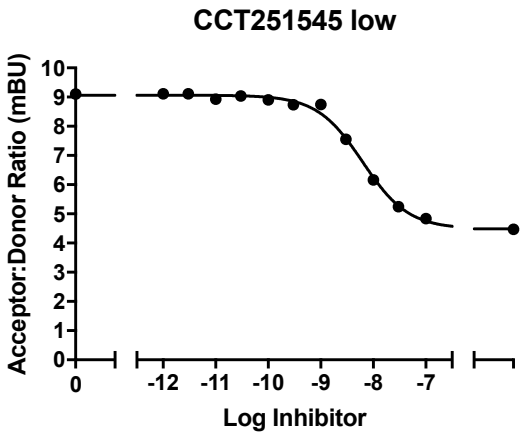
List of kinases inhibited < 10% control



Cellular target engagement in HEK293 cells

NLuc - CDK19 (N term)

CDK19 IC_{50} = 6.3 nM



CDK19 IC_{50} = 6.3 nM

Cellular target engagement of CCT251545 with CDK19 / Cyclin C