

JA397: A panTAIRE Chemical Probe

Version 1.0 (17th July 2023)

Web link for more details: <https://www.thesgc.org/chemical-probes/ja397>

Overview

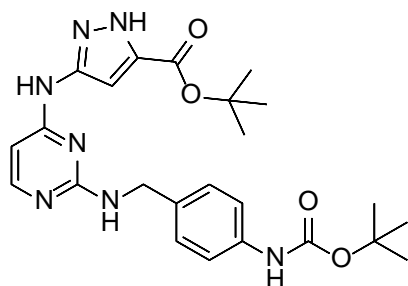
The TAIRE family of protein kinases can be subdivided into the PCTAIRE (CDK16–18) and PFTAIRE (CDK14–15) families and both of them belong to the CDKs (cyclin dependent kinases). While other members of the CDKs already have FDA-approved drugs, such as CDK4/6, relatively little is known about the TAIRE family of CDKs, and they are assigned to the dark kinome.

Summary

Chemical Probe Name	JA397
Negative control compound	JA314
Target(s) (synonyms)	CDK14 / CDK15 / CDK16 / CDK17 / CDK18; Cyclin-dependent kinase 14/15/16/17/18
Recommended cell assay concentration	Use at concentration of 1 μ M; use with negative control JA314 for best interpretation of data.
Suitability for <i>in vivo</i> use and recommended dose	JA397 was not tested <i>in vivo</i> .
Publications	https://doi.org/10.3390/ijms232314834
Orthogonal chemical probes	
<i>In vitro</i> assay(s) used to characterise	NanoBRET™ -lysed mode, biochemical activity assay (Reaction Biology)
Cellular assay(s) for target-engagement	NanoBRET™

Chemical Probe & Negative Control Structures and Use

JA397 Chemical Probe



SMILES:

O=C(OC(C)(C)C)C1=CC(NC2=NC(NCC3=CC=C(NC(OC(C)(C)C)=O)C=C3)=NC=C2)=NN1

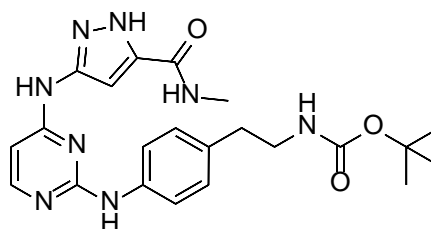
InChiKey: JQLMEZBHIJSVKR-UHFFFAOYSA-N

Molecular weight: 481.56

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 mM; use only 1 freeze/thaw cycle per aliquot

JA314 Negative Control



SMILES:

O=C(NC)C1=CC(NC2=NC(NC3=CC=C(CCNC(OC(C)(C)C)=O)C=C3)=NC=C2)=NN1

InChiKey: VJWCJKXRULCPCJ-UHFFFAOYSA-N

Molecular weight: 452.52

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 mM; use only 1 freeze/thaw cycle per aliquot

Chemical Probe Profile

In vitro Potency & Selectivity:

JA397 had an EC₅₀ of 27.1 nM, 252.2 nM, 39.0 nM, 77.2 nM and 172.3 nM to CDK14, CDK15, CDK16, CDK 17 and CDK18, respectively in the NanoBRET-lysed mode assay.

Potency in Cells and Cellular Target Engagement:

JA397 displayed an EC₅₀ of 72.1 nM, 307 nM, 33.4 nM, 21.2 nM and 121 nM on CDK14, CDK15, CDK16, CDK 17 and CDK18 respectively in intact cells in the NanoBRET assay.

In the FUCCI cell cycle assay JA397 showed a G2/M phase arrest at a concentration of 1 μ M after 24 h in HCT116 cells in comparison to DMSO. JA397 showed metabolic stability with a recovery rate of \sim 80% after 60 min in a microsomal stability assay.