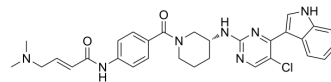


## THZ531

Cat. No.:	HY-103618		
CAS No.:	1702809-17-3		
Molecular Formula:	C <sub>30</sub> H <sub>32</sub> ClN <sub>7</sub> O <sub>2</sub>		
Molecular Weight:	558		
Target:	CDK		
Pathway:	Cell Cycle/DNA Damage		
Storage:	Powder	-20°C	3 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

In Vitro	DMSO : 250 mg/mL (448.03 mM; Need ultrasonic)					
	Preparing Stock Solutions	Solvent Concentration	Mass			
			1 mg	5 mg	10 mg	
			1 mM	1.7921 mL	8.9606 mL	17.9211 mL
			5 mM	0.3584 mL	1.7921 mL	3.5842 mL
10 mM	0.1792 mL	0.8961 mL	1.7921 mL			
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 1.43 mg/mL (2.56 mM); Clear solution					
	2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 1.43 mg/mL (2.56 mM); Suspended solution; Need ultrasonic					
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 1.43 mg/mL (2.56 mM); Clear solution					

### BIOLOGICAL ACTIVITY

Description	THZ531 is a selective and covalent inhibitor of both CDK12 and CDK13 with IC <sub>50</sub> s of 158 nM and 69 nM, respectively <sup>[1]</sup> .			
IC <sub>50</sub> & Target	CDK12 158 nM (IC <sub>50</sub> )	CDK13 69 nM (IC <sub>50</sub> )	CDK7 8.5 μM (IC <sub>50</sub> )	CDK9 10.5 μM (IC <sub>50</sub> )
In Vitro	The results from Kinase assays demonstrate that THZ531 potently inhibits CDK12 and CDK13 with IC <sub>50</sub> s of 158 nM and 69 nM, respectively; whereas inhibition of CDK7 and CDK9 is more than 50-fold weaker with IC <sub>50</sub> s of 8.5 and 10.5 μM, respectively. THZ531 treatment leads to a dramatic and irreversible decrease in Jurkat cell proliferation with an IC <sub>50</sub> of 50 nM. FACS cell			

cycle analysis following treatment with escalating doses of THZ531 displays a dose and time-dependent increase in the number of cells exhibiting sub-G1 content. At 50 nM THZ531, no increase in the percentage of apoptotic cells is observed over DMSO control for the time course of the experiment. Higher doses of THZ531 leads to pronounced Annexin V signal with 30 to 40% annexin V-positively stained cells by 72 hrs. A dramatic reduction in elongating Pol II following THZ531 treatment is also observed<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

### Kinase Assay <sup>[1]</sup>

Cells are treated with THZ531 or DMSO for 6 hrs. Following treatment cells are washed 2-fold with cold PBS and then lysed in the following lysis buffer: 50 mM Hepes pH 7.4, 150 mM NaCl, 1% Nonidet P40 substitute, 5 mM EDTA, 1 mM DTT, and protease/phosphatase cocktails. Following clearance, lysates are treated with bio-THZ1 or bio-TH531 for pulldown overnight at 4°C. Lysates are further incubated at room temperature for 3 hrs to increase the efficiency of covalent bond formation. Lysates are then incubated with streptavidin agarose for pulldown for an additional 2 to 3 hrs at 4°C<sup>[1]</sup>.

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### Cell Assay <sup>[1]</sup>

Jurkat cells are plated in 96-well plates at 20,000 cells/well in fresh media and treated with THZ531 or DMSO at the indicated concentrations for 72 hours. HAP1 cells are seeded in 96-well plates at 12,000 cells/well in fresh media and 24 hours later are treated with THZ531 at the indicated concentrations for 72 hours. Anti-proliferative effect of THZ531 is assessed. To assess the effect of inhibitor washout on anti-proliferation of Jurkat cells, cells are treated with THZ531 or DMSO for 6 hrs. Inhibitor-containing medium is then removed and incubated with or without THZ531 for 66 hrs. Anti-proliferative effect of THZ531 is assessed. All proliferation assays are performed in biological triplicate. IC<sub>50</sub>s are determined using non-linear regression curve fit<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Nature. 2020 Sep;585(7824):293-297.
- Nucleic Acids Res. 2021 Apr 19;49(7):3748-3763.
- Nat Chem Biol. 2020 Nov;16(11):1199-1207.
- J Exp Clin Cancer Res. 2023 Aug 21;42(1):214.
- J Biomed Sci. 2022 Feb 14;29(1):13.

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## REFERENCES

[1]. Zhang T, et al. Covalent targeting of remote cysteine residues to develop CDK12 and CDK13 inhibitors. Nat Chem Biol. 2016 Oct;12(10):876-84.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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