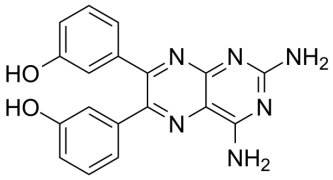
TG100-115

Cat. No.:	HY-10111
CAS No.:	677297-51-7
Molecular Formula:	$C_{18}H_{14}N_6O_2$
Molecular Weight:	346.34
Target:	PI3K
Pathway:	PI3K/Akt/mTOR
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (96.23 mM; ultrasonic and warming and adjust pH to 2 with HCl and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8873 mL	14.4367 mL	28.8734 mL
	5 mM	0.5775 mL	2.8873 mL	5.7747 mL
	10 mM	0.2887 mL	1.4437 mL	2.8873 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: 2.5 mg/mL (7.22 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (7.22 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

TG100-115 is a selective PI3Kγ/PI3Kδ inhibitor with IC_{50}s of 83 and 235 nM, respectively.

IC_{50} & Target

PI3Kγ	PI3Kδ
83 nM (IC_{50})	235 nM (IC_{50})

In Vitro

TG100-115 inhibits PI3Kγ and PI3Kδ with IC_{50}s of 83 and 235 nM, respectively, whereas both PI3Kα and PI3Kβ are relatively unaffected (IC_{50} values >1 μM). As a gauge of general specificity, TG100-115 is also assayed against a 133 protein kinase panel, none of which are inhibited at IC_{50} values <1 μM. TG100-115 potently inhibits edema and inflammation in response to multiple mediators known to participate in myocardial infarction, including vascular endothelial growth factor and platelet-activating factor; by contrast, endothelial cell mitogenesis, a repair process important to tissue survival after ischemic

	damage[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	To correlate these in vivo responses with the molecular target of interest, PI3K pathway signaling is monitored through western blot analyses of Akt phosphorylation (a PI3K-mediated event). VEGF injection i.v. in mice induces a rapid Akt phosphorylation readily detectable in lung lysates, pretreatment with TG100-115 blocks this response. Blockade is seen with TG100-115 doses as low as 0.5 mg/kg and persists over a period of several hours. In initial dose-ranging studies, generally equivalent responses are observed using TG100-115 doses of 0.5-10 mg/kg, and we therefore elected to conduct a statistically powered test at the lowest dose. Animals dosed with TG100-115 as a single 0.5 mg/kg i.v. bolus 30 min after reperfusion developed smaller infarcts vs. vehicle-treated controls. Measuring infarct area as percent of total LV ischemic area, infarct size is reduced by 35% (P=0.04). Viable tissue within the ischemic zone is increased by 37% (P=0.04), directly demonstrating the cardioprotective effect of PI3Kγ/δ inhibition[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	PI3K reactions are constructed by using recombinant human kinases, 3 μM ATP, phosphatidylinositol substrate, and cofactors, and reaction progression measured by using a luminescent-based detection system to quantify ATP consumption. Protein kinase assays are performed by using commercial screening services[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Human umbilical vein EC plated in 96-well cluster plates (5,000 cells/well) are cultured in assay medium (containing 0.5% serum and 50 ng/mL VEGF) in the presence or absence of test compounds (e.g., TG100-115) (10 μM), and cell numbers are quantified by XTT assay 24, 48, or 72 h later[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Rats[1] Sprague-Dawley rats (175-200 g) are dosed i.v. with either TG100-115 (1 mg/kg) or vehicle, and 1-4 h later Evans blue dye is administered i.v. as 500 μl of a 2% sterile saline solution. Immediately after dye injection, animals are injected intradermally on each shaved flank with 100 μL of saline, VEGF (2 μg/mL stock), or histamine (10 μg/mL stock). Thirty minutes later, injection sites are photographed. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Molecules. 2020 Apr 23;25(8):1980.

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REFERENCES

[1]. Doukas J, et al. Phosphoinositide 3-kinase gamma/delta inhibition limits infarct size after myocardial ischemia/reperfusion injury. Proc Natl Acad Sci U S A. 2006 Dec 26;103(52):19866-71.

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

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