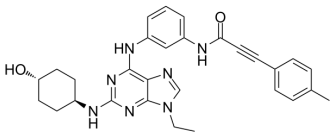
TN1

Cat. No.:	HY-100826
CAS No.:	289479-94-3
Molecular Formula:	$C_{29}H_{31}N_7O_2$
Molecular Weight:	509.6
Target:	Others
Pathway:	Others

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 : 100 mg/mL (196.23 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9623 mL	9.8116 mL	19.6232 mL
5 mM	0.3925 mL	1.9623 mL	3.9246 mL
10 mM	0.1962 mL	0.9812 mL	1.9623 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 (4.91 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TN1 is a potent fetal hemoglobin (HbF) inducer.

IC_{50} & Target

fetal hemoglobin (HbF)[1]

In Vitro

A high-throughput screen of a large chemical library identifies a 2,6-diamino-substituted purine, TN1, which induces fetal hemoglobin (HbF) more potently than hydroxyurea in KU812 and K562 leukemia cell lines.TN1 increases HbF protein in both leukemic KU812 and K562 cells in a dose-dependent manner. At 100 nM concentration, Western blot analysis indicated that TN1 increased γ-globin expression (2.9- and 3.7-fold increase in KU812 cell and K562 cell, respectively) to higher levels than 50-100 μM HU (1.8- and 1.9-fold increase in KU812 cell and K562 cell, respectively), the first drug approved for the treatment of SCD. The EC_{50} value for TN1-mediated HbF induction is approximately three orders of magnitude lower than that of HU

(HU: EC_{50}=50-100 μM; TN1: EC_{50}=100 nM). In addition, TN1 is more potent than a number of previously reported small-molecule HbF inducers including sodium butyrate and other histone deacetylase (HDAC) inhibitors. At the concentrations tested, TN1, as well as hemin and HU, increase γ-globin mRNA transcription (greater than fourfold), indicating that TN1 increases γ-globin levels at both the transcriptional and protein level. The time course of TN1-induced γ-globin mRNA and protein synthesis is measured and both increase after approximately 24 h of treatment. TN1 also induces β-globin mRNA in addition to γ-globin mRNA, similar to hydroxyurea[1].

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

PROTOCOL

Cell Assay [1]

Representative images of PBMC culture in the presence of test compounds. PBMC are cultured in methylcellulose medium containing 0.9% methylcellulose, 30% fetal bovine serum (FBS), 2 mM glutamine, 1% deionized bovine serum albumin (BSA), 100 μM 2-mercaptoethanol, 10 ng recombinant human (rh) IL-3, and 3 U/mL rh erythropoietin (EPO) for 16 days in the presence of TN1 (30 nM) or HU (50 μM). HU treatment leads to smaller colonies and inhibition of maturation towards the erythrocyte lineage; b) Western blot of HbF with BFU-E colonies treated with DMSO, TN1 (30 nM), and HU (50 μM) after incubation for 18 days. β-actin is used as an internal control[1].

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

REFERENCES

[1]. Nam TG, et al. Identification and characterization of small-molecule inducers of fetal hemoglobin. ChemMedChem. 2011 May 2;6(5):777-80.

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