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产品名称：TN1
产品别名：TN1

生物活性：

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 EC50 value for TN1-mediated HbF induction is approximately three orders of magnitude lower than that of HU (HU: EC50=50-100 μM; TN1: EC50=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].
Solvent&Solubility	***In Vitro:*** **DMSO : 100 mg/mL** (**196.23 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (4.91 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.91 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.91 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.91 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Nam TG, et al. Identification and characterization of small-molecule inducers of fetal hemoglobin. ChemMedChem. 2011 May 2;6(5):777-80.

实验参考：

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