Product Data Sheet

Product Name: TN1
Cat. No.: GC34024

Chemical Properties

Cas. No.	289479-94-3		
SMILES	O=C(NC1=CC=CC(NC2=C3N=CN(CC)C3=NC(N[C@H]4CC[C@H](O)CC4)=N2)=C1)C#CC5=CC=C(C)C=C5		
Formula	$C_{29}H_{31}N_7O_2$	M.Wt	509.6
Solubility	DMSO : 100 mg/mL (196.23 mM);Water : < 0.1 mg/mL (insoluble)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	TN1		

Protocol

Cell experiment: 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].

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References:

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

Background

TN1 is a potent fetal hemoglobin (HbF) inducer.

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].

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