Product Data Sheet

Product Name: 6-Thio-dG
Cat. No.: GC12193

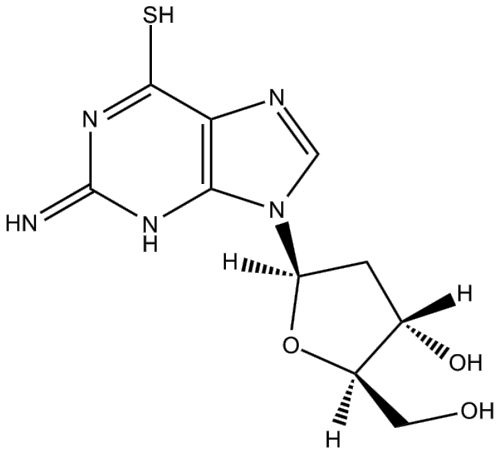
Chemical Properties

Cas. No.	789-61-7
Chemical Name	(2R,3S,5R)-2-(hydroxymethyl)-5-(2-imino-6-mercapto-2H-purin-9(3H)-yl)tetrahydrofuran-3-ol
SMILES	N=C1NC2=C(N=CN2[C@@]3([H])C[C@@](O)([H])[C@@](O3)([H])CO)C(S)=N1

Formula	$C_{10}H_{13}N_5O_3S$	M.Wt	283.31
Solubility	≥ 62.5mg/mL in DMSO	Storage	Store at -20°C,protect from light

General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C 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



Protocol

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Cell experiment: HCT116, A549, and H2882, HCC2429, HCC827, HCC15, H2087, HCC4017, HCC515, H2009, BJ and HCEC1 cells are plated in growth media in 96 well plates. Cells are incubated for 1 week and treated with varying concentrations of 6-Thio-2'-Deoxyguanosine and 6-thioguanine or DMSO every three days. The 96 well plates are analyzed for the CellTiterGlo luminescent cell viability assay[1].

Animal experiment: Athymic NCR nu/nu female mice (6 weeks old) are used. A549 cells are inoculated subcutaneously into the left and right dorsal flanks of the nude mice in 100 µL phosphate buffered saline (PBS). When tumors reach 40 mm3 average volume, mice are randomly divided into control, 6-thio-dG and 6-thioguanine treatment groups (3 animals in each group). Animals are injected intraperitoneally every two days for 17 days at a dose of 2mg/kg in 100 µL DMSO/PBS mixture per mouse. In addition, different animals are injected intratumorally every day for 16 days at a dose of Athymic NCR nu/nu female mice2.5mg/kg in 50 µL DMSO/PBS mixture per mouse. Tumor size is measured by calipers and recorded either every day or every two days[1].

References:

[1]. Mender I, et al. Induction of telomere dysfunction mediated by the telomerase substrate precursor 6-thio-2'-deoxyguanosine. Cancer Discov. 2015 Jan;5(1):82-95.

Background

6-thio-dG is a nucleoside analogue [1], is a telomerase-mediated telomere disrupting compound [2]. It is an anti-cancer inhibitor [1]. Cancer cells were very sensitive to 6-thio-dG with observed IC50 values ranging from 0.7-2.9 µM, depending on cell types [3].

Telomeres are found at the end of eukaryotic linear chromosomes. They are essential for genomic stability and chromosome maintenance [3].

In HCT116 human colon cancer cell line, treatment with 6-thio-dG made progressive telomere

shortening independent of telomerase activity inhibition and induced telomere dysfunction. GRN163L is a telomerase inhibitor. In HCT116 cells, treatment with GRN163L and 6-thio-dG together increased telomere shortening. Within 1 week, 6-thio-dG killed most of HCT116 cells and altered cellular morphology. Normal BJ fibroblast cells are telomerase silent. After 1 week, treatment with 6-thio-dG showed no effect on cell morphology. After long-term treatment with 6-thio-dG, no effect on telomere shortening was found [1].

In murine mode with xenograft derived from A549 lung cancer cell line, as compared to controls, intraperitoneal injection with 2 mg/kg of 6-thio-dG every other day completely prevented progressive tumor growth. Ki67 is a biomarker correlating with proliferation levels. Compared to controls, 6-thio-dG decreased Ki67 staining. Treatment with 6-thio-dG through local injection resulted in even more dramatic decrease in the tumor growth rate compared to untreated controls [3].

References:
[1]. Mender I, Gryaznov S, Dikmen ZG, et al. Abstract LB-125: A novel telomerase inhibitor. Cancer Research, 2013, 73(8 Supplement): LB-125-LB-125.
[2]. Mender I, Gryaznov S, Shay JW. A novel telomerase substrate precursor rapidly induces telomere dysfunction in telomerase positive cancer cells but not telomerase silent normal cells. Oncoscience, 2015, 2(8): 693.
[3]. Mender I, Gryaznov S, Dikmen ZG, et al. Induction of telomere dysfunction mediated by the telomerase substrate precursor 6-thio-2-deoxyguanosine. Cancer discovery, 2015, 5(1): 82-95.