

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

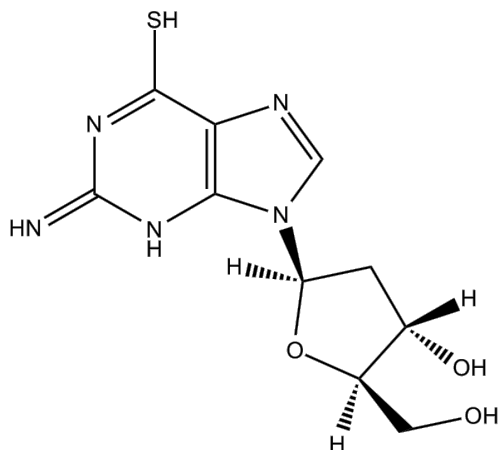
Formula $C_{10}H_{13}N_5O_3S$ M.Wt 283.31

Solubility $\geq 62.5\text{mg/mL}$ 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

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

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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 μ L 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 μ L 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 mice 2.5mg/kg in 50 μ L 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 μ M, 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

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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.

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