Product Data Sheet

Product Name: SGI-110
Cat. No.: GC17428

Chemical Properties

Cas. No.	929901-49-5		
Chemical Name	[(2S,3R,5R)-5-(2-amino-6-oxo-3H-purin-9-yl)-3-hydroxyoxolan-2-yl]methyl [5-(4-amino-2-oxo-1,3,5-triazin-1-yl)-2-(hydroxymethyl)oxolan-3-yl] hydrogen phosphate		
SMILES	C1C(C(OC1N2C=NC3=C2NC(=NC3=O)N)COP(=O)(O)OC4CC(OC4CO)N5C=NC(=NC5=O)N)O		
Formula	$C_{18}H_{24}N_9O_{10}P$	M.Wt	557.41
Solubility	DMSO : 50 mg/mL (86.30 mM); Water	Storage	Store at -20°C,unstable in solution, ready to use.
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	SGI-110		

Protocol

Cell experiment [1]:

Cell lines	Parental A2780 cells and A2780-CDDP resistant cells
Preparation method	This compound is soluble in DMSO. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below - 20 °C for several months.

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Reacting condition	0.1, 0.3, 1 or 5 μM; 48 hrs
Applications	At the moderate dose of 5 μM, SGI-110 increased the sensitivity of OC cells to CDDP, resulting in a > 2-fold reduction in the IC50 for CDDP: 28 μM CDDP IC50 for A2780-CDDP resistant cells and 42 μM CDDP IC50 for parental A2780 cells. SGI-110 increased the sensitivity of both the parental and the resistant A2780 cells to CDDP. It was demonstrated that SGI-110 chemosensitized the A2780 cells by demethylation and reexpression of MLH1, RASSF1A and HOXA11.

Animal experiment [2]:

Animal models	Nude rats bearing Calu6 cells
Dosage form	20 mg/kg; s.c.; twice per week, for 4 weeks
Applications	In nude rats bearing Calu6 cells, SGI-110 alone reduced tumor burden by 35%, and the combination treatment with SGI-110 □ Entinostat significantly reduced tumor burden by 56%. Besides, SGI-110 alone or in combination with Entinostat decreased the pleomorphic cell population similarly, to approximately 25%. However, compared with the control group, these 2 treatment groups showed some cumulative toxicity. After 4 weeks of treatment, body weights of rats reduced by 13 ~ 18%.

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Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:

[1]. Fang F, Munck J, Tang J, Taverna P, Wang Y, Miller DF, Pilrose J, Choy G, Azab M, Pawelczak KS, VanderVere-Carozza P, Wagner M, Lyons J, Matei D, Turchi JJ, Nephew KP. The novel, small-molecule DNA methylation inhibitor SGI-110 as an ovarian cancer chemosensitizer. Clin Cancer Res. 2014 Dec 15;20(24):6504-16.

[2]. Tellez CS1, Grimes MJ, Picchi MA, Liu Y, March TH, Reed MD, Oganesian A, Taverna P, Belinsky SA. SGI-110 and entinostat therapy reduces lung tumor burden and reprograms the epigenome. Int J Cancer. 2014 Mar 26.

Background

SGI-110 is a second generation DNA methyltransferase (DNMT) inhibitor that is synthesized as a dinucleotide consisting of a deoxyguanosine (5’-DACpG-3’) and 5-AZA-CdR bonds with a natural phosphodiester linkage. Unlike other DNMT inhibitors that are susceptible to rapid inactivation by cytidine deaminase (CDA), SGI-110 is highly resistant

to deamination by CDA. In previous studies, SGI-110 has been demonstrated to effectively retard tumor growth in human bladder cancer xenografts through both intraperitoneal (i.p.) and subcutaneous (s.c.) administration and to exhibit epigenetic remodeling activity, in which the expression of p16 in cancer cells is restored through demethylation of the 5’-end region of the gene.

References:

[1]Tellez CS1, Grimes MJ, Picchi MA, Liu Y, March TH, Reed MD, Oganesian A, Taverna P, Belinsky SA. SGI-110 and entinostat therapy reduces lung tumor burden and reprograms the epigenome. Int J Cancer. 2014 Mar 26. doi: 10.1002/ijc.28865. [Epub ahead of print]
[2]Coral S1, Parisi G, Nicolay HJ, Colizzi F, Danielli R, Fratta E, Covre A, Taverna P, Sigalotti L, Maio M. Immunomodulatory activity of SGI-110, a 5-aza-2'-deoxycytidine-containing demethylating dinucleotide. Cancer Immunol Immunother. 2013 Mar;62(3):605-14. doi: 10.1007/s00262-012-1365-7. Epub 2012 Nov 9.
[3]Foulks JM1, Parnell KM, Nix RN, Chau S, Swierczek K, Saunders M, Wright K, Hendrickson TF, Ho KK, McCullar MV, Kanner SB. Epigenetic drug discovery: targeting DNA methyltransferases. J Biomol Screen. 2012 Jan;17(1):2-17. doi: 10.1177/1087057111421212. Epub 2011 Sep 30.