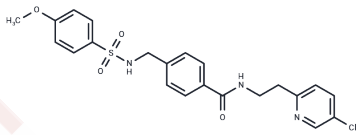
Data Sheet (Cat.No.T4339)

TargetMol

YU238259

Chemical Properties



CAS No. : 1943733-16-1

Formula: C22H22ClN3O4S

Molecular Weight: 459.95

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	YU238259 is a novel inhibitor of homology-dependent DNA repair(HDR), but does not inhibit non-homologous end-joining (NHEJ), in cell-based GFP reporter assays.
Targets(IC50)	DNA-PK
In vitro	YU238259 sensitizes tumor cells to radiation therapy and DSB-inducing chemotherapy. Treatment with YU238259 is not only synergistic with ionizing radiation (IR), etoposide, and PARP inhibition, but this synergism is heightened by BRCA2-deficiency. Synthetic lethality of YU238259 in HDR-deficient cells results from accumulation of unresolved DSBs following additional inhibition of residual HDR pathway activity. Inhibition of HDR activity by YU238259 has little to no effect on the NHEJ pathway.
In vivo	Growth of BRCA2-deficient human tumor xenografts in nude mice is significantly delayed by YU238259 treatment even without concomitant DNA-damaging therapy.
Kinase Assay	The cloning, expression and purification of USP21 from BL21 (DE3) bacteria are performed using standard molecular biology techniques. USP2, USP5, USP7, USP8, USP28, USP47, Ub-PLA2 (Ub-CHOP) and Ub-EKL (Ub-CHOP2) are generated. Caspase 3 and the caspase 3 substrate DEVD-Rh110 are used. Deubiquitylating enzyme, cathepsin B and 20S proteasome chymotrypsin like protease activities are measured. Caspase 3 activity is determined using a similar protocol. Briefly, dose ranges of compound (including USP7/USP47 inhibitor) are incubated with caspase 3 for 30 minutes before the addition of DEVD-Rh110 and reading on a fluorometric plate reader using excitation and emission maxima of 485 nm and 531 nm respectively. The final concentrations of caspase 3 and DEVD-Rh110 are 2 nM and 100 nM respectively
Cell Research	U2OS cells were pretreated with 25 μM YU238259 or DMSO vehicle for 1 h and cells were then irradiated with 10 Gy IR. Cells were fixed at 8 h post-IR, stained with antibodies and Hoechst dye, and imaged. Foci were quantified using the InCell Analyzer algorithm developed by YCMD. Cells were scored as foci-positive if they contained ≥15 foci (BRCA1, pDNA-PK) or ≥20 foci (53BP1).
Animal Research	Animal Models: 069(nu)/070(nu/+) athymic nude mice. Formulation: 3:1 DMSO:PBS. Dosages: 3 mg/kg . Administration: i.p

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 84 mg/mL (182.63 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Corn Oil: 3.3 mg/mL (7.17 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1741 mL	10.8707 mL	21.7415 mL
5 mM	0.4348 mL	2.1741 mL	4.3483 mL
10 mM	0.2174 mL	1.0871 mL	2.1741 mL
50 mM	0.0435 mL	0.2174 mL	0.4348 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Stachelek GC,etal.YU238259 Is a Novel Inhibitor of Homology-Dependent DNA Repair That Exhibits Synthetic Lethality and Radiosensitization in Repair-Deficient Tumors.Mol Cancer Res. 2015 Oct;13(10):1389-97.