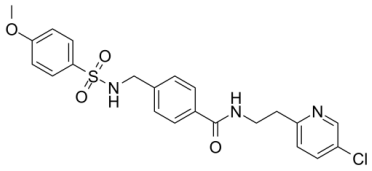
Data Sheet

Product Name:	YU238259
Cat. No.:	CS-0017546
CAS No.:	1943733-16-1
Molecular Formula:	C22H22ClN3O4S
Molecular Weight:	459.95
Target:	DNA-PK
Pathway:	Cell Cycle/DNA Damage; PI3K/Akt/mTOR
Solubility:	DMSO : ≥ 300 mg/mL (652.24 mM)



BIOLOGICAL ACTIVITY:

YU238259 is an inhibitor of homology-dependent DNA repair (**HDR**), used for cancer research. IC50 & Target: HDR[1] **In Vitro:** YU238259 is an inhibitor of homology-dependent DNA repair, with no effect on PARP activity. YU238259 shows cytotoxicity in BRCA2-deficient cells, with a low LD_{50} of 8.5 μM. YU238259 (0-5 μM) causes a potent, dose-dependent decrease in HDR efficiency in U2OS DR-GFP or U2OS EJ5-GFP cells, but with no effect on NHEJ frequency. YU238259 (0-10 μM) exhibits synthetic lethality with loss of frequently mutated tumor suppressors, and shows synergism with radiotherapy (IR) and DNA-damaging chemotherapy that is potentiated by BRCA2 loss[1]. **In Vivo:** YU238259 (3 mg/kg, i.p.) inhibits the growth of BRCA2-deficient tumor xenografts in nude mice [1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]**U2OS reporter cell lines (DR-GFP or EJ5-GFP)** are pretreated in triplicate with **varying concentrations of YU238259 for 24 h**, after which 4 μg of SCE-I plasmid is transfected into **1 × 10^6 cells/replicate** using an Amaxa Nucleofector. Transfected cells are reseeded on 6-well plates and cultured with YU238259 for an additional 72 h. The percentage of GFP-positive cells is quantified by flow cytometry. Data analysis is performed using FlowJo software. Error bars represent the standard deviation[1]. **Animal Administration:** YU238259 is formulated in 3:1 DMSO:PBS.[1]**069(nu)/070(nu/$^+$) athymic nude mice, at 4-5 weeks age**, are injected subcutaneously with **3 × 10^6 DLD-1 or DLD-1 BRCA2-KO cells** suspended in 100 μL PBS. Tumor take rate is >80%. When tumors reach 100 mm^3 geometric mean volume, the mice are injected with **3 mg/kg YU238259 or its 3:1 DMSO:PBS vehicle**, or 5 mg/kg YU128440 or its 1:19 DMSO:PBS vehicle (IP, 100 μL total in each case). Treatment is repeated 3×/week (Mon/Wed/Fri) for a total of 12 doses of YU238259 and 4 doses of YU128440. Tumor growth is assessed by external caliper. Mice are euthanized when individual tumor volumes exceed 1000 mm^3[1].

References:

[1]. Stachelek GC, et al. 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.

CAIndexNames:

Benzamide, N-[2-(5-chloro-2-pyridinyl)ethyl]-4-[[[(4-methoxyphenyl)sulfonyl]amino]methyl]-

SMILES:

COC1=CC=C(S(NCC2=CC=C(C(NCCC3=CC=C(Cl)C=N3)=O)C=C2)(=O)=O)C=C1

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

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