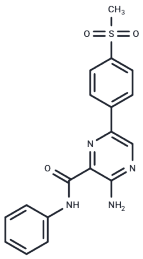
Data Sheet (Cat.No.T3032)

TargetMol

VE-821

Chemical Properties



CAS No. : 1232410-49-9

Formula: C18H16N4O3S

Molecular Weight: 368.41

Storage: Store at low temperature
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	VE-821 (ATR Inhibitor IV) is a selective ATP competitive inhibitor of ATR(Ki/IC50: 13/26 nM in cell-free assays).
Targets(IC50)	ATM/ATR
In vitro	VE-821 exhibits high selectivity for ATR with minimal cross-reactivity against related PIKKs, including ATM, DNA-dependent protein kinase (DNA-PK), mammalian target of rapamycin, and phosphoinositol 3-kinase-γ (Kis of 16 μM, 2.2 μM, >1 μM and 3.9 μM, respectively). It inhibits H2AX phosphorylation in hydroxyurea-treated HT29 cancer cells without affecting M059J or HT144 lines treated with neocarzinostatin [1]. VE-821 significantly increases the sensitivity of PSN-1, MiaPaCa-2, and primary PancM pancreatic cancer cells to radiation and gemcitabine under both normoxic and hypoxic conditions, leading to the inhibition of radiation-induced G2/M arrest [2]. Additionally, VE-821 (1 and 4 μM) enhances H2AX phosphorylation at Ser139 in OVCAR-8 cells induced by topotecan and cisplatin but does not block ATR-mediated Ser345 Chk1 or Ser296 autophosphorylation induced by gemcitabine, topotecan, or cisplatin [3].
Kinase Assay	The ability of compounds (e.g., VE-821) to inhibit ATR, ATM or DNAPK kinase activity is tested using a radiometric-phosphate incorporation assay. A stock solution is prepared consisting of the appropriate buffer, kinase, and target peptide. To this is added the compound of interest, at varying concentrations in DMSO to a final DMSO concentration of 7%. Assays are initiated by addition of an appropriate [g-33P]ATP solution and incubated at 25°C. Assays are stopped, after the desired time course, by addition of phosphoric acid and ATP to a final concentration of 100 mM and 0.66 μM, respectively. Peptides are captured on a phosphocellulose membrane, prepared, and washed six times with 200 μL of 100 mM phosphoric acid, prior to the addition of 100 μL of scintillation cocktail and scintillation counting on a 1450 Microbeta Liquid Scintillation Counter. Dose-response data are analyzed using GraphPad Prism software [4].
Cell Research	Clonogenic survival assays were performed as described before. Briefly, logarithmically growing cells were plated in triplicate in 6-well tissue culture dishes under oxic (21% O2) or hypoxic conditions (0.5% O2) using an InVivo2 300 chamber. Cells were incubated for 6 h before irradiation under oxia or hypoxia using tightly sealed chambers. The target O2 level was achieved within 6 h of gassing and maintained during irradiation, as confirmed by an OxyLite oxygen probe. Cells irradiated under hypoxia were exposed to

Cell Research	normoxia at 1 h post-irradiation. As standard, VE-821 (1 μM) was added 1 h prior to irradiation (6 Gy) and was washed away 72 h after irradiation. For the chemotherapy experiments, cells were initially exposed to increasing concentrations of gemcitabine (5, 10 and 20 nM) for 24 h before addition of the VE-821 (1 μM) for another 72 h. The effect of triple combination of irradiation with VE-821 and gemcitabine was examined as well. Cells were incubated for 10–21 d until colonies were stained with 0.5% crystal violet and counted in a CellCount automated colony counter. Clonogenic survival was calculated and data were fitted in GraphPad Prism 4.0 [2].

Solubility Information

Solubility	DMSO: 69 mg/mL (187.29 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.7144 mL	13.5718 mL	27.1437 mL
5 mM	0.5429 mL	2.7144 mL	5.4287 mL
10 mM	0.2714 mL	1.3572 mL	2.7144 mL
50 mM	0.0543 mL	0.2714 mL	0.5429 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

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