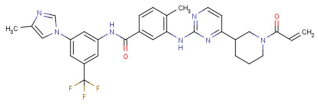
Data Sheet (Cat.No.T15943)

TargetMol
A DRUG SCREENING EXPERT

M443

Chemical Properties



CAS No.:	1820684-31-8
Formula:	C31H30F3N7O2
Molecular Weight:	589.61
Appearance:	N/A
Storage:	0-4℃ for short term (days to weeks), or -20℃ for long term (months).

Biological Description

Description	M443 is an irreversible and specific MRK inhibitor (IC50<125 nM).
Targets(IC_{50})	MRK: <125 nM
In vitro	Similarly, the clonogenic assay displays a significant decrease in survival with a dose enhancement factor (DEF) of 1.6 at 10% viability. MRK depletion reduces cell viability after IR by 33% of control at 3 Gy. In both cell cultures, the IR-stimulated activation of MRK, Chk2, and p38 are greatly inhibited by 500 nM M443. Cells are seeded on coverslips, pretreated with 500 nM M443 or vehicle, exposed to 6 Gy of IR, fixed at different times after IR, and processed for immunofluorescence with the MPM2 phospho-specific antibody that specifically stains mitotic cells. The M443-treated cells fail to arrest after IR and maintained a similar mitotic index as the nonirradiated cells, in contrast to control cells. Thus, inhibition of MRK leads to inhibition of Chk2 and failure to arrest in the cell cycle in response to IR-induced DNA damage.
In vivo	Treatment with M443 alone adds 5.5 days to this survival, whereas the chosen low dose of radiation does not significantly increase survival. Control mice survive with a median of 32 days after tumor cell implantation. It is displayed that the tumor-containing fraction has elevated levels of both total and active MRK (lane RB in the vehicle-treated brain). The combination of M443 and IR extend survival with a median of 16 days longer than control. Treatment with M443 does not affect the animal weight, as the weight loss observed is observed in all groups just a few days before the animals became moribund. The tumor-containing fraction from the M443-treated brain shows the total loss of MRK activity. The fractions containing the normal brain, which in the control brain show some level of MRK protein, in the treated brain also has lost MRK, suggesting that diffusion of M443 across the whole cerebellum inhibits normal MRK as well.

Solubility Information

Solubility	DMSO: 55 mg/mL (93.28 mM) (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.696 mL	8.48 mL	16.96 mL
5 mM	0.339 mL	1.696 mL	3.392 mL
10 mM	0.17 mL	0.848 mL	1.696 mL
50 mM	0.034 mL	0.17 mL	0.339 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. The storage conditions and period of the stock solution: - 80 ℃ for 6 months; - 20 ℃ for 1 month. Please use it as soon as possible.

Reference

1. Markowitz D, et al. Pharmacological Inhibition of the Protein Kinase MRK/ZAK Radiosensitizes Medulloblastoma. Mol Cancer Ther. 2016 Aug;15(8):1799-808.

Inhibitors · Natural Compounds · Compound Libraries

This product is for Research Use Only · Not for Human or Veterinary or Therapeutic Use.

Tel:781-999-4286 E-mail:info@targetmol.com Address:36 Washington Street,Wellesley Hills,MA 02481