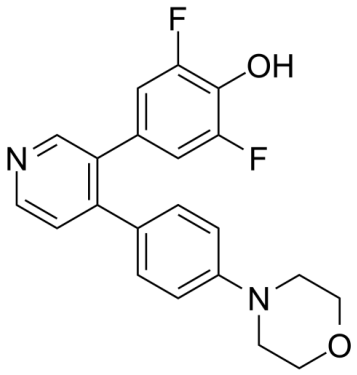
Data Sheet

Product Name:	LJI308
Cat. No.:	CS-5380
CAS No.:	1627709-94-7
Molecular Formula:	$C_{21}H_{18}F_2N_2O_2$
Molecular Weight:	368.38
Target:	Ribosomal S6 Kinase (RSK)
Pathway:	MAPK/ERK Pathway
Solubility:	DMSO : 25 mg/mL (67.86 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

LJI308 is a potent pan-**ribosomal S6 kinase (RSK)** inhibitor, with **IC_{50}**s of 6 nM, 4 nM, and 13 nM for RSK1, RSK2, and RSK3, respectively. LJI308 inhibits the phosphorylation of RSK (T359/S363) and YB-1 (S102) after irradiation, treatment with EGF, and in cells expressing a KRAS mutation[1][2]. **In Vitro:** LJI308 inhibits S6K1 with an IC_{50} of 0.8 μM[1].
LJI308 inhibits YB-1 phosphorylation in CRC cells at concentrations of 5 to 25 μM. In a dose kinetics experiment, LJI308, starting at 2.5 μM, inhibits YB-1 phosphorylation in the KRAS mutated TNBC cell line MDA-MB-231 by approximately 86%. LJI308 effectively blocks RSK and YB-1 phosphorylation after EGF stimulation and after irradiation in KRAS wild-type HBL-100 cells[2].
LJI308 (1-10 μM; 96 hours) decreases cell viability by up to 90%[3].

PROTOCOL (Extracted from published papers and Only for reference)

Enzyse assay [1] Enzymatic activity of RSK isoforms 1, 2, and 3 (PV4049, PV4051, and PV3846) was assessed using recombinant full-length RSK protein purchased from Invitrogen RSK1 (1 nM), RSK2 (0.1 nM), or RSK3 (1 nM) was allowed to phosphorylate 200 nmol/L peptide substrate (biotin-AGAGRSRHSSYPAGT-OH) in the presence of ATP at concentration equal to the Km for ATP for each enzyme (RSK1, 5 μM; RSK2, 20 μM; and RSK3, 10 μM) and appropriate dilutions of RSK inhibitors.

References:

[1]. Aronchik I, et al. Novel potent and selective inhibitors of p90 ribosomal S6 kinase reveal the heterogeneity of RSK function in MAPK-driven cancers. Mol Cancer Res. 2014 May;12(5):803-12.

[2]. Lettau K, et al. Simultaneous Targeting of RSK and AKT Efficiently Inhibits YB-1-Mediated Repair of Ionizing Radiation-Induced DNA Double-Strand Breaks in Breast Cancer Cells. Int J Radiat Oncol Biol Phys. 2021;109(2):567-580.

[3]. Jain R, et al. Discovery of Potent and Selective RSK Inhibitors as Biological Probes. J Med Chem. 2015 Sep 10;58(17):6766-83.

[4]. Davies AH, et al. Inhibition of RSK with the novel small-molecule inhibitor LJI308 overcomes chemoresistance by eliminating cancer stem cells. Oncotarget. 2015;6(24):20570-20577.

CAIndexNames:

Phenol, 2,6-difluoro-4-[4-[4-(4-morpholinyl)phenyl]-3-pyridinyl]-

SMILES:

OC1=C(F)C=C(C2=C(C3=CC=C(N4CCOCC4)C=C3)C=CN=C2)C=C1F

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

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