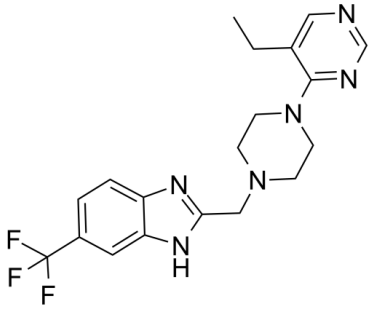
Data Sheet

Product Name:	PF-4708671
Cat. No.:	CS-1739
CAS No.:	1255517-76-0
Molecular Formula:	$C_{19}H_{21}F_3N_6$
Molecular Weight:	390.41
Target:	Autophagy; Ribosomal S6 Kinase (RSK)
Pathway:	Autophagy; MAPK/ERK Pathway
Solubility:	DMSO : 33.33 mg/mL (85.37 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

PF-4708671 is a potent cell-permeable **S6K1** inhibitor with a $\mathbf{K_i}$ of 20 nM and $\mathbf{IC_{50}}$ of 160 nM. **In Vitro:** PF-4708671 inhibits the activity of full-length S6K1 in vitro with a K_i of 20 nM, and S6K1 isolated from IGF1-stimulated HEK293 cells with an IC_{50} of 0.16 μM, and only inhibits very weakly the closely related S6K2 isoform (IC_{50} of 65 μM). PF-4708671 inhibits RSK1 (IC_{50} of 4.7 μM) and RSK2 (IC_{50} of 9.2 μM) over 20-fold less potently than S6K1. PF4708671 inhibits MSK1 (IC_{50} of 0.95 μM) 4-fold more weakly than S6K1[1]. HCT116 cells are treated with (i) vehicle (DMSO), (ii) OSI-906 (5 μM), (iii) PF-4708671 (10 μM), and (iv) OSI-906 (5 μM)+PF-4708671 (10 μM) for various amounts of time. HCT116 cells treated with OSI-906 alone (closed square) or PF4708671 alone (open circle) slightly inhibit cell growth. In contrast, proliferation in HCT116 cells is significantly inhibited after a 2-day treatment with the combination of OSI-906 and PF-4708671 (closed circle). A similar result is also observed when SW480 cells are treated with the combination of OSI-906 and PF-4708671. Colony formation also significantly reduces in OSI-906+PF-4708671-treated cells comparing with vehicle, OSI-906 alone, or PF-4708671 alone treated HCT116 or SW480 cells[2]. **In Vivo:** The tumor growth rate in mice treated with the combination of OSI-906+PF-4708671 is significantly slower than that of OSI-906 alone (P=0.0189) or PF4708671 alone (P=0.0165) treated mice. The average tumor volume in the OSI-906+PF-4708671-treated mice is approximately 50% of that in mice treated with OSI-906 (P=0.0056) or PF-4708671 alone (P<0.001) at the end of a 15-day treatment[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]**GEO, HT29, SW480, and HCT116 cells** are used. The effects of OSI-906 or the combination of OSI-906 and PF-4708671 on cell proliferation is determined with XTT and clonogenic assays. XTT assays are performed using the Cell Proliferation Kit II (XTT). For clonogenic assays, cells (1×10^3 cells/well) are seeded on a 6-well plate and subsequently treated with drugs (OSI-906 5 μM, **PF-4708671 10 μM**). After 1 week of incubation, cells are stained with 1% crystal violet, and the number of colonies is counted and recorded[2]. **Animal Administration:** [2]Mice[2]

Five- to 6-week-old female athymic nude mice (Hsd:Athymic Nude-Foxn1nu) are randomly assigned to the following groups (5 mice/group). For injection of HT29-L and HT29-P cells, mice are treated with vehicle (25 mM tartaric acid) or OSI-906 (30 mg/kg) for 12 days. For injection of HCT116 cells, mice are treated with (i) vehicle (25 mM tartaric acid); (ii) OSI-906 alone (30 mg/kg); (iii) **PF-4708671** alone (**60 mg/kg**); and (iv) OSI-906 (30 mg/kg)+PF-4708671 (60 mg/kg) and treated with drugs **orally** for 14 days. Vehicle and OSI-906 are given once per day and PF-4708671 is given once every other day. Twenty-four hours after the last treatment, the mice are sacrificed and the tumor weights were measured[2].

References:

[1]. Pearce LR, et al. Characterization of PF-4708671, a novel and highly specific inhibitor of p70 ribosomal S6 kinase (S6K1). Biochem J. 2010 Oct 15;431(2):245-55.

[2]. Zhang Y, et al. Inhibition of p70S6K1 Activation by Pdcd4 Overcomes the Resistance to an IGF-1R/IR Inhibitor in Colon Carcinoma Cells. Mol Cancer Ther. 2015 Mar;14(3):799-809.

CAIndexNames:

1H-Benzimidazole, 2-[[4-(5-ethyl-4-pyrimidinyl)-1-piperazinyl]methyl]-6-(trifluoromethyl)-

SMILES:

FC(C1=CC=C2N=C(CN3CCN(C4=NC=NC=C4CC)CC3)NC2=C1)(F)F

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