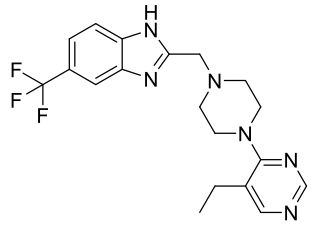
Product data sheet

MedKoo Cat#: 406432 Name: PF-4708671 CAS#: 1255517-76-0 Chemical Formula: $C_{19}H_{21}F_3N_6$ Exact Mass: 390.17798 Molecular Weight: 390.41	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

PF-4708671 is a novel cell-permeable inhibitor of S6K1. PF-4708671 specifically inhibits the S6K1 isoform with a Ki of 20 nM and IC50 of 160 nM. PF-4708671 prevents the S6K1-mediated phosphorylation of S6 protein in response to IGF-1 (insulin-like growth factor 1), while having no effect upon the PMA-induced phosphorylation of substrates of the highly related RSK (p90 ribosomal S6 kinase) and MSK (mitogen- and stress-activated kinase) kinases.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	20.0	51.2

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.56 mL	12.81 mL	25.61 mL
5 mM	0.51 mL	2.56 mL	5.12 mL
10 mM	0.26 mL	1.28 mL	2.56 mL
50 mM	0.05 mL	0.26 mL	0.51 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Shen H, Wang GC, Li X, Ge X, Wang M, Shi ZM, Bhardwaj V, Wang ZX, Zinner RG, Peiper SC, Aplin AE, Jiang BH, He J. S6K1 blockade overcomes acquired resistance to EGFR-TKIs in non-small cell lung cancer. Oncogene. 2020 Dec;39(49):7181-7195. doi: 10.1038/s41388-020-01497-4. Epub 2020 Oct 9. PMID: 33037411; PMCID: PMC7718330.
2. Archambault AS, Turcotte C, Martin C, Lefebvre JS, Provost V, Laviolette M, Flamand N. Leukotriene B_4 Metabolism and p70S6 Kinase 1 Inhibitors: PF-4708671 but Not LY2584702 Inhibits CYP4F3A and the ω-Oxidation of Leukotriene B_4 In Vitro and In Cellulo. PLoS One. 2017 Jan 9;12(1):e0169804. doi: 10.1371/journal.pone.0169804. PMID: 28068410; PMCID: PMC5222342.

In vivo study

1. Kam K, Kang M, Eren CY, Pettibone WD, Bowling H, Taveras S, Ly A, Chen RK, Berryman NV, Klann E, Varga AW. Interactions between sleep disruption, motor learning, and p70 S6 kinase 1 signaling. Sleep. 2020 Mar 12;43(3):zsz244. doi: 10.1093/sleep/zsz244. PMID: 31608388; PMCID: PMC7315768.
2. Shum M, Houde VP, Bellemare V, Junges Moreira R, Bellmann K, St-Pierre P, Viollet B, Foretz M, Marette A. Inhibition of mitochondrial complex 1 by the S6K1 inhibitor PF-4708671 partly contributes to its glucose metabolic effects in muscle and liver cells. J Biol Chem. 2019 Aug 9;294(32):12250-12260. doi: 10.1074/jbc.RA119.008488. Epub 2019 Jun 26. PMID: 31243102; PMCID: PMC6690709.

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7. Bioactivity

Biological target:

PF-4708671 is a potent cell-permeable S6K1 inhibitor with a Ki of 20 nM and IC50 of 160 nM.

In vitro activity

To determine whether PF-4708671 can synergistically enhance the cytotoxicity of TKI in resistant cells, a MTT assay was used to examine the effects of PF and TKI on cell viabilities. More than 60% cells were still viable when treated with osimertinib or PF alone at the highest doses (Fig.5B, C). Notably, the combination of osimertinib and PF induced higher cytotoxicity in HCC827-OR cells (Fig.5D). The combination index (CI) analyzed by CompuSyn software showed the strong synergism between osimertinib and PF (Fig. 5E). Similar results were obtained in PC-9/G cells treated with gefitinib (Fig.S4D, E, F, G), indicating that PF-4708671 was able to re-sensitize resistant cells to TKI.

Reference: Oncogene. 2020 Dec; 39(49): 7181–7195. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7718330/

In vivo activity

This study used differentiated muscle cells from WT mice or mice lacking both AMPKα1 and AMPKα2 catalytic subunits (AMPK α1/2 dKO muscle cells). After 5 and 48 h of treatment with PF (PF-4708671), AMPK phosphorylation on Thr-172 and ACC phosphorylation on Ser-79 were increased in differentiated WT myocytes but, as expected, not in AMPK α1/2 dKO muscle cells (Fig. 2A). In both AMPK WT and dKO muscle cells, PF treatment decreased basal and insulin-stimulated S6 phosphorylation in both WT and AMPK α1/2 dKO muscle cells. PF treatment of both WT and AMPK α1/2 dKO muscle cells for 5 and 48 h increased glucose uptake compared with vehicle-treated cells (Fig. 2B). However, lack of AMPK activation did not reduce the stimulatory effects of PF treatment on muscle glucose uptake. These data demonstrate that AMPK is dispensable for the stimulatory effect of PF on muscle glucose uptake.

Reference: J Biol Chem. 2019 Aug 9; 294(32): 12250–12260. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6690709/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.