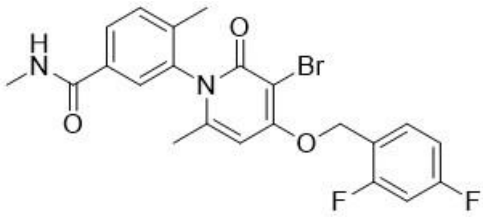
Product data sheet

MedKoo Cat#: 206022 Name: PH-797804 CAS#: 586379-66-0 Chemical Formula: $C_{22}H_{19}BrF_2N_2O_3$ Exact Mass: 476.05471 Molecular Weight: 477.3	
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:

PH-797804 is a potent and selectiove inhibitor of p38 mitogen-activated protein (MAP) kinase. PH-797804 reduces tumor growth of the three PDXs, which correlates with impaired colon tumor cell proliferation and survival. The inhibition of p38 MAPK in PDXs results in downregulation of the IL-6/STAT3 signaling pathway, which is a key regulator of colon tumorigenesis. PH-797804 may have therapeutic interest for colon cancer treatment.

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	14.0	29.3

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.10 mL	10.48 mL	20.95 mL
5 mM	0.42 mL	2.10 mL	4.19 mL
10 mM	0.21 mL	1.05 mL	2.10 mL
50 mM	0.04 mL	0.21 mL	0.42 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. Revuelta M, Elicegui A, Scheuer T, Endesfelder S, Bührer C, Moreno-Cugnon L, Matheu A, Schmitz T. In vitro P38MAPK inhibition in aged astrocytes decreases reactive astrocytes, inflammation and increases nutritive capacity after oxygen-glucose deprivation. Aging (Albany NY). 2021 Feb 9;13(5):6346-6358. doi: 10.18632/aging.202651. Epub 2021 Feb 9. PMID: 33563843; PMCID: PMC7993689.

2. Moreno-Cugnon L, Arrizabalaga O, Llarena I, Matheu A. Elevated p38MAPK activity promotes neural stem cell aging. Aging (Albany NY). 2020 Apr 3;12(7):6030-6036. doi: 10.18632/aging.102994. Epub 2020 Apr 3. PMID: 32243258; PMCID: PMC7185101.

In vivo study

1. Hope HR, Anderson GD, Burnette BL, Compton RP, Devraj RV, Hirsch JL, Keith RH, Li X, Mbalaviele G, Messing DM, Saabye MJ, Schindler JF, Selness SR, Stillwell LI, Webb EG, Zhang J, Monahan JB. Anti-inflammatory properties of a novel N-phenyl pyridinone inhibitor of p38 mitogen-activated protein kinase: preclinical-to-clinical translation. J Pharmacol Exp Ther. 2009 Dec;331(3):882-95. doi: 10.1124/jpet.109.158329. Epub 2009 Aug 31. PMID: 19720877.

2. Gupta J, Igea A, Papaioannou M, Lopez-Casas PP, Llonch E, Hidalgo M, Gorgoulis VG, Nebreda AR. Pharmacological inhibition of p38 MAPK reduces tumor growth in patient-derived xenografts from colon tumors. Oncotarget. 2015 Apr 20;6(11):8539-51. doi: 10.18632/oncotarget.3816. PMID: 25890501; PMCID: PMC4496165.

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7. Bioactivity

Biological target:

PH-797804 is a ATP-competitive, selective p38α/p38β inhibitor (IC50=26 nM and Ki=5.8 nM for p38α; Ki=40 nM for p38β) and does not inhibit JNK2.

In vitro activity

The aim of this study was to investigate the effect of OGD in young and aged primary rat astrocyte cultures and to analyze the expression and effect of p38MAPK in these cultures. For this, this study cultured young and aged astrocytes with PH-797804, MAPK14 (p38α) inhibitor, the most abundant isoform of p38MAPK in the brain, to define changes in supporting and protective properties of astrocytes that can be critical for survival of brain cells. For assays with P38MAPK inhibitor, astrocytes were treated with 2 μM PH-797804 (Selleckchem) added to the medium when seeded and included in every medium change. the addition of PH-797804 to aged astrocyte cultures lowered levels of P-P38MAPK and Mapk14 (p38alpha) gene expression by 50% after OGD and after reperfusion in comparison to control cells. Analysis of TNFα, GFAP and P-p38MAPK protein expression after OGD revealed that there was a reduction of all these proteins in aged astrocytes treated with PH-797804 after OGD. In the results, the inactivation of p38α in aged astrocyte cultures treated by PH-797804 attenuated astroglial activation and inflammation that occur after OGD. It was also found that PH-797804 treatment in aged astrocytes can prevent OGD-induced changes of growth factors igf and ngf, of the free radical clearance factors sod2 and gclc, and of the glutamate metabolism system gs that were increased after OGD.

Reference : Aging (Albany NY). 2021 Mar 15; 13(5): 6346–6358. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7993689/

In vivo activity

To investigate the role of p38 MAPK signaling in the PDXs from CRC, the inhibitor PH797804 was used. This chemical compound effectively inhibits the p38α and p38β MAPKs, without affecting other MAPKs such as ERK1/2 and JNK, and it is used in clinical trials for inflammatory diseases. Tumors in PDXs were allowed to grow up to a measurable size (150-200 mm3) and then mice were randomized into two groups, which received either PH797804 or vehicle. Models CCR-010 and CCR-024 showed a decrease in tumor size when treated with PH797804 during the first 5-7 days. Then, tumors started to grow again although significantly slower than the vehicle treated tumors. These two models were treated for 10 days (Figure2). Model CCR-038 showed a more pronounced growth inhibition during all the treatment with PH797804. Due to the different response observed, in this case the treatment was extended until day 16 to confirm that tumor growth inhibition was maintained (Figure2). Therefore, tumor growth was significantly reduced in the PH797804-treated mice for the three PDX models of CRC, although there were slight differences in the response of each model.

Reference: Oncotarget. 2015 Apr 20; 6(11): 8539–8551. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4496165/