

Product Data Sheet

Product Name: C188-9
Cat. No.: GC34076

Chemical Properties

Cas. No. 432001-19-9

SMILES O=S(C1=CC=C(OC)C=C1)(NC2=C3C=CC=CC3=C(O)C(C4=C5C=CC=CC5=CC=C4O)=C2)=O

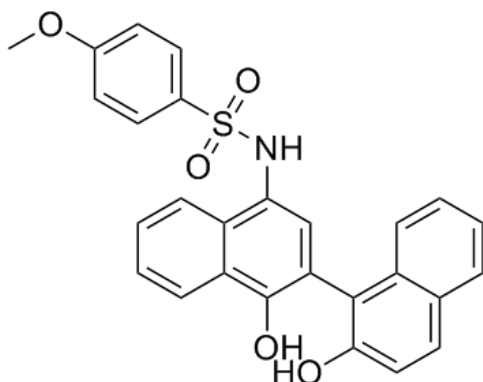
Formula $C_{27}H_{21}NO_5S$ M.Wt 471.52

Solubility DMSO : ≥ 62 mg/mL (131.49 mM) Storage 4°C, protect from light

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

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

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Cell experiment: Cell lines are plated at 2 to 5×10^5 cells/mL in growth medium and treated with increasing doses of inhibitor for 24 hours. CD34+ AML cells are plated at 1 to 2×10^5 cells/mL in IMDM with 20% FBS and Pen/Strep, and incubated with C188-9 (0.3 to 100 μ M) for 48 hours. Cells are then harvested and labeled. The fraction of spontaneous apoptosis is determined from an untreated sample and then subtracted from the drug-treated samples to yield the percentage of apoptosis attributed to drug treatment[1].

Animal experiment: Mice[3]UM-SCC-17B cells (1.5×10^6) are injected into the tongues of athymic, 8-10 week old, male, nude mice. Once tumors are established, mice (20 total; 10/group) are randomized (average tumor vol ~ 15 -20 mm³) to receive 5 times a week, intraperitoneal injections of either DMSO or C188 (50 mg/kg) or C188-9 (100 mg/kg). Tumor volumes are measured twice weekly. Average tumor volumes $6/\pi \times (\text{long dimension}) \times (\text{short dimension})^2$) are calculated and normalized to the volume at first day of treatment and plotted comparison is done by t test (* $p < 0.05$) [3].

References:

- [1]. Silva KA, et al. Inhibition of Stat3 activation suppresses caspase-3 and the ubiquitin-proteasome system, leading to preservation of muscle mass in cancer cachexia. J Biol Chem. 2015 Apr 24;290(17):11177-87.
- [2]. Redell MS, et al. Stat3 signaling in acute myeloid leukemia: ligand-dependent and -independent activation and induction of apoptosis by a novel small-molecule Stat3 inhibitor. Blood. 2011 May 26;117(21):5701-9.
- [3]. Bharadwaj U, et al. Small-molecule inhibition of STAT3 in radioresistant head and neck squamous cell carcinoma. Oncotarget. 2016 May 3;7(18):26307-30.

Background

C188-9 is a Stat3 inhibitor, with a Kd of 4.7 nM.

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C188-9 is a Stat3 inhibitor, with a K_d of 4.7 nM[1]. The IC_{50} s of C188-9 to inhibit Stat3 activation in AML cell lines are in the range of 4-7 μ M, and in primary AML samples the IC_{50} s are in the range of 8-18 μ M. For apoptosis studies, AML cell lines and primary samples are treated for 24 hours with C188-9, then apoptotic cells are quantified by FACS analysis for annexin V-labeled cells. The EC_{50} s for apoptosis induction are quite variable, ranging from 6 μ M to over 50 μ M[2].

Of the approximately 13,528 discernible genes, levels of 37 gene transcripts are altered by C188 (17 down and 20 up-regulated, $fdr < 0.01$, fold change ≥ 1.5), of which 7 are known STAT3 gene targets. In comparison, C188-9 affects a much greater number of genes involved in oncogenesis (384 total, 95 down- and 289 up-regulated), including 76 genes previously reported as regulated by STAT3 (38 down-regulated and 38 up-regulated). Among the 38 genes previously shown to be upregulated by STAT3, 24 (63%) genes are downregulated by C188-9 treatment, as expected. Additionally, 10 more genes downregulated by C188-9 ($fdr < 0.01$, fold change ≥ 1.5) that previously are shown to be upregulated by STAT1. Thus, 40 of 48 (83.3%) genes downregulated by C188-9 previously are shown to be positively regulated by STAT1, including sixteen genes shown to be co-regulated by STAT3 and STAT1. This analysis raises the possibility that the effect of C188-9 on gene transcript levels in HNSCC tumors is mediated by its effects on both STAT3 and STAT1[3].

[1]. Silva KA, et al. Inhibition of Stat3 activation suppresses caspase-3 and the ubiquitin-proteasome system, leading to preservation of muscle mass in cancer cachexia. J Biol Chem. 2015 Apr 24;290(17):11177-87. [2]. Redell MS, et al. Stat3 signaling in acute myeloid leukemia: ligand-dependent and -independent activation and induction of apoptosis by a novel small-molecule Stat3 inhibitor. Blood. 2011 May 26;117(21):5701-9. [3]. Bharadwaj U, et al. Small-molecule inhibition of STAT3 in radioresistant head and neck squamous cell carcinoma. Oncotarget. 2016 May 3;7(18):26307-30.

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