

Product Data Sheet

Product Name: PF-06260933

Cat. No.: GC31675

Chemical Properties

Cas. No. 1811510-56-1

SMILES NC1=C(C2=CC=C(CI)C=C2)C=C(C(C=N3)=CC=C3N)C=N1

Formula $C_{16}H_{13}ClN_4$ M.Wt 296.75

Solubility DMSO : 30 mg/mL (101.10 mM) Storage Store at -20°C

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.

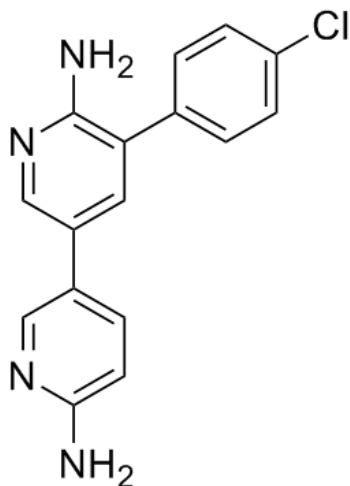
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment: HUVECs are maintained in EGM2 media at 37°C and 5% CO₂. HUVECs or peritoneal macrophages are treated with vehicle or PF-06260933 in vitro to determine whether pharmacological inhibition of MAP4K4 alters MAPK signalling in response to TNF- α [2].

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Animal experiment: Compound PF-06260933 (10 mg/kg, dissolved in dH₂O) is orally administered to 8 to 10-week-old male Apoe^{-/-} mice twice daily for 6 weeks. Ldlr^{-/-} male mice are placed on high-fat diet (HFD) for 10 weeks before drug administration. Compound PF-06260933 is administered to male 8 to 10-week-old Ldlr^{-/-} mice as above for 10 weeks. Oral administration of water is used as vehicle control in all studies. Mice are euthanized by CO₂ inhalation followed by bilateral pneumothorax[2].

References:

- [1]. Ammirati M, et al. Discovery of an in Vivo Tool to Establish Proof-of-Concept for MAP4K4-Based Antidiabetic Treatment. ACS Med Chem Lett. 2015 Oct 6;6(11):1128-33.
[2]. Roth Flach RJ, et al. Endothelial protein kinase MAP4K4 promotes vascular inflammation and atherosclerosis. Nat Commun. 2015 Dec 21;6:8995.

Background

PF-06260933 is a highly selective small-molecule inhibitor of MAP4K4 with IC₅₀s of 3.7 and 160 nM for kinase and cell, respectively.

PF-06260933 treatment of human aortic endothelial cell (EC) robustly prevents TNF- α -mediated endothelial permeability in vitro, similar to MAP4K4 knockdown[2].

In the mice model, PF-06260933 treatment does not alter plasma lipid content, although reductions in glucose levels are observed, which is consistent with whole-body-inducible Map4k4 knockout animals. PF-06260933 administration ameliorates further plaque development and/or promotes plaque regression in this animal model (46.0% versus 25.5%), and a reduction in plasma glucose as well as lipid content is also observed[2].

- [1]. Ammirati M, et al. Discovery of an in Vivo Tool to Establish Proof-of-Concept for MAP4K4-Based Antidiabetic Treatment. ACS Med Chem Lett. 2015 Oct 6;6(11):1128-33. [2]. Roth Flach RJ, et al. Endothelial protein kinase MAP4K4 promotes vascular inflammation and atherosclerosis. Nat Commun. 2015 Dec 21;6:8995.

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