Small Molecules

BIRB-796

p38 MAPK inhibitor

Catalog # 72682 1 mg
72684 10 mg

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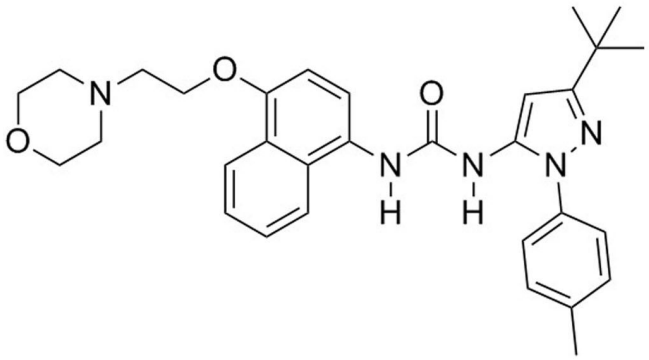
Product Description

BIRB-796 inhibits the stress-activated p38 mitogen-activated protein kinase (MAPK), which plays a critical role in regulating the production of proinflammatory cytokines such as tumor necrosis factor (TNF) and interleukin 1 (IL-1). BIRB-796 is a highly potent inhibitor of p38 MAPK (Kd = 0.1 nM) that blocks TNFα release in LPS-stimulated THP-1 cells (IC_{50} = 18 nM; Pargellis et al.). At 10 µM, BIRB-796 inhibits c-Jun N-terminal kinase (JNK) 2α2 in vitro, but at the low concentration necessary to inhibit p38 MAPK, it does not affect the phosphorylation of JNK substrates in cells (Bain et al.; Kuma et al.).

Molecular Name:	BIRB-796
Alternative Names:	Doramapimod
CAS Number:	285983-48-4
Chemical Formula:	$C_{31}H_{37}N_5O_3$
Molecular Weight:	527.7 g/mol
Purity:	≥ 98%
Chemical Name:	N-[3-(1, 1-dimethylethyl)-1-(4-methylphenyl)-1H-pyrazol-5-yl]-N'-[4-[2-(4-morpholinyl)ethoxy]-1-naphthalenyl]-urea
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect from prolonged exposure to light. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 56 mM · Absolute ethanol ≤ 5.6 mM For example, to prepare a 10 mM stock solution in DMSO, resuspend 1 mg in 190 µL of fresh DMSO. Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application. Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

Published Applications

MAINTENANCE AND SELF-RENEWAL
· Rescues the self-renewal ability of muscle satellite cells from aged mice (Bernet et al.).
· Increases the regenerative capacity of functional aged skeletal muscle stem cells grown in hydrogel (Cosgrove et al.).
· Blocks GADD45G-induced differentiation of long-term repopulating hematopoietic stem cells (Thalheimer et al.).
· Enhances stem cell activity of cultured umbilical cord blood-derived hematopoietic cells cultured in serum-free medium supplemented with SCF (Catalog #78062), TPO (Catalog #02522), and FLT3L (Baudet et al.).
· Blocks the osteogenic differentiation effect of myocilin on human mesenchymal stem cells (Kwon et al.).

References

Bain J et al. (2007) The selectivity of protein kinase inhibitors: a further update. Biochem J 408(3): 297–315.
Baudet A et al. (2012) RNAi screen identifies MAPK14 as a druggable suppressor of human hematopoietic stem cell expansion. Blood 119(26): 6255–8.
Bernet JD et al. (2014) p38 MAPK signaling underlies a cell-autonomous loss of stem cell self-renewal in skeletal muscle of aged mice. Nat Med 20(3): 265–71.
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Kuma Y et al. (2005) BIRB796 inhibits all p38 MAPK isoforms in vitro and in vivo. J Biol Chem 280(20): 19472–9.
Kwon HS et al. (2013) Myocilin stimulates osteogenic differentiation of mesenchymal stem cells through mitogen-activated protein kinase signaling. J Biol Chem 288(23): 16882–94.
Pargellis C et al. (2002) Inhibition of p38 MAP kinase by utilizing a novel allosteric binding site. Nat Struct Biol 9(4): 268–72.
Thalheimer FB et al. (2014) Cytokine-regulated GADD45G induces differentiation and lineage selection in hematopoietic stem cells. Stem Cell Reports 3(1): 34–43.

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