

Product Data Sheet

Product Name: MRT67307

Cat. No.: GC17136

Chemical Properties

Cas. No. 1190378-57-4

Chemical Name N-[3-[[5-cyclopropyl-2-[3-(morpholin-4-ylmethyl)anilino]pyrimidin-4-yl]amino]propyl]cyclobutanecarboxamide

SMILES C1CC(C1)C(=O)NCCCNC2=NC(=NC=C2C3CC3)NC4=CC=CC(=C4)CN5CCOCC5

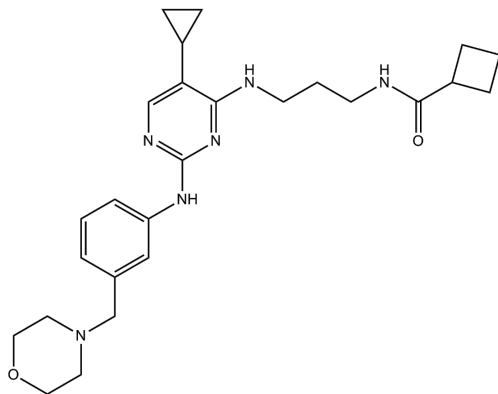
Formula $C_{26}H_{36}N_6O_2$ M.Wt 464.62

Solubility ≥ 23.25 mg/mL in DMSO, ≥ 30.67 mg/mL in EtOH, ≥ 52.5 mg/mL in Water with gentle warming
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.

Structure



Protocol

Kinase experiment [1]:

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

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Kinase assays Substrates and kinases were diluted in 50 mM Tris/HCl (pH 7.5), 0.1% 2-mercaptoethanol, 0.1 mM EGTA and 10 mM magnesium acetate. Reactions were initiated with [γ -³²P]ATP (2500 c.p.m./pmol) to a final concentration of 0.1 mM and terminated after 15 min at 30 °C by the addition of SDS and EDTA (pH 7.0) to final concentrations of 1.0% (w/v) and 20 mM respectively. After heating for 5 min at 100 °C and separation by SDS/PAGE, the phosphorylated proteins.

Cell experiment [1]:

Cell lines Mouse bone-marrow-derived macrophages

Preparation method The solubility of this compound in DMSO is >23.3 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37°C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting condition 0-10000 nM

Applications Treatment of macrophages with MRT67307 led to an increase in the poly(I:C)- and LPS-stimulated phosphorylation of p105 and RelA and enhanced NF- κ B transcriptional activity. In addition, MRT67307 prevented the production of IFN β and the phosphorylation of IRF3 without suppressing the activation of NF- κ B, which showed that MRT67307 blocked the induction of Pellino 1 through inhibiting TBK1/IKK ϵ kinase activity.

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References:

[1] Clark K, et al. Novel cross-talk within the IKK family controls innate immunity. *Biochem J*. 2011 Feb 15;434(1):93-104.

Background

MRT67307 is an inhibitor for TBK1, IKK ϵ , MARK1-4 and NUA1 with IC₅₀ value of 19, 160, 27-52 and 230nM, respectively [1]. It is an inhibitor for ULK1 and ULK2 with IC₅₀ value of 45 and 38nM, respectively [2]. Also, it is a salt inducible kinase (SIK) inhibitor with IC₅₀ value of 250, 67 and 430nM for SIK1, SIK2 and SIK3, respectively.

SIKs prevent the formation of regulatory macrophages and their inhibition induces increasing in some markers of regulatory macrophages, such as IL-10 and other anti-inflammatory molecules. IKK ϵ and TBK-1 mediate the phosphorylation of interferon regulatory factor 3 (IRF3). MARK1 is a Serine/threonine-protein kinase.

In macrophages, MRT67307 prevented the production of IFN β and the phosphorylation of IRF3 without suppressing the activation of NF- κ B, which showed that MRT67307 blocked the induction of Pellino 1 through inhibiting TBK1/IKK ϵ kinase activity [1] [3]. Also, MRT67307 completely blocked the TBK1- or IKK ϵ -induced decrease in the mobility of Pellino 1 [3]. Exposed macrophages to MRT67307 increased the levels of the anti-inflammatory cytokines IL-1 α and IL-10 and decreased the levels of proinflammatory cytokines (such as IL-6, IL-12, and TNF) in response to bacterial lipopolysaccharide (LPS) [4].

References:

[1]. Clark K, Pegg M, Plater L, et al. Novel cross-talk within the IKK family controls innate immunity. *Biochem J*, 2011, 434(1): 93-104.

[2]. Petherick KJ, Conway OJ, Mpamhanga C, et al. Pharmacological Inhibition of ULK1 Blocks mTOR-Dependent Autophagy. *J Biol Chem*, 2015, pii: jbc.C114.627778.

[3]. Smith H, Liu XY, Dai L, et al. The role of TBK1 and IKK ϵ in the expression and activation of Pellino 1. *Biochem J*, 2011, 434(3): 537-548.

[4]. Clark K, MacKenzie KF, Petkevicius K, et al. Phosphorylation of CRT3 by the salt-inducible kinases controls the interconversion of classically activated and regulatory macrophages. *Proc Natl Acad Sci U S A*, 2012, 109(42): 16986-16991.

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