

Product Data Sheet

Product Name: ZL0420
Cat. No.: GC19455

Chemical Properties

Cas. No. 2230496-80-5

SMILES OC1=CC(N)=C(/N=N/C2=CC(CCC(N3)=O)=C3C=C2)C=C1C

Formula $C_{16}H_{16}N_4O_2$ M.Wt 296.32

Solubility DMF: 30 mg/ml, DMSO: 30 mg/ml, DMSO:PBS (pH 7.2) (1:9): 0.1 mg/ml
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

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

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Cell experiment: hSAECs are first pretreated with a series final concentrations of BRD4 inhibitors from 0.01 nM to 100 μ M for 24 hours and are then added poly(I:C) at 10 μ g/mL for another 4 hours prior to harvesting the cells. The harvested cells are first washed with PBS twice and then the total RNA is extracted using acid guanidinium phenol extraction. The total RNA is further reverse-transcribed for gene expression analysis by Q-RT-PCR[1].

Animal experiment: Mice[1]C57BL/6 mice are pre-treated in the absence or presence of the ZL0420 [10 mg/kg body weight, via the intraperitoneal route] one day prior to poly(I:C) stimulation. The next day, animals are given another dose of ZL0420 immediately followed by intranasal (i.n.) administration of phosphate-buffered saline (PBS, 50 μ L) or poly(I:C) (300 μ g dissolved in 50 μ L PBS). One day later, the mice are euthanized. The bronchoalveolar lavage fluid (BALF) and lung tissues of treated mice are collected for further analysis[1].

References:

[1]. Liu Z, et al. Discovery of potent and selective BRD4 inhibitors capable of blocking TLR3-induced acute airway inflammation. Eur J Med Chem. 2018 May 10;151:450-461.

Background

ZL0420 is a potent and selective BRD4 inhibitor with IC₅₀ values of 27 nM against BRD4 BD1 and 32 nM against BRD4 BD2.

ZL0420 is well docked into the acetyl-lysine (KAc) binding pocket of BRD4, forming key interactions including the critical hydrogen bonds with Asn140 directly and Tyr97 indirectly via a H₂O molecule. ZL0420 exhibits submicromolar potency of inhibiting the TLR3-dependent innate immune gene program, including ISG54, ISG56, IL-8, and Gro β genes in cultured human small airway epithelial cells (hSAECs) with IC₅₀s of 0.49-0.86 μ M[1].

ZL0420 demonstrates potent efficacy reducing airway inflammation in a mouse model with low toxicity. ZL0420 displays high efficacy and almost completely blocks the profound accumulation of

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neutrophils around the small and medium sized airways induced by poly(I:C) administration[1].

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