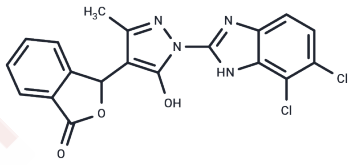
Data Sheet (Cat.No.T5486)

TargetMol

RU.521

Chemical Properties



CAS No. : 2262452-06-0

Formula: C19H12Cl2N4O3

Molecular Weight: 415.23

Storage: Keep away from direct sunlight,Keep away from moisture
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	RU.521 (RU3205217) is a selective cyclic GMP-AMP synthetase (cGAS) inhibitor (mouse: IC50=0.11 μM), (human: IC50=2.94 μM). RU.521 is an inhibitor of the receptor activated by dsDNA (IC50=700 nM). RU.521 inhibits cGAS-mediated interferon upregulation. RU.521 reduces constitutive interferon expression in macrophages derived from a mouse model of Aicardi-Goutieres syndrome.
Targets(IC50)	cGAS,DNA
In vitro	**METHODS**: Human THP1-Dual cells were treated with RU.521 for 24 hours, and the cytotoxicity was determined using the CCK-8 assay. **RESULTS**: RU.521 inhibited cell growth (CC50=38.4 μM). [1]
In vivo	**METHODS**: To study the effect of RU.521 on sepsis, mice were intraperitoneally injected with RU.521 (5 mg/kg) (injected with LPS) in a single dose. **RESULTS**: RU.521 enhanced cardiac function, reduced cardiac inflammation, oxidative stress and apoptosis, and alleviated the symptoms of sepsis in mice. [2]
Cell Research	Small-molecule compounds were serially diluted to concentrations spanning the range tested in the response curves were added to 6.7?×?10^5 RAW-Blue macrophages plated 16?h prior in 96-well dishes, then harvested 72?h after compound addition. ATP was measured using CellTiter Glo Viability Assay using 50?μM Tamoxifen as a positive control for cytotoxicity. Viability values were generated using vehicle (DMSO) or the first dose as 100% and Tamoxifen as 0%. Outliers were removed.
Animal Research	the chronically elevated levels of cytokines observed in Trex1 null mice are a consequence of constitutively activated cGAS, due to the inability to eliminate aberrantly localized self-DNA. We harvested BMDMs from 6-8-week old Trex1 ?/? mice, treated them with each compound, and measured expression levels of IFNB1 by quantitative reverse transcription PCR (qRT-PCR). Treatment of primary BMDMs with RU.521 or its analogs reduced IFNB1 expression, indicating their effectiveness in suppressing intrinsic DNA-dependent, constitutively-activated type I interferon expression in cells deficient of a cytoplasmic DNA exonuclease.

Solubility Information

Solubility	DMSO: 126.3 mg/mL (304.17 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	5% DMSO+40% PEG300+5% Tween 80+50% Saline: 2 mg/mL (4.82 mM) *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4083 mL	12.0415 mL	24.083 mL
5 mM	0.4817 mL	2.4083 mL	4.8166 mL
10 mM	0.2408 mL	1.2042 mL	2.4083 mL
50 mM	0.0482 mL	0.2408 mL	0.4817 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Tan J, et al. Synthesis and Pharmacological Evaluation of Tetrahydro-γ-carboline Derivatives as Potent Anti-inflammatory Agents Targeting Cyclic GMP-AMP Synthase. J Med Chem. 2021 Jun 10;64(11):7667-7690.
Li B, Xu L, Wang Z, et al.Neutrophil Extracellular Traps Regulate Surgical Brain Injury by Activating the cGAS-STING Pathway.Cellular and Molecular Neurobiology.2024, 44(1): 36.
Wang Z, Zhang X, Luo Y, et al.Therapeutic targeting of ARID1A-deficient cancer cells with RITA (Reactivating p53 and inducing tumor apoptosis).Cell Death & Disease.2024, 15(5): 375.
Xu Q, et al. Small molecule inhibition of cyclic GMP-AMP synthase ameliorates sepsis-induced cardiac dysfunction in mice. Life Sci. 2020 Nov 1;260:118315.