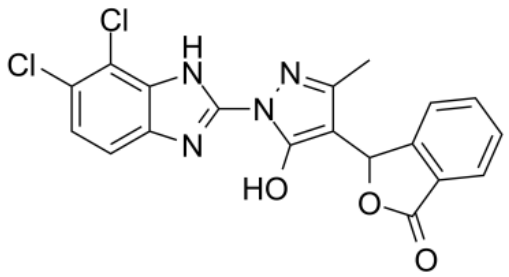
Product Data Sheet

Product Name: RU.521
Cat. No.: GC37570

Chemical Properties

Cas. No.	2262452-06-0		
SMILES	O=C1OC(C2=C(O)N(C3=NC4=CC=C(Cl)C(Cl)=C4N3)N=C2C)C5=C1C=CC=C5		
Formula	$C_{19}H_{12}Cl_2N_4O_3$	M.Wt	415.23
Solubility	DMSO: ≥ 125 mg/mL (301.04 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.		

Structure



Protocol

Cell experiment [1]:

Cell lines 16HBE cells

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Preparation Method	16HBE cells were pretreated with 1, 10 and 20μM of the cGAS inhibitor RU.521 for 24h, and then infected with Human metapneumovirus (hMPV) for 48h.
Reaction Conditions	1, 10 and 20μM, 24h
Applications	HMPV replication decreased significantly after 16HBE cells were treated with different concentrations of inhibitors, and 10μM RU.521 had a significant inhibitory effect.

Animal experiment [2]:

Animal models	Lung ischemia/reperfusion（I/R）Sprague-Dawley rats model
Preparation Method	Sprague-Dawley rats were subjected to left hilar occlusion reperfusion surgery to establish a pulmonary I/R model. Rats were intraperitoneally administered with cGAS-specific inhibitor RU.521, STING agonist SR-717, and ERS inhibitor 4-phenylbutyric acid (4-PBA).
Dosage form	5mg/kg, 1h, i.p.
Applications	RU.521 attenuates pulmonary ischemia/reperfusion injury by inhibiting the cGAS-STING pathway.

Caution: Product has not been fully validated for medical applications. For research use only.
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Address: 10292 Central Ave. #205, Montclair, CA, USA

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References:

[1] Wu G, Zhang Y, Niu L, Hu Y, Yang Y, Zhao Y. Interleukin-1β promotes human metapneumovirus replication via activating the cGAS-STING pathway. Virus Res. 2024 May;343:199344.

[2] Vincent J, Adura C, Gao P, Luz A, Lama L, Asano Y, Okamoto R, Imaeda T, Aida J, Rothamel K, Gogakos T, Steinberg J, Reasoner S, Aso K, Tuschl T, Patel DJ, Glickman JF, Ascano M. Small molecule inhibition of cGAS reduces interferon expression in primary macrophages from autoimmune mice. Nat Commun. 2017 Sep 29;8(1):750.

Background

RU.521 (RU320521) is a potent and selective cyclic GMP-AMP synthase (cGAS) inhibitor that binds to the catalytic domain of cGAS, thereby inhibiting the activation of cGAS by dsDNA. The IC_{50} value of RU.521 in inhibiting cGAS-mediated signal transduction is 700nM[1].

RU.521 (10μM) can inhibit the replication of human metapneumovirus (hMPV) in 16HBE cells, and exogenous addition of interleukin 1 beta (IL-1β) in the presence of RU.521 does not affect hMPV replication (IL-1β can promote hMPV replication) [2]. RU.521 (700nM) can reverse the damage of HUVEC cells caused by neutrophil extracellular traps (NETs) by inhibiting the cGAS/STING pathway[3].

RU.521 (5mg/kg) can inhibit the cGAS-STING pathway and reduce endoplasmic reticulum stress (ERS), thereby alleviating lung injury and promoting pulmonary ventilation function in rats with pulmonary ischemia/reperfusion (I/R)[4]. Intracisternary infusion of RU.521 (0.4mg/kg) in hypertensive mice reduced the expression of cGAS and STING in the paraventricular nucleus (PVN) of mice, and also reduced the LC3II/I ratio and p62 expression level[5].

References:
[1] Vincent J, Adura C, Gao P, Luz A, Lama L, Asano Y, Okamoto R, Imaeda T, Aida J, Rothamel K, Gogakos T, Steinberg J, Reasoner S, Aso K, Tuschl T, Patel DJ, Glickman JF, Ascano M. Small molecule inhibition of cGAS reduces interferon expression in primary macrophages from autoimmune mice. Nat Commun. 2017 Sep 29;8(1):750. doi: 10.1038/s41467-017-00833-9. Erratum in: Nat Commun. 2017 Nov 23;8(1):1827.

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[2] Wu G, Zhang Y, Niu L, Hu Y, Yang Y, Zhao Y. Interleukin-1β promotes human metapneumovirus replication via activating the cGAS-STING pathway. Virus Res. 2024 May;343:199344.
[3] Zhang B, Fang Z, Lin Y, et al. RU. 521 protects against neutrophil extracellular traps-induced vascular endothelial injury by inhibiting cGAS/STING pathway[J]. ||| Bangladesh Journal of Pharmacology|||, 2024, 19(2): 59-64.
[4] Vincent J, Adura C, Gao P, Luz A, Lama L, Asano Y, Okamoto R, Imaeda T, Aida J, Rothamel K, Gogakos T, Steinberg J, Reasoner S, Aso K, Tuschl T, Patel DJ, Glickman JF, Ascano M. Small molecule inhibition of cGAS reduces interferon expression in primary macrophages from autoimmune mice. Nat Commun. 2017 Sep 29;8(1):750.
[5] Han C, Qian X, Ren X, Zhang S, Hu L, Li J, Huang Y, Huang R, Ooi K, Lin H, Xia C. Inhibition of cGAS in Paraventricular Nucleus Attenuates Hypertensive Heart Injury Via Regulating Microglial Autophagy. Mol Neurobiol. 2022 Nov;59(11):7006-7024.

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