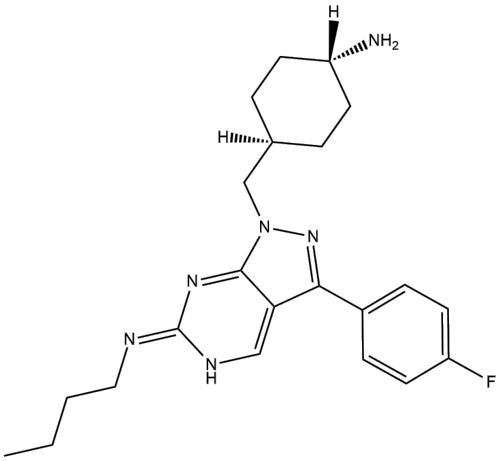
Product Data Sheet

Product Name: UNC569
Cat. No.: GC18308

Chemical Properties

Cas. No.	1350547-65-7		
Chemical Name	1-[(trans-4-aminocyclohexyl)methyl]-N-butyl-3-(4-fluorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-6-amine		
SMILES	CCCCNC1=NC=C2C(N(C[C@H]3CC[C@H](N)CC3)N=C2C4=CC=C(F)C=C4)=N1		
Formula	$C_{22}H_{29}FN_6$	M.Wt	396.5
Solubility	DMF: 2.5 mg/ml,DMF:PBS (pH 7.2) (1:4): 0.2 mg/ml,DMSO: 0.2 mg/ml,Ethanol: 2 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

Cell experiment [1]:

Product Data Sheet

Cell lines	Jurkat or 697 cells
Preparation Method	Jurkat or 697 cells were plated at a density of 3×10^5 cells/ml and treated with UNC569 (0, 400, 800, 1000, 1200, 1400, 1600, 1800 and 2000nM) for 48h. Alternatively, cells were treated with UNC569 for 24h, then harvested and cultured in fresh medium containing UNC569 or vehicle only for an additional 24h. Cells were collected by centrifugation at 240g for 5min. Cell pellets were resuspended in PBS containing 1μM YO-PRO-1 and 1.5μM propidium iodide. Samples were incubated for 15min, and fluorescence was detected using a FC500 flow cytometer and analyzed with CXP data analysis software.
Reaction Conditions	0, 400, 800, 1000, 1200, 1400, 1600, 1800 and 2000nM; 48h
Applications	UNC569 reduces proliferation and induces apoptosis in acute lymphoblastic leukemia (ALL) cells.

Animal experiment [2]:

Animal models	Male BALB/c AnNCrlCrlj mice

Product Data Sheet

Preparation Method	UNC569 was administered orally once daily at doses of 60, 100, and 150mg/kg for 14 days. Animals receiving 0.5 w/v% methyl cellulose in the same manner served as the control group. During the experiment, light was introduced into the room at 7:00, and dosing was conducted at 10:30. The first day of dosing was defined as day 1. Animals were euthanized by exsanguinations under isoflurane anesthesia and necropsied at 10:30 on day 15. Eyes were removed from all animals. The right eyes were fixed in Davidson's fixative, embedded in paraffin, and prepared as histopathological specimens, which were stained with hematoxylin and eosin (HE) for light microscopy. The left eyes were fixed in 2.5% glutaraldehyde, postfixed in 2% osmium tetroxide, and embedded in resin. Semithin sections were stained with toluidine blue (TB) for light microscopy, and ultrathin sections were stained with uranyl acetate and lead for electron microscopy.
Dosage form	60, 100 and 150mg/kg; 14 days; p.o.
Applications	In a mouse animal experiment, the MerTK inhibitor UNC569 impaired the phagocytic function of the retinal pigment epithelium (RPE), leading to accumulation of photoreceptor outer segments (POS) and increased phagosomes and phagolysosomes in the RPE.

References:

[1] Christoph S, Deryckere D, et al. UNC569, a novel small-molecule mer inhibitor with efficacy against acute lymphoblastic leukemia in vitro and in vivo. Mol Cancer Ther. 2013 Nov;12(11):2367-77.
[2] Sayama A, Okado K, Nakamura K, et al. UNC569-induced Morphological Changes in Pigment Epithelia and Photoreceptor Cells in the Retina through MerTK Inhibition in Mice. Toxicol Pathol. 2018 Feb;46(2):193-201.

Background

UNC569 is a novel small molecule Mer tyrosine kinase inhibitor with potent activity against Mer (Mer IC_{50} = 2.9nM)[1].

Product Data Sheet

In vitro, UNC569 (0, 400, 800, 1000, 1200, 1400, 1600, 1800, and 2000nM; 48h) reduces proliferation and induces apoptosis in acute lymphoblastic leukemia (ALL) cells[1]. In macrophages derived from THP-1 cells, UNC569 (5μM; 48h) significantly inhibits Gas-6-induced MerTK phosphorylation and Akt activation[2]. In the presence and absence of exogenous galectin-3, UNC569 (5μM; 48h) strongly inhibited microglial phagocytosis of bacteria, without affecting microglial viability[3].

In vivo, In a mouse animal experiment, the MerTK inhibitor UNC569 (60, 100 and 150mg/kg or 100mg/kg; 14 days or 15, 17, 18.5 and 20h; p.o.) impaired the phagocytic function of the retinal pigment epithelium (RPE), leading to accumulation of photoreceptor outer segments (POS) and increased phagosomes and phagolysosomes in the RPE[4].

References:
[1] Christoph S, Deryckere D, et al. UNC569, a novel small-molecule mer inhibitor with efficacy against acute lymphoblastic leukemia in vitro and in vivo. Mol Cancer Ther. 2013 Nov;12(11):2367-77.
[2] Pastore M, Caligiuri A, Raggi C, et al. Macrophage MerTK promotes profibrogenic cross-talk with hepatic stellate cells via soluble mediators. JHEP Rep. 2022 Feb 1;4(4):100444.
[3] Cockram TOJ, Puigdellívol M, Brown GC. Calreticulin and Galectin-3 Opsonise Bacteria for Phagocytosis by Microglia. Front Immunol. 2019 Nov 12;10:2647.
[4] Sayama A, Okado K, Nakamura K, et al. UNC569-induced Morphological Changes in Pigment Epithelia and Photoreceptor Cells in the Retina through MerTK Inhibition in Mice. Toxicol Pathol. 2018 Feb;46(2):193-201.

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