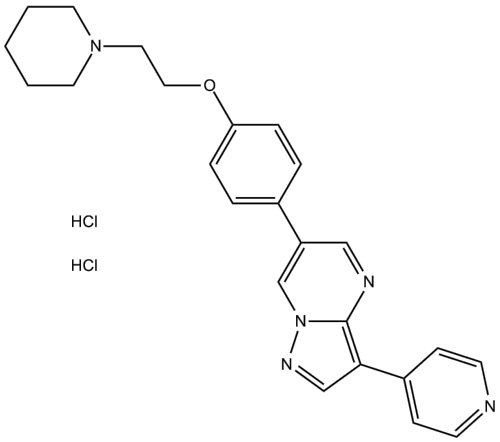
Product Data Sheet

Product Name: Dorsomorphin (Compound C) 2HCl
Cat. No.: GC12560

Chemical Properties

Cas. No.	1219168-18-9		
Chemical Name	6-[4-(2-piperidin-1-ylethoxy)phenyl]-3-pyridin-4-ylpyrazolo[1,5-a]pyrimidine;dihydrochloride		
SMILES	C1CCN(CC1)CCOC2=CC=C(C=C2)C3=CN4C(=C(C=N4)C5=CC=NC=C5)N=C3.Cl.Cl		
Formula	$C_{24}H_{25}N_5O.2HCl$	M.Wt	472.41
Solubility	≥100mg/mL in Water, ≥ 5.9mg/mL in DMSO, ≥ 11.34 mg/mL in 0.9% NS	Storage	Store at -20°C,protect from light
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]:

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Cell lines	Jurkat, Molt4, CEM, REH, Nalm6 (acute lymphoblastic leukemia, ALL), U937, THP.1, ML-1, HL-60, KG1A, MV-4-11, SET2 (acute myeloid leukemia, AML), K562, HEL (blast phase of chronic myeloid leukemia) cell lines
Preparation Method	Above acute leukemia cell lines were maintained in RPMI 1640 containing 10% heat-inactivated fetal bovine serum (FBS), 100U/mL penicillin G, 100μg/mL streptomycin and 2mM glutamine at densities below 10^6 cells/mL. Cells were treated with Dorsomorphin for 24h.
Reaction Conditions	5μM; 24h
Applications	Dorsomorphin induced cell death. Dorsomorphin suppressed AMPKα autophosphorylation and phosphorylation of downstream AMPK substrates including Beclin 1, Raptor, ULK1 and ACC, promoted dephosphorylation of the proapoptotic protein BAD at Ser75 and Ser99, facilitated BAD translocation to mitochondria to bind BCLXL, and further increased BAK activation, procaspase-9/procaspase-3/PARP1 cleavage, with partial involvement of GSDME-mediated pyroptosis.

Animal experiment [2]:

Animal models	Male CD-1 (ICR) mice, subarachnoid hemorrhage (SAH) model established by intra-arterial puncture
Preparation Method	Male CD-1 mice were anesthetized and subjected to SAH induction via intra-arterial puncture. Dorsomorphin was administered via tail vein injection at 1h after successful SAH modeling. Mice were allocated into 4 groups: sham, SAH+vehicle, SAH+recombinant human GPNMB (rGPNMB, 3.3μg/10μL, intracerebroventricular injection at 1h post-SAH) and SAH+Dorsomorphin.
Dosage form	10mg/kg; i.v.; single injection at 1h post-SAH

Caution: Product has not been fully validated for medical applications. For research use only.
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Applications	Dorsomorphin reduced the rGPNMB-elevated p-AMPK/AMPK ratio in SAH mice, reversed the rGPNMB-mediated downregulation of p-NFκB, IL-1β, IL-6 and TNF-α at both protein and secretion levels, and counteracted the alleviative effects of rGPNMB on brain edema, blood-brain barrier impairment and neurological deficits in SAH mice.

References:

[1] Jia J, Ji W, Saliba AN, et al. AMPK inhibition sensitizes acute leukemia cells to BH3 mimetic-induced cell death. Cell Death Differ. 2024;31(3):405-416.

[2] Li T, Zhang Y, Lu Q, et al. GPNMB Ameliorates Neuroinflammation Via the Modulation of AMPK/NFkB Signaling Pathway After SAH in Mice. J Neuroimmune Pharmacol. 2023;18(6):628-639.

Background

Dorsomorphin (Compound C) 2HCl is a potent, cell-permeable dual inhibitor of AMPK and BMP pathways (K_i value of 109nM for AMPK).Dorsomorphin competitively binds to the ATP site of AMPK to inhibit AMPK activity and block cellular energy sensing. At the same time, Dorsomorphin inhibits BMP type I receptors ALK2/ALK3/ALK6 to block SMAD1/5/8 phosphorylation. Dorsomorphin can be used in stem cell differentiation, tumor and metabolism research[1-4].

In vitro, Dorsomorphin (5μM) treated Jurkat, U937, Molt4 and other acute lymphoblastic leukemia and acute myeloid leukemia cell lines for 24h. Dorsomorphin inhibited AMPKα autophosphorylation and phosphorylation of downstream AMPK substrates including Beclin 1, Raptor, ULK1, ACC in cells. Dorsomorphin enhanced mitochondrial pathway cell death[5]. Dorsomorphin (5μM) combined with differentiation inducers (3-isobutyl-1-methylxanthine 0.5mM, dexamethasone 0.25μM, insulin 10μg/ml) treated 3T3-L1 preadipocytes for 8 days. Dorsomorphin significantly reduced lipid accumulation in 3T3-L1 preadipocytes[6].

In vivo, Dorsomorphin (10mg/kg; single tail vein injection) combined with recombinant human GPNMB (rGPNMB; single intracerebroventricular injection) was given to CD-1 male mice with

subarachnoid hemorrhage (SAH) model at 1h after SAH modeling. Dorsomorphin reduced the p-AMPK/AMPK ratio in mice. Dorsomorphin reversed the downregulation of p-NFκB, IL-1β, IL-6 and TNF-α caused by rGPNMB. Dorsomorphin counteracted the alleviation of brain edema, blood-brain barrier disruption and neurological deficits mediated by rGPNMB[7]. Dorsomorphin (10mg/kg) was intraperitoneally injected into APP/PS1 mice 1h before each aerobic exercise session for 8 weeks. Dorsomorphin eliminated the promotion of p300 nuclear translocation, upregulation of hippocampal H4K5ac and H4K12ac, and enrichment of histone acetylation at GluN1 promoter region induced by aerobic exercise. Dorsomorphin counteracted the improvements in CA1 dendritic spine density, LTP and contextual fear memory enhanced by aerobic exercise[8].

References:

[1] Zhou G, Myers R, Li Y, et al. Role of AMP-activated protein kinase in mechanism of metformin action. J Clin Invest. 2001 Oct;108(8):1167-74.

[2] Kim YM, Kim MY, Kim HJ, et al. Compound C independent of AMPK inhibits ICAM-1 and VCAM-1 expression in inflammatory stimulants-activated endothelial cells in vitro and in vivo. Atherosclerosis. 2011 Nov;219(1):57-64.

[3] Saito S, Furuno A, Sakurai J, et al. Compound C prevents the unfolded protein response during glucose deprivation through a mechanism independent of AMPK and BMP signaling. PLoS One. 2012;7(9):e45845.

[4] Guo Y, Zhang Y, Hong K, et al. AMPK inhibition blocks ROS-NFκB signaling and attenuates endotoxemia-induced liver injury. PLoS One. 2014 Jan 24;9(1):e86881.

[5] Jia J, Ji W, Saliba AN, et al. AMPK inhibition sensitizes acute leukemia cells to BH3 mimetic-induced cell death. Cell Death Differ. 2024;31(3):405-416.

[6] Suenaga M, Matsui T, Funaba M. BMP Inhibition with Dorsomorphin Limits Adipogenic Potential of Preadipocytes. J Vet Med Sci. 2010;72(3):373-377.

[7] Li T, Zhang Y, Lu Q, et al. GPNMB Ameliorates Neuroinflammation Via the Modulation of AMPK/NFkB Signaling Pathway After SAH in Mice. J Neuroimmune Pharmacol. 2023;18(6):628-639.

[8] Chai G, Gao T, Bi S, et al. Aerobic exercise facilitates p300 nuclear translocation via ADRB2-AMPKα signaling, leading to enhanced histone acetylation and mitigation of cognitive decline in

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APP/PS1 mice. Alzheimer's Res Ther. 2026;18:62.