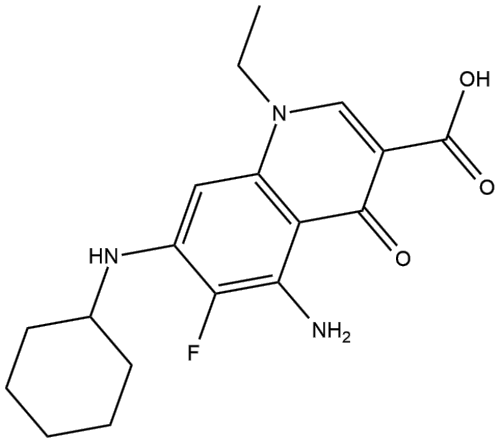
Product Data Sheet

Product Name: AS1842856
Cat. No.: GC19040

Chemical Properties

Cas. No.	836620-48-5		
SMILES	O=C(C1=CN(CC)C2=C(C(N)=C(F)C(NC3CCCCC3)=C2)C1=O)O		
Formula	$C_{18}H_{22}FN_3O_3$	M.Wt	347.38
Solubility	DMSO : 7.6 mg/mL (21.88 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]:

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Cell lines	3T3L1 preadipocytes
Preparation Method	Cell were cultured(with or without AS1842856) in basal medium (0-2 days), adipocyte differentiation was induced with differentiation medium I(3-4 days) and differentiation medium (5-6 days), and then the cells were maintained in basal medium (7-12 days).
Reaction Conditions	1.0 μM AS1842856; 0-12 days
Applications	AS1842856 continued to inhibit Foxo1, preventing adipocyte differentiation.

Animal experiment [2]:

Animal models	Foxc2 $^{+/-}$ mice(lymphedema-distichiasis mouse model)
Preparation Method	Mice were injected with AS1842856 for 2 weeks.
Dosage form	10 mg/kg AS1842856;i.p.;(P) 7-21(2 weeks)
Applications	AS1842856 treatment increases the valve number in Foxc2 heterozygous mice.

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

[1]. Zou P, Liu L, et,al. Targeting Foxo1 with AS1842856 suppresses adipogenesis. Cell Cycle. 2014;13(23):3759-67. doi: 10.4161/15384101.2014.965977. PMID: 25483084; PMCID: PMC4613185.
[2]. Ogunsina O, Banerjee R, et,al. Pharmacological inhibition of Foxo1 promotes lymphatic valve growth in a congenital lymphedema mouse model. Front Cell Dev Biol. 2023 Jan 5;10:1024628. doi: 10.3389/fcell.2022.1024628. PMID: 36742198; PMCID: PMC9890395.

Background

AS1842856 is a cell permeable inhibitor that inhibits Foxo1 transcriptional activity with IC_{50}=33 nM.AS1842856 can directly bind activated Foxo1, but does not bind Foxo1 phosphorylated at Ser256. AS1842856 reduces Foxo1 activity only by binding to Foxo1, without affecting its transcription and protein expression. AS1842856 can inhibit autophagy[1-3].

AS1842856(1.0 μM; 0-12 days) continued to inhibit Foxo1, preventing adipocyte differentiation [4]. Treatment of BBC and GBM cancer cells with AS1842856(0.2-1.0 μM)led to increases in FAS (FAS cell surface death receptor) and BIM (BCL2L11) gene expression, as well as increased positivity for markers for apoptosis such as annexin V and propidium iodide[5].

AS1842856-mediated(10 days ;5 mg/kg) chemical inhibition of Foxo1 reduced the expression of the atrophy-related ubiquitin ligases and significantly reversed the adverse cardiac remodeling while improving the contractile functions in the TLR2-KO mice[6].AS1842856(10 mg/kg;i.p.;(P) 7-21(2 weeks)) treatment increases the valve number in Foxc2 heterozygous mice[7].

References:
[1]. Nagashima T, Shigematsu N, et,al. Discovery of novel forkhead box O1 inhibitors for treating type 2 diabetes: improvement of fasting glycemia in diabetic db/db mice. Mol Pharmacol. 2010 Nov;78(5):961-70. doi: 10.1124/mol.110.065714. Epub 2010 Aug 24. PMID: 20736318.
[2]. He J, Zhang A, et,al. The resistant effect of SIRT1 in oxidative stress-induced senescence of rat nucleus pulposus cell is regulated by Akt- Foxo1 pathway. Biosci Rep. 2019 May 10;39(5):BSR20190112. doi: 10.1042/BSR20190112. PMID: 30967498; PMCID: PMC6509061.

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[3]. Tanaka H, Nagashima T, et,al. Effects of the novel Foxo1 inhibitor AS1708727 on plasma glucose and triglyceride levels in diabetic db/db mice. Eur J Pharmacol. 2010 Oct 25;645(1-3):185-91. doi: 10.1016/j.ejphar.2010.07.018. Epub 2010 Jul 23. PMID: 20655898.
[4]. Zou P, Liu L, et,al. Targeting Foxo1 with AS1842856 suppresses adipogenesis. Cell Cycle. 2014;13(23):3759-67. doi: 10.4161/15384101.2014.965977. PMID: 25483084; PMCID: PMC4613185.
[5]. Flores D, Lopez A, et,al. The Foxo1 inhibitor AS1842856 triggers apoptosis in glioblastoma multiforme and basal-like breast cancer cells. FEBS Open Bio. 2023 Feb;13(2):352-362. doi: 10.1002/2211-5463.13547. Epub 2023 Jan 16. PMID: 36602390; PMCID: PMC9900086.
[6]. Spurthi KM, Sarikhani M, et,al.Toll-like receptor 2 deficiency hyperactivates the Foxo1 transcription factor and induces aging-associated cardiac dysfunction in mice. J Biol Chem. 2018 Aug 24;293(34):13073-13089. doi: 10.1074/jbc.RA118.001880. Epub 2018 Jun 21. PMID: 29929978; PMCID: PMC6109936.
[7]. Ogunsina O, Banerjee R, et,al.Pharmacological inhibition of Foxo1 promotes lymphatic valve growth in a congenital lymphedema mouse model. Front Cell Dev Biol. 2023 Jan 5;10:1024628. doi: 10.3389/fcell.2022.1024628. PMID: 36742198; PMCID: PMC9890395.

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