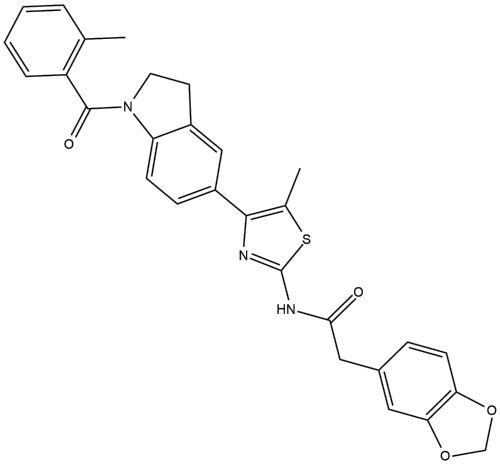
Product Data Sheet

Product Name: ML385
Cat. No.: GC19254

Chemical Properties

Cas. No.	846557-71-9		
SMILES	O=C(NC1=NC(C2=CC=C(N(C(C3=C(C)C=CC=C3)=O)CC4)C4=C2)=C(C)S1)CC5=CC(OCO6)=C6C=C5		
Formula	$C_{29}H_{25}N_3O_4S$	M.Wt	511.59
Solubility	DMSO : ≥ 30 mg/mL (58.64 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	FaDu cells (human hypopharyngeal squamous cell carcinoma cell line), YD9 cells (human oral squamous cell carcinoma cell line)

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Preparation Method	FaDu and YD9 cells were maintained in MEM or RPMI-1640 supplemented with 10% FBS at 37°C, 5% CO_2. Cells were treated with 1-20μM ML385 for 48h (FaDu) or 72h (YD9). After treatment, cell viability (EZ-Cytox), Western blot for p-NRF2/NRF2/HO-1, colony formation assay, transwell migration assay, wound-healing assay, cell cycle analysis (PI staining, 5μM ML385 24h), and apoptosis assay (Annexin V-FITC/PI, 5μM ML385 72h) were performed.
Reaction Conditions	1-20μM; 48h or 72h
Applications	ML385 decreased cell viability in a dose- and time-dependent manner, reduced NRF2 phosphorylation and NRF2 and HO-1 protein levels, reduced colony number, transwell migration cell number and wound closure area, arrested cells at G1/S phase, and did not significantly increase apoptosis in FaDu and YD9 cells.
Animal experiment [2]:	
Animal models	CAV1-knockout (CAV1-KO) mice on C57BL/6J background (male, 6-8 weeks old)
Preparation Method	Type 1 diabetes was induced by intraperitoneal injection of streptozotocin (50mg/kg) for 5 consecutive days; mice with fasting blood glucose >11.1mM were included. After establishment of the diabetic model, CAV1-KO diabetic mice received intraperitoneal injection of ML385 (an NRF2 inhibitor, 30mg/kg) and were maintained for 8 weeks. At 8 weeks, mice were euthanized under anesthesia; echocardiography (EF, FS), serum CK-MB and LDH ELISA, heart weight/body weight ratio, WGA staining for cardiomyocyte cross-sectional area, Masson staining for fibrosis, DHE staining and cardiac MDA assay, qRT-PCR for GCLC and PTGS2 mRNA, and Western blot for NRF2 were performed.

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Dosage form	30mg/kg; i.p.; single injection after diabetic model establishment
Applications	ML385 reduced cardiac NRF2 protein level, reversed the protective effects of CAV1 deficiency on diabetes-induced cardiac dysfunction (decreased EF and FS), increased serum CK-MB and LDH levels, increased cardiomyocyte cross-sectional area, heart weight/body weight ratio, Masson fibrosis, DHE ROS signal and cardiac MDA level, and decreased cardiac GCLC mRNA level in CAV1-KO diabetic mice.

References:

[1] Jeong EJ, Choi JJ, Lee SY, et al. The Effects of ML385 on Head and Neck Squamous Cell Carcinoma: Implications for NRF2 Inhibition as a Therapeutic Strategy. International Journal of Molecular Sciences. 2024 Jun 27;25(13):7011.

[2] Li G, Liu R, Peng Z, et al. Inhibition of CAV1 attenuates diabetic cardiomyopathy through reducing ferroptosis via activating NRF2/GCLC signaling pathway. Theranostics. 2025;15(11):4989-5006.

Background

ML385 is a cell-active NRF2 inhibitor (IC_{50}=1.9μM). ML385 binds to the Neh1 CNC-bZIP domain of NRF2 and interferes with NRF2-MAFG complex formation and antioxidant response element DNA binding. ML385 reduces the expression of NRF2-regulated cytoprotective and detoxification genes. ML385 can be used in research related to cancer, oxidative stress, ferroptosis, chemotherapy resistance, and neurodegenerative diseases[1-4].

In vitro, FaDu and YD9 cells were treated with 1-20μM ML385 for 48-72 hours. ML385 reduced cell viability, decreased NRF2 phosphorylation and NRF2 and HO-1 protein levels, reduced colony number, migration cell number and wound healing area, and arrested the cell cycle at the G1/S phase[5]. RAW264.7 cells were pretreated with 5μM ML385 for 1 hour, then treated with 4μM Plumbagin for 1 hour and 1μg/mL LPS for 24 hours. ML385 decreased Nrf2 and HO-1 protein

expression and increased TNF-α, IL-1β and IL-6 secretion[6]. A549 cells were treated with 5μM ML385 for 72 hours. ML385 reduced NRF2 transcriptional activity, decreased NRF2, NQO1, ABCC2 and ABCG2 mRNA levels, reduced NRF2 protein level, and decreased NQO1 enzyme activity, total cellular antioxidant capacity and glutathione levels[7].

In vivo, C57BL/6 mice were intraperitoneally injected with a single dose of 30mg/kg ML385 1 hour before middle cerebral artery occlusion surgery. ML385 eliminated the improvement of neurological function by remote ischemic conditioning, increased cerebral infarct volume, decreased brain TAC, SOD and GSH/GSSG levels, and increased MDA levels[8]. C57BL/6 mice were intraperitoneally injected with a single dose of 30mg/kg ML385 1 hour after aseptic laparotomy under isoflurane anesthesia. ML385 worsened cognitive impairment, decreased the novel object recognition discrimination index, and increased hippocampal IL-1β and IL-6 levels[9]. Cav1-knockout diabetic mice were intraperitoneally injected with a single dose of 30mg/kg ML385. ML385 decreased cardiac ejection fraction and fractional shortening, increased serum creatine kinase isoenzyme MB and lactate dehydrogenase levels, increased cardiomyocyte cross-sectional area, increased cardiac DHE staining reactive oxygen species signal, increased cardiac malondialdehyde levels, and decreased cardiac GCLC mRNA levels[10].

References:

[1] Gelerstein-Claro S, Méndez-Valdés G, Rodrigo R. Effects of the Pharmacological Modulation of NRF2 in Cancer Progression. Medicina (Kaunas). 2025 Dec 16;61(12):2224.

[2] Yan L, Hu H, Feng L, et al. ML385 promotes ferroptosis and radiotherapy sensitivity by inhibiting the NRF2-SLC7A11 pathway in esophageal squamous cell carcinoma. Med Oncol. 2024 Nov 7;41(12):309.

[3] Xu C, Chen Y, Zhou Z, et al. ML385, an Nrf2 Inhibitor, Synergically Enhanced Celastrol Triggered Endoplasmic Reticulum Stress in Lung Cancer Cells. ACS Omega. 2024 Oct 15;9(43):43697-43705.

[4] Cao Y, Zhou W, Cai J, et al. ML385 Attenuates Malignant Progression of Silica-induced Lung Adenocarcinoma Cells through the ROS/NRF2-autophagy Axis Pathway. J Vis Exp. 2025 Oct 31;(224).

[5] Jeong EJ, Choi JJ, Lee SY, et al. The Effects of ML385 on Head and Neck Squamous Cell

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Carcinoma: Implications for NRF2 Inhibition as a Therapeutic Strategy. International Journal of Molecular Sciences. 2024 Jun 27;25(13):7011.

[6] Liu Z, Wei J, Sun H, et al. Plumbagin ameliorates LPS-induced acute lung injury by regulating PI3K/AKT/mTOR and Keap1-Nrf2/HO-1 signalling pathways. J Cell Mol Med. 2024;28:e18386.

[7] Singh A, Venkannagari S, Oh KH, et al. Small molecule inhibitor of NRF2 selectively intervenes therapeutic resistance in KEAP1-deficient NSCLC tumors. ACS Chem Biol. 2016 Nov 18;11(11):3214-25.

[8] Sun YY, Zhu HJ, Zhao RY, et al. Remote ischemic conditioning attenuates oxidative stress and inflammation via the Nrf2/HO-1 pathway in MCAO mice. Redox Biology. 2023;66:102852.

[9] Kong X, Lyu W, Lin X, et al. Itaconate alleviates anesthesia/surgery-induced cognitive impairment by activating a Nrf2-dependent anti-neuroinflammation and neurogenesis via gut-brain axis. Journal of Neuroinflammation. 2024 Apr 22;21:104.

[10] Li G, Liu R, Peng Z, et al. Inhibition of CAV1 attenuates diabetic cardiomyopathy through reducing ferroptosis via activating NRF2/GCLC signaling pathway. Theranostics. 2025;15(11):4989-5006.

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