

Data Sheet

Product Name:	ML385
Cat. No.:	CS-6447
CAS No.:	846557-71-9
Molecular Formula:	C ₂₉ H ₂₅ N ₃ O ₄ S
Molecular Weight:	511.59
Target:	Ferroptosis; Keap1-Nrf2
Pathway:	Apoptosis; NF-кВ
Solubility:	$DMSO: 25 \ mg/mL \ (ultrasonic); H_2O: < 0.1 \ mg/mL$

BIOLOGICAL ACTIVITY:

ML385 is a specific nuclear factor erythroid 2-related factor 2 (**NRF2**) inhibitor with an **IC**₅₀ of 1.9 μ M. IC50 & Target:IC50: 1.9 μ M (NRF2)^[1] *In Vitro:*ML385 interacts with NRF2 and affects the DNA binding activity of the NRF2-MAFG protein complex. The addition of ML385 decreases anisotropy in a dose-dependent manner, with an IC₅₀ of 1.9 μ M. A dose-dependent reduction in the NRF2 transcriptional activity is observed and the maximum inhibitory concentration is 5 μ M by ML385. Treatment with ML385 leads to a significant reduction in NRF2 and downstream target gene expression selectively in KEAP1 mutant H460 cells. ML385 selectively affects the colony forming ability or growth of lung cancer cells with gain of NRF2 function^[1]. *In Vivo:*ML385 in combination with carboplatin leads to a significant reduction in tumor cell proliferation, demonstrated by fewer Ki-67 positive cells. Tumor samples treated with ML385 show a significant reduction in NRF2 protein level and its downstream target genes^[1]. ML385 (intraperitoneal injection; 30 mg/kg; 7 days) weakens the therapeutic effects of MSC-Exo on inflammation-induced astrocytic

activation (e.g., reduced reactive astrogliosis, NF-kB deactivation) in mice^[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay:^[1]cells are treated with ML385 for 36 h. An equal amount of CellTiter-Blue reagent is added to the wells and the fluorescence is measured after 30 min. The CellTiter-Blue reagent is discarded and the Caspase-Glo (100 μ L) reagent is added to the cells and incubated at 37°C for an additional 60-90 min. The resulting luminescence is recorded and the caspase activity is normalized to cell number^[1]. **Animal Administration:**ML385 is prepared in Solutol/Cremophor EL/polyethylene glycol 400/water [15/10/35/40,v/v/v/v].^[1]Mice: Mice tumor xenografts are randomly allocated into 4 groups: vehicle, ML385, carboplatin, and ML385 in combination with carboplatin. Vehicle, carboplatin (5 mg/kg daily Monday to Friday)18, ML385 (30 mg/kg daily Monday to Friday), or ML385 in combination with carboplatin are administered intraperitoneally for 3 weeks. At the end of treatment period, mice are sacrificed and the tumor, blood, lung, and liver samples are collected^[1].

References:

[1]. Singh A, et al. Small Molecule Inhibitor of NRF2 Selectively Intervenes Therapeutic Resistance in KEAP1-Deficient NSCLC Tumors. ACS Chem Biol. 2016 Nov 18;11(11):3214-3225.

[2]. Xinnong Liu, et al. Isoliquiritigenin ameliorates acute pancreatitis in mice via inhibition of oxidative stress and modulation of the Nrf2/HO-1 pathway. Oxid Med Cell Longev. 20 March 2018. [3]. Xian P, et al. Mesenchymal stem cell-derived exosomes as a nanotherapeutic agent for amelioration of inflammationinduced astrocyte alterations in mice. Theranostics. 2019 Aug 14;9(20):5956-5975.

CAIndexNames:

1,3-Benzodioxole-5-acetamide, N-[4-[2,3-dihydro-1-(2-methylbenzoyl)-1H-indol-5-yl]-5-methyl-2-thiazolyl]-

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

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

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