# Menin-MLL inhibitor MI-2

**Cat. No.:** HY-15222

**CAS No.:** 1271738-62-5

**Molecular Formula:** $C_{18}H_{25}N_5S_2$

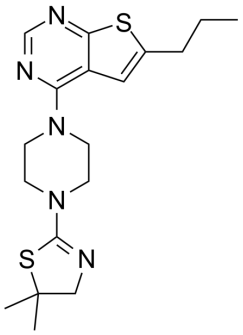
**Molecular Weight:** 375.55

**Target:** Epigenetic Reader Domain; Apoptosis

**Pathway:** Epigenetics; Apoptosis

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 2 years |
| | -20°C | 1 year |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 50 mg/mL (133.14 mM; Need ultrasonic)

| Preparing Stock Solutions | Mass / Solvent / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.6628 mL | 13.3138 mL | 26.6276 mL |
| | 5 mM | 0.5326 mL | 2.6628 mL | 5.3255 mL |
| | 10 mM | 0.2663 mL | 1.3314 mL | 2.6628 mL |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.66 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.66 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.66 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

Menin-MLL inhibitor MI-2 is a Menin-MLL interaction inhibitor with $IC_{50}$ of 446±28 nM.

**$IC_{50}$ & Target**

IC50: 446±28 nM (Menin-MLL)[1]

**In Vitro**

Menin-MLL inhibitor MI-2 very effectively blocks proliferation of MLL-AF9 and MLL-ENL transduced BMC, with $GI_{50}$ values of about 5 μM. Assessment of diverse hydrophobic groups at R1 led to the development of several compounds with $IC_{50}$ values in the nanomolar range, including MI-2 ($IC_{50}$= 446±28 nM) and MI-3 ($IC_{50}$=648±25 nM).The dissociation constants measured

for the menin-MLL inhibitors are at the nanomolar level, $K_d$=158 nM for MI-2. MI-2 can access the protein target and very effectively inhibit the menin-MLL-AF9 interaction in human cells. Furthermore, MI-2 shows only a small effect on the cell growth of E2A-HLF transduced BMC ($GI_{50}$>50 μM), which may be due to inhibition of the menin interaction with wild-type MLL. Treatment with MI-2 results in $GI_{50}$ values below 10 μM in MV4;11 (harboring MLL-AF4; $GI_{50}$=9.5 μM), KOPN-8 (MLL-ENL; $GI_{50}$=7.2 μM) and ML-2 (MLL-AF6; $GI_{50}$=8.7 μM), and in MonoMac6 (MLL-AF9; $GI_{50}$=18 μM)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

**Cell Assay** [1]

$5\times10^5$ HEK 293 cells/mL are plated in 12-well plates (1 mL/well) and treated with compounds (e.g., MI-2) (0.25% final concentration of DMSO for each condition) or 0.25% DMSO control and incubated for 48h at 37°C in a 5% $CO_2$ incubator. After incubation, $1.5\times10^5$ cells are harvested and resuspended in 100 μL 1× Annexin V binding buffer from the Annexin V-FITC Apoptosis kit, incubated with 4 μL of AnnexinV-FITC and 6 μL of Propidium iodide at room temperature in the dark for 10 minutes and analyzed by flow cytometry on a LSR II instrument. Data analysis is performed using WinList software. The experiments are performed three times in triplicates with calculation of mean and standard deviation for each condition[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Cell Syst. 2018 Apr 25;6(4):424-443.e7.
- Patent. US20180263995A1.

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## REFERENCES

[1]. Grembecka J, et al. Menin-MLL inhibitors reverse oncogenic activity of MLL fusion proteins in leukemia. Nature Chemical Biology (2012), 8(3), 277-284.



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