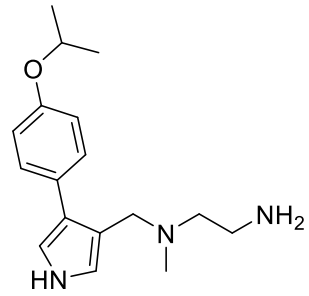
Product data sheet

MedKoo Cat#: 407274 Name: MS023 free base CAS#: 1831110-54-3 (free base) Chemical Formula: $C_{17}H_{25}N_3O$ Exact Mass: 287.1998 Molecular Weight: 287.407	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
MS023 is a Potent, Selective, and Cell-Active Inhibitor of Human Type I Protein Arginine Methyltransferases. MS023 displayed high potency for type I PRMTs including PRMT1, -3, -4, -6, and -8 but was completely inactive against type II and type III PRMTs, protein lysine methyltransferases and DNA methyltransferases. MS023 is a useful chemical tool for investigating the role of type I PRMTs in health and disease.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	62.0	215.72
H2O	39.0	135.70

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	3.48 mL	17.40 mL	34.79 mL
5 mM	0.70 mL	3.48 mL	6.96 mL
10 mM	0.35 mL	1.74 mL	3.48 mL
50 mM	0.07 mL	0.35 mL	0.70 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Plotnikov A, Kozer N, Cohen G, Carvalho S, Duberstein S, Almog O, Solmesky LJ, Shurrush KA, Babaev I, Benjamin S, Gilad S, Kupervaser M, Levin Y, Gershovits M, Ben-Avraham D, Barr HM. PRMT1 inhibition induces differentiation of colon cancer cells. Sci Rep. 2020 Nov 18;10(1):20030. doi: 10.1038/s41598-020-77028-8. PMID: 33208761; PMCID: PMC7676271.
2. Cai T, Yu Z, Wang Z, Liang C, Richard S. Arginine methylation of SARS-Cov-2 nucleocapsid protein regulates RNA binding, its ability to suppress stress granule formation, and viral replication. J Biol Chem. 2021 May 23;297(1):100821. doi: 10.1016/j.jbc.2021.100821. Epub ahead of print. PMID: 34029587; PMCID: PMC8141346.

In vivo study

1. Plotnikov A, Kozer N, Cohen G, Carvalho S, Duberstein S, Almog O, Solmesky LJ, Shurrush KA, Babaev I, Benjamin S, Gilad S, Kupervaser M, Levin Y, Gershovits M, Ben-Avraham D, Barr HM. PRMT1 inhibition induces differentiation of colon cancer cells. Sci Rep. 2020 Nov 18;10(1):20030. doi: 10.1038/s41598-020-77028-8. PMID: 33208761; PMCID: PMC7676271.
2. Zhu Y, He X, Lin YC, Dong H, Zhang L, Chen X, Wang Z, Shen Y, Li M, Wang H, Sun J, Nguyen LX, Zhang H, Jiang W, Yang Y, Chen J, Müschen M, Chen CW, Konopleva MY, Sun W, Jin J, Carlesso N, Marcucci G, Luo Y, Li L. Targeting PRMT1-mediated

Product data sheet

FLT3 methylation disrupts maintenance of MLL-rearranged acute lymphoblastic leukemia. Blood. 2019 Oct 10;134(15):1257-1268. doi: 10.1182/blood.2019002457. PMID: 31395602; PMCID: PMC6788006.

7. Bioactivity

Biological target:

MS023 is a potent, selective, and cell-active inhibitor of human type I protein arginine methyltransferases (PRMTs) inhibitor, with IC50s of 30, 119, 83, 4 and 5 nM for PRMT1, PRMT3, PRMT4, PRMT6, and PRMT8, respectively.

In vitro activity

Entinostat was toxic for normal cells, while its effect on colon cancer cells was stronger (Growth Inhibition of 50% (GI50) was 8.3 µM and 1.2 µM, respectively). The most pronounced ALP-inducing hit was PRMT type 1 inhibitor MS023. Figure 2a shows that MS023 moderately increased ALP activity in comparison to entinostat (e.g. 5-fold increase versus about 30-fold increase respectively at 2.5 µM). Effective concentration of 50% (EC50) of MS023 was 5.8 µM, and it significantly delays HT-29 cell proliferation (GI50 was 2.3 µM). Importantly, MS023 had no effect on either ALP activity or proliferation of CCD-841 cells. Interestingly, MS023 reduced cell growth in four colon cancer cell lines, previously reported as irresponsive to SB treatment25: HCT-116, Colo-205, SW-620, and HCT-15 (Table1). This suggests that MS023 effect was not cell line specific. Following formation of established spheroids (5 days), MS023, entinostat or vehicle (DMSO) were added and growth was monitored during 6 additional days. In order to detect dead cells, propidium iodide (PI) staining of the spheroids was perofmed shortly before imaging (Fig. 2b,c). While entinostat rapidly induced cytotoxic effect, MS023 showed reduced growth, but low toxicity. Thus, PRMT type 1 inhibition induces effects associated with cell differentiation in both monolayer and 3D culture.

Reference: Sci Rep. 2020; 10: 20030. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7676271/

In vivo activity

MS023 efficacy in-vivo was examined using HT-29 xenograft model in nude mice. In order to calculate desirable frequency of MS023 injection, a preliminary experiment was performed, where cell growth medium containing MS023 was replaced 5 days later with a fresh one containing or not a second dose of MS023. The absence of MS023 led to restoration of the proliferative potential, while addition of a second dose kept the cells in low-proliferating status (data not shown). Therefore, the animals received 2 doses of the compound/week. The treatment started when tumors reached 6–7 mm diameter. MS023 treatment significantly delayed tumor growth (Fig. 8a) without any signs of toxicity. This data shows that MS023 was able to reduce tumor growth and proliferation in vivo through differentiation of malignant cells, demonstrating a tractable model of pharmacological manipulation of colon cancer differentiation, with clinical implications.

Reference: Sci Rep. 2020; 10: 20030. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7676271/