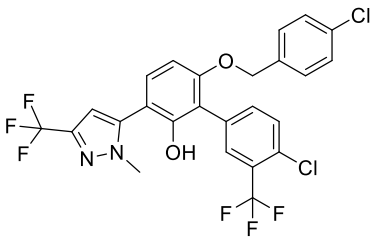
Product data sheet

MedKoo Cat#: 408061 Name: MYCi975 CAS#: 2289691-01-4 Chemical Formula: $C_{25}H_{16}Cl_2F_6N_2O_2$ Exact Mass: 560.0493 Molecular Weight: 561.31	
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:
MYCi975, also known as NUCC-0200975, is a potent and selective MYC Inhibitor. MYCi975 disrupts MYC/MAX interaction, promotes MYC T58 phosphorylation and MYC degradation, and impairs MYC driven gene expression.

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	56	99.8

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.78 mL	8.91 mL	17.82 mL
5 mM	0.36 mL	1.78 mL	3.56 mL
10 mM	0.18 mL	0.89 mL	1.78 mL
50 mM	0.04 mL	0.18 mL	0.36 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. Han H, Jain AD, Truica MI, Izquierdo-Ferrer J, Anker JF, Lysy B, Sagar V, Luan Y, Chalmers ZR, Unno K, Mok H, Vatapalli R, Yoo YA, Rodriguez Y, Kandela I, Parker JB, Chakravarti D, Mishra RK, Schiltz GE, Abdulkadir SA. Small-Molecule MYC Inhibitors Suppress Tumor Growth and Enhance Immunotherapy. Cancer Cell. 2019 Nov 11;36(5):483-497.e15. doi: 10.1016/j.ccell.2019.10.001. Epub 2019 Oct 31. PMID: 31679823; PMCID: PMC6939458.

In vivo study

1. Han H, Jain AD, Truica MI, Izquierdo-Ferrer J, Anker JF, Lysy B, Sagar V, Luan Y, Chalmers ZR, Unno K, Mok H, Vatapalli R, Yoo YA, Rodriguez Y, Kandela I, Parker JB, Chakravarti D, Mishra RK, Schiltz GE, Abdulkadir SA. Small-Molecule MYC Inhibitors Suppress Tumor Growth and Enhance Immunotherapy. Cancer Cell. 2019 Nov 11;36(5):483-497.e15. doi: 10.1016/j.ccell.2019.10.001. Epub 2019 Oct 31. PMID: 31679823; PMCID: PMC6939458.

2. Truica MI, Burns MC, Han H, Abdulkadir SA. Turning Up the Heat on MYC: Progress in Small-Molecule Inhibitors. Cancer Res. 2021 Jan 15;81(2):248-253. doi: 10.1158/0008-5472.CAN-20-2959. Epub 2020 Oct 21. PMID: 33087323; PMCID: PMC7855142.

7. Bioactivity
Biological target:

Product data sheet

MYCi975 (NUCC-0200975) is a potent, selective and orally active inhibitor of MYC that disrupts MYC/MAX interaction, promotes MYC T58 phosphorylation and MYC degradation, and impairs MYC driven gene expression.

In vitro activity

MYCi975 (975) inhibited cell viability in a MYC-dependent manner (Figure 7A, S8A and S8B) and selectively suppressed E-box-luciferase activity (Figure 7B). To assess the molecular pathways modulated by MYCi treatment in an unbiased manner, RNA-seq experiments were performed using P493–6 and PC3 cells. The ability to repress MYC with tetracycline treatment in the P493–6 model allowed us to directly compare empirical MYC targets in these cells after turning MYC "off" to the genes regulated by 975 treatment. The results, shown in Figure 7C, indicate that 975 affected the expression of 3647 genes, the majority (69%) of which are MYC responsive. Among the 975-regulated genes that did not respond to MYC (and may therefore represent off-target effects), the top altered pathways were related to small molecule compound metabolism process, consistent with a general cellular response to exposure to organic small molecule (Figure 7D). Next, the effects of 975 were compared to those of 361 by RNA-seq in PC3 cells. 975 affected the expression of a smaller number of genes (n = 3095) compared to 361 (n = 5033), of which 66.4% were common between the two compounds (Figure 7E). GO biological process analysis of the common genes showed that cell cycle and DNA replication were among the top down regulated pathways, while pathways related to cell death, response to organic compound and ER stress were upregulated (Table S3). GSEA analysis of genes uniquely regulated by 361 (n = 2978) showed suppression of several sets that all share common leading edge genes encoding HIST1H proteins and the TCA cycle/respiratory electron transport (Table S4). However, no gene sets were significantly enriched in GSEA analysis of genes uniquely regulated by 975 in PC3 cells. These findings may partly explain the improved tolerability of 975 compared to 361 as will be shown below.

Reference: Cancer Cell. 2019 Nov 11;36(5):483-497.e15. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/31679823/

In vivo activity

975 exhibited excellent pharmacokinetic profiles following p.o., i.p. or i.v. administration (Figure S8C and S8D). The half-lives observed were 7 hr and 12 hr when dosed at 100 mg/kg and 250 mg/kg p.o. respectively. The Cmax values attained were 41533 ng/ml (74 μM) and 54000 ng/ml (96 μM) respectively. 975 significantly inhibited tumor growth (Figures 8A) and increased survival (Figures 8B) in the MycCaP allograft model with animals tolerating a 100 mg/kg/day i.p. dosing for 14 days. Analysis of tumor tissue showed increased pT58 and PD-L1 levels (Figure 8C) and enhanced tumor infiltration of CD3+ T cells (Figure 8D), B220+ B Cells (Figure 8E), and NKp46+ NK cells (Figure 8F) after 975 treatment. Therefore, the effect of combining 975 with anti-PD1 treatment was examined. 975 alone dosed at 100 mg/kg/day, 2 days on/2 days off slowed tumor growth, while the combination treatment with anti-PD1 (100 μg/day, on alternating 2 days on/2 days off) resulted in a synergistic suppression of tumor growth (Figure 8G and S8E). Similar to 361, 975 treatment inhibited MycCaP tumors grown in immunocompetent FVB mice more strongly than in immunodeficient NSG mice (Figure 8H), indicating that full anti-tumor efficacy of 975 is also dependent on an intact immune system. Treatment of Lewis Lung Carcinoma (LLC1)-bearing mice with 975 (100 mg/kg/day) inhibited tumor growth with no changes in body weight (Figure 8I and S8F). NSG mice bearing MV-411 AML xenografts were treated with 975 (50 mg/kg/day) or Ara-C (20 mg/kg/day) 5 days a week. In this model, the lower dose of 975 and the immunodeficient host background may explain reduced efficacy as a single agent. 975 synergized with Ara-C with no obvious impact on mouse body weight (Figure 8J and S8G).

Reference: Cancer Cell. 2019 Nov 11;36(5):483-497.e15. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/31679823/