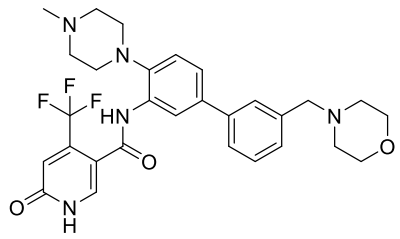
Product data sheet

MedKoo Cat#: 406821 Name: OICR-9429 CAS#: 1801787-56-3 Chemical Formula: $C_{29}H_{32}F_3N_5O_3$ Exact Mass: 555.2457 Molecular Weight: 555.6	
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:

OICR-9429 is a potent and selective chemical probe suitable to help dissect the biological role of WDR5 (Kdisp < 100 nM). OICR-9429 selectively inhibited proliferation and induced differentiation in p30-expressing human AML cells. OICR-9429 disrupts the interaction of Wdr5 with MLL in cells, thereby selectively triggering a differentiation program in p30-expressing leukemia cells.

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	10.0	18.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.80 mL	9.00 mL	18.00 mL
5 mM	0.36 mL	1.80 mL	3.60 mL
10 mM	0.18 mL	0.90 mL	1.80 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. Grebien F, Vedadi M, Getlik M, Giambruno R, Grover A, Avellino R, Skucha A, Vittori S, Kuznetsova E, Smil D, Barsyte-Lovejoy D, Li F, Poda G, Schapira M, Wu H, Dong A, Senisterra G, Stukalov A, Huber KVM, Schönegger A, Marcellus R, Bilban M, Bock C, Brown PJ, Zuber J, Bennett KL, Al-Awar R, Delwel R, Nerlov C, Arrowsmith CH, Superti-Furga G. Pharmacological targeting of the Wdr5-MLL interaction in C/EBPα N-terminal leukemia. Nat Chem Biol. 2015 Aug;11(8):571-578. doi: 10.1038/nchembio.1859. Epub 2015 Jul 13. Erratum in: Nat Chem Biol. 2015 Oct;11(10):815. PMID: 26167872; PMCID: PMC4511833.
2. Neilsen BK, Chakraborty B, McCall JL, Frodyma DE, Sleightholm RL, Fisher KW, Lewis RE. WDR5 supports colon cancer cells by promoting methylation of H3K4 and suppressing DNA damage. BMC Cancer. 2018 Jun 20;18(1):673. doi: 10.1186/s12885-018-4580-6. PMID: 29925347; PMCID: PMC6011590.

In vivo study

1. Shimoda H, Doi S, Nakashima A, Sasaki K, Doi T, Masaki T. Inhibition of the H3K4 methyltransferase MLL1/WDR5 complex attenuates renal senescence in ischemia reperfusion mice by reduction of $p16^{INK4a}$. Kidney Int. 2019 Nov;96(5):1162-1175. doi: 10.1016/j.kint.2019.06.021. Epub 2019 Aug 1. PMID: 31570196.
2. Zhou Q, Chen X, He H, Peng S, Zhang Y, Zhang J, Cheng L, Liu S, Huang M, Xie R, Lin T, Huang J. WD repeat domain 5 promotes chemoresistance and Programmed Death-Ligand 1 expression in prostate cancer. Theranostics. 2021 Mar 4;11(10):4809-4824. doi: 10.7150/thno.55814. PMID: 33754029; PMCID: PMC7978315.

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7. Bioactivity

Biological target:

OICR-9429 is a small-molecule antagonist of the Wdr5-MLL interaction with IC50 of 5 uM.

In vitro activity

First this study tested whether OICR-9429 was able to disrupt the C/EBPα p30-Wdr5 interaction. Wdr5 was readily detected in C/EBPα immunoprecipitates from lysates of Cebpap30/p30 cells in the presence of OICR-9429, suggesting that the interaction of Wdr5 with MLL did not influence p30 binding (Supplementary Fig. 13). This study next tested the effect of OICR-9429 on Wdr5-dependent protein-protein interactions in cells using a biotinylated variant of the compound in a chemical proteomics experiment. Although this study was able to efficiently isolate Wdr5 using the biotinylated variant of OICR-9429, this enrichment was lost upon competition with excess unmodified OICR-9429 (Fig. 5a). Bioinformatic analysis of LC/MS/MS data revealed that Wdr5 was the primary target protein of OICR-9429 in cells (Fig. 5b). Notably, analysis did not identify any other components of SET/MLL HMT complexes, indicating that OICR-9429 disrupts integral protein-protein interactions between Wdr5 and its binding partners. Indeed, OICR-9429 reduced the amount of endogenous MLL and RBBP5 that coimmunoprecipitated with exogenously expressed Flag-tagged WDR5 in a dose-dependent manner (Fig. 5c).

Reference: Nat Chem Biol. 2015 Oct;11(10):815. https://www.nature.com/articles/nchembio.1859

In vivo activity

Protein levels of $p16^{INK4a}$ increased in IRI (ischemia reperfusion injury) mice following vehicle treatment compared with those in sham-operated mice, whereas they decreased in IRI mice with MM-102 or OICR-9429 injection (Figure 2a). Similarly, gene expression of $p16^{INK4a}$ also increased in IRI mice and was suppressed by MM-102 or OICR-9429 administration (Figure 2b). Meanwhile, expansion of the $p16^{INK4a}$-positive area was observed mainly in the interstitial region of the kidney in IRI mice following vehicle treatment, but this area shrank with MM-102 treatment.

Reference: Kidney Int. 2019 Nov;96(5):1162-1175. https://www.kidney-international.org/article/S0085-2538(19)30773-2/fulltext

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.