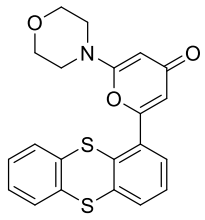
Product data sheet

MedKoo Cat#: 201681 Name: KU-55933 CAS#: 587871-26-9 Chemical Formula: $C_{21}H_{17}NO_3S_2$ Exact Mass: 395.06498 Molecular Weight: 395.49	
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:

KU-55933 is an ATM inhibitor, which blocks the phosphorylation of Akt induced by insulin and insulin-like growth factor I in cancer cells that exhibit abnormal Akt activity. Moreover, KU-55933 inhibits cancer cell proliferation by inducing G(1) cell cycle arrest. It does so through the downregulation of the synthesis of cyclin D1, a protein known to be elevated in a variety of tumors. In addition, KU-55933 treatment during serum starvation triggers apoptosis in these cancer cells. Research results suggest that KU-55933 may be a novel chemotherapeutic agent targeting cancer resistant to traditional chemotherapy or immunotherapy due to aberrant activation of Akt. Furthermore, KU-55933 completely abrogates rapamycin-induced feedback activation of Akt. Combination of KU-55933 and rapamycin not only induces apoptosis, which is not seen in cancer cells treated only with rapamycin, but also shows better efficacy in inhibiting cancer cell proliferation than each drug alone. For detail see: http://www.ncbi.nlm.nih.gov/pubmed/20053781.

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	42.14	106.55
DMF	30.0	75.86
DMF:PBS (pH 7.2) (1:1)	0.5	1.26
Ethanol	14.89	37.65

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.53 mL	12.64 mL	25.29 mL
5 mM	0.51 mL	2.53 mL	5.06 mL
10 mM	0.25 mL	1.26 mL	2.53 mL
50 mM	0.05 mL	0.25 mL	0.51 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. Munera López J, Ganuza A, Bogado SS, Muñoz D, Ruiz DM, Sullivan WJ Jr, Vanagas L, Angel SO. Evaluation of ATM Kinase Inhibitor KU-55933 as Potential Anti-Toxoplasma gondii Agent. Front Cell Infect Microbiol. 2019 Feb 13;9:26. doi: 10.3389/fcimb.2019.00026. PMID: 30815397; PMCID: PMC6381018.
2. Li Y, Yang DQ. The ATM inhibitor KU-55933 suppresses cell proliferation and induces apoptosis by blocking Akt in cancer cells with overactivated Akt. Mol Cancer Ther. 2010 Jan;9(1):113-25. doi: 10.1158/1535-7163.MCT-08-1189. Epub 2010 Jan 6. PMID: 20053781.

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In vivo study

1. Zhao J, Zhang L, Lu A, Han Y, Colangelo D, Bukata C, Scibetta A, Yousefzadeh MJ, Li X, Gurkar AU, McGowan SJ, Angelini L, O'Kelly R, Li H, Corbo L, Sano T, Nick H, Pola E, Pilla SPS, Ladiges WC, Vo N, Huard J, Niedernhofer LJ, Robbins PD. ATM is a key driver of NF-κB-dependent DNA-damage-induced senescence, stem cell dysfunction and aging. Aging (Albany NY). 2020 Mar 22;12(6):4688-4710. doi: 10.18632/aging.102863. Epub 2020 Mar 22. PMID: 32201398; PMCID: PMC7138542.
2. Uehara M, Kusaba T, Ida T, Nakai K, Nakata T, Tomita A, Watanabe-Uehara N, Ikeda K, Kitani T, Yamashita N, Kirita Y, Matoba S, Humphreys BD, Tamagaki K. Pharmacological inhibition of ataxia-telangiectasia mutated exacerbates acute kidney injury by activating p53 signaling in mice. Sci Rep. 2020 Mar 10;10(1):4441. doi: 10.1038/s41598-020-61456-7. PMID: 32157166; PMCID: PMC7064514.

7. Bioactivity

Biological target:

KU-55933 is a potent ATM inhibitor with an IC50 and Ki of 12.9 and 2.2 nM, respectively.

In vitro activity

These results indicate that KU-55933 has a detrimental effect on intracellular tachyzoite replication. However, the indirect effect of PI3K inhibitors on tachyzoite replication due to HFF alterations, specifically at high doses, cannot be ruled out. To investigate if KU-55933 can have an effect directly on Toxoplasma, extracellular tachyzoites were incubated 4 h in presence of different doses of KU-55933 at room temperature. After that HFF monolayers were infected and incubated in absence of the drug for 12 h. Figure 3E shows a significant reduction in tachyzoite replication from 2.5 μM, suggesting that KU-55933 has a direct impact on Toxoplasma.

Reference: Front Cell Infect Microbiol. 2019; 9: 26. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6381018/

In vivo activity

Treatment of DNA repair deficient *Ercc1*$^{-/-}$ MEFs with KU-55933 (10 μM) reduced the percent of SA-βgal positive cells to a level similar to WT MEFs (Figure 2A and 2B). Additional markers of senescence, including the cell-cycle regulators p21^{Cip1} and p16^{INK4A}, also were decreased by KU-55933 treatment (Figure 2C). As expected, autophosphorylation of ATM at Ser1981 was downregulated by the ATM inhibitor, as were the levels of p-KAP1 and γH2AX (Figure 2D). Interestingly, ATM inhibition also decreased Poly [ADP-ribose] polymerase 1 (PARP1) abundance (Figure 2D), an enzyme that promotes DNA repair and chromatin remodeling, utilizing NAD^+ as a cofactor. Interestingly, these results also suggest that inhibition of ATM activity may regulate ATM expression at protein level as indicated by reduced ATM level (Figure 2D). Furthermore, ATM inhibition reduced the abundance of nuclear-localized p65 and NEMO and the level of p-p65 (Figure 2E), as well as NF-κB transcriptional activity, measured using a NF-κB luciferase reporter assay (Figure 2F). Finally, treatment with the ATM inhibitor significantly reduced expression of multiple senescence and SASP markers as determined by qRT-PCR (Figure 2G). Taken together, these results suggest that ATM activation triggered by endogenous DNA damage plays a critical role in driving cellular senescence, SASP and NF-κB activation in a NEMO-dependent manner.

Reference: Aging (Albany NY). 2020 Mar 31; 12(6): 4688–4710. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7138542/

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.