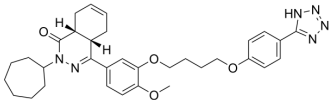
(4aS,8aR)-NPD-001

Cat. No.:	HY-150025
CAS No.:	2366272-43-5
Molecular Formula:	$C_{33}H_{40}N_6O_4$
Molecular Weight:	584.71
Target:	DNA Methyltransferase; Apoptosis
Pathway:	Epigenetics; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	(4aS,8aR)-NPD-001 is a potent and allosteric inhibitor of DNMT3A. (4aS,8aR)-NPD-001 inhibits DNMT3A activity by disrupting protein-protein interactions. (4aS,8aR)-NPD-001 induces apoptosis of acute myeloid leukemia (AML) cell lines. (4aS,8aR)-NPD-001 induces differentiation of distinct AML cell lines including cells with mutated DNMT3A R882[1].
IC_{50} & Target	DNMT3A
In Vitro	(4aS,8aR)-NPD-001 (compound 2) (60 μM) disrupts DNMT3A-DNMT3L interactions at the DNMT3A tetramer interface, inhibits the stimulation of DNMT3A_WT activity by DNMT3L, but does not inhibit the activation of DNMT3A_WT by H3 peptides[1]. (4aS,8aR)-NPD-001 (0-120 μM, 100 min) inhibits the activation of DNMT3A_R882H by DNMT3L[1]. (4aS,8aR)-NPD-001 (0-30 μM, 72 h) induces apoptosis and and differentiation in AML cell lines in a concentration-dependent manner[1]. (4aS,8aR)-NPD-001 (5 μM, 20 days) leads to a time-dependent decrease of global 5-methylcytosine[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	Human AML cell lines
Concentration:	0, 1, 5, 10, 20, and 30 μM
Incubation Time:	72 h
Result:	Showed a dose-response effect with a marked increase in apoptosis in the 7-12 μM range. Led to a concentration-dependent increase in the myeloid differentiation marker, CD11b, in multiple PI-negative AML cell lines: MV411 (biphenotypic B myelomonocytic leukemia), MOLM13 (acute monocytic leukemia), THP-1 (acute monocytic leukemia), OCI-AML3 (DNMT3A R882 mutant, AML), KASUMI (acute myeloblastic leukemia), HL60 (acute promyelocytic leukemia), and K562 (chronic myelogenous leukemia).

REFERENCES

[1]. Sandoval JE, et al. First-in-Class Allosteric Inhibitors of DNMT3A Disrupt Protein-Protein Interactions and Induce Acute Myeloid Leukemia Cell Differentiation. J Med Chem. 2022 Jul 22.

Caution: Product has not been fully validated for medical applications. For research use only.

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