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EPZ004777 (Formate)

Histone modifier; Inhibits disruptor of telomeric silencing 1-like (DOT1L)

Catalog #100-1655 10 mg

Product Description

EPZ004777 (Formate) is a potent inhibitor of disruptor of telomeric silencing 1-like (DOT1L) histone lysine methyltransferase (IC_{50} = 400 pM). By inhibiting DOT1L, EPZ004777 (Formate) prevents DOT1L-mediated methylation of lysine 79 of histone 3 (H3K79; Daigle et al.). H3K79 methylation impacts telomeric silencing, transcriptional regulation, DNA-damage repair, and cell cycle progression (Nguyen & Zhang). Dysregulation of DOTL1-mediated H3K79 methylation is involved in the development of mixed-lineage leukemia (MLL) and the pathophysiology of other cancers (McLean et al.).

Alternative Names: Not applicable

CAS Number: Not applicable

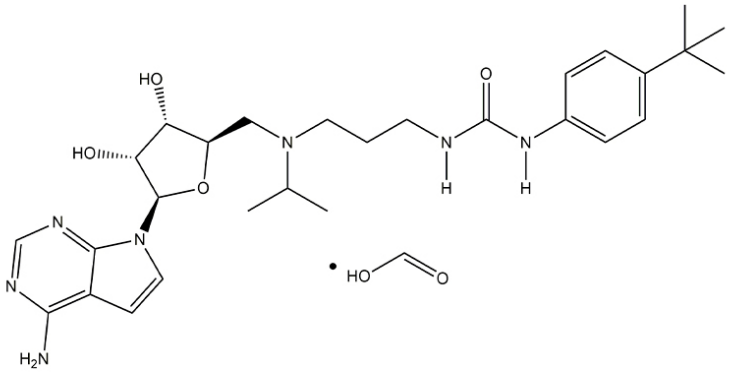
Chemical Formula: $C_{28}H_{41}N_7O_4 \bullet CH_2O_2$

Molecular Weight: 585.7 g/mol

Purity: ≥ 98%

Chemical Name: 7-[5-deoxy-5-[[3-[[[[4-(1,1-dimethylethyl)phenyl]amino]carbonyl]amino]propyl](1-methylethyl)amino]-β-D-ribofuranosyl]-7H-pyrrolo[2,3-d]pyrimidin-4-amine, monoformic acid

Structure:



Properties

Product Format: A crystalline solid

Stability and Storage: Product stable at -20°C as supplied. As a precaution, STEMCELL recommends storing all small molecules away from direct light. For long-term storage, store with a desiccant. Stable as supplied for 12 months from date of receipt.

Preparation:

- DMSO ≤ 17 mM
- Absolute ethanol ≤ 17 mM

For example, to prepare a 10 mM stock solution in DMSO, resuspend 10 mg in 1.71 mL of DMSO.

Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported; however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application.

Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO or absolute ethanol concentration above 0.1% due to potential cell toxicity.

Published Applications

CANCER RESEARCH

- Reduces cell viability and colony formation in human prostate cancer cell lines and patient-derived xenograft model (Vatapalli et al.).
- Inhibits cell growth and upregulates pro-apoptotic genes in a mouse xenograft model of ovarian cancer and human ovarian cancer cell lines (Chava et al.).
- Reduces mouse pancreatic and colon cancer cell viability and colony formation and reduces tumor growth in a mouse xenograft model (Zhou et al.).
- Induces apoptosis, cell-cycle arrest, and terminal differentiation in human acute myeloid leukemia cells and suppresses leukemic tumor growth in a mouse xenograft model (Rau et al.).

References

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Daigle SR et al. (2011) Selective killing of mixed lineage leukemia cells by a potent small-molecule DOT1L inhibitor. Cancer Cell 20(1): 53–65.
McLean CM et al. (2014) The emerging roles of DOT1L in leukemia and normal development. Leukemia 28(11): 2131–8.
Nguyen AT & Zhang Y. (2011) The diverse functions of Dot1 and H3K79 methylation. Genes Dev 25(13): 1345–58.
Rau RE et al. (2016) DOT1L as a therapeutic target for the treatment of DNMT3A-mutant acute myeloid leukemia. Blood 128(7): 971–81.
Vatapalli R et al. (2020) Histone methyltransferase DOT1L coordinates AR and MYC stability in prostate cancer. Nat Commun 11(1): 4153.
Zhou Z et al. (2019) Epigenetically modulated FOXM1 suppresses dendritic cell maturation in pancreatic cancer and colon cancer. Mol Oncol 13 (4): 873–93.

Related Products

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