

Product Data Sheet

Product Name: YL-5092
Cat. No.: GC75826

Chemical Properties

Cas. No. 3056857-07-6

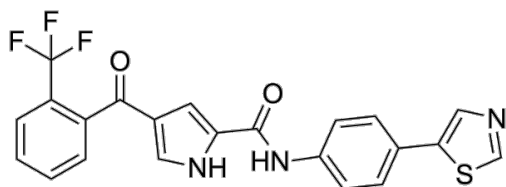
Formula $C_{22}H_{14}F_3N_3O_2S$ M.Wt 441.43

Solubility DMSO: 100 mg/mL (226.54 mM; Storage -20°C
Need ultrasonic)

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

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Cell lines	MOLM-13, MV4-11, HL-60, THP-1, KG-1, U937, OCI-AML3 human acute myeloid leukemia (AML) cell lines, primary human AML specimens (CD34 ⁺ leukemia stem/progenitor cells), HEK293T cells transfected with EGFP-tagged YTHDC1, normal human umbilical cord blood (CB) CD34 ⁺ hematopoietic stem/progenitor (HSPC) cells
Preparation Method	AML cell lines and primary specimens were maintained in standard culture medium supplemented with 10% heat-inactivated fetal bovine serum (FBS) at 37°C, 5% CO ₂ . YL-5092 diluted to indicated working concentrations in culture medium for cell treatment.
Reaction Conditions	0.1–10µM, 72h
Applications	YL-5092 selectively engaged YTHDC1 in living AML cells without affecting other YTH family proteins or m ⁶ A reader proteins. YL-5092 blocked the binding of YTHDC1 to its m ⁶ A substrates (including MYC, FOXM1, GINS1, MCM2, MCM4, MCM5), reduced the stability and mRNA levels of these targets, and suppressed YTHDC1-mediated liquid-liquid phase separation and nuclear condensate formation in MV4-11 cells. YL-5092 dose-dependently inhibited the viability of all tested AML cell lines and primary AML specimens (half-maximum inhibitory concentration IC ₅₀ : 0.28–2.87µM), induced G ₀ /G ₁ phase arrest, apoptosis and myeloid differentiation in AML cells, and suppressed the colony-forming capacity of CD34 ⁺ leukemia stem/progenitor cells, while exerting minimal impact on normal human umbilical cord blood CD34 ⁺ HSPCs and their lineage differentiation.

Animal experiment [2]:

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Animal models	C57BL/6J mice, MOLM-13-luciferase or U937-luciferase cell-derived xenograft (CDX) immunodeficient mice, four independent patient-derived xenograft (PDX) models of acute myeloid leukemia (AML), human umbilical cord blood (CB) CD34+ hematopoietic stem/progenitor cell (HSPC)-engrafted immunodeficient mice
Preparation Method	For CDX model establishment, MOLM-13 or U937 cells expressing luciferase were transplanted into immunodeficient mice via tail vein; YL-5092 (70mg/kg; i.p.; twice per day) was initiated 4 days post-transplant and continued for 18 consecutive days. For PDX model establishment, immunodeficient mice were transplanted with primary AML cells from four independent patients via tail vein; YL-5092 (70mg/kg; i.p.; twice per day) was initiated 10 days post-transplant and continued for 21 days; bone marrow (BM) cells isolated from primary PDX mice treated with vehicle or YL-5092 were serially transplanted into secondary recipient immunodeficient mice to evaluate leukemia stem cell (LSC) function. For combination efficacy test, YL-5092 (50mg/kg; i.p.; twice per day) was administered together with standard AML therapy venetoclax plus azacitidine (Ven/Aza) in CDX and PDX models.
Dosage form	50 or 70mg/kg; i.p.; twice per day for 18 days

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Applications

In CDX models, YL-5092 monotherapy significantly alleviated leukemia burden, reduced the proportion of human CD45⁺CD33⁺ leukemia cells in peripheral blood, spleen and bone marrow, downregulated the expression of YTHDC1 target genes (MYC, FOXM1, GINS1, MCM2, MCM4, MCM5) in BM-derived leukemia cells, and prolonged the overall survival of recipient mice. In PDX models YL-5092 monotherapy reduced leukemia burden in bone marrow across four PDX models with distinct genetic backgrounds, extended the survival of PDX-4 mice, and serial transplantation assays showed that YL-5092-treated primary PDX BM cells had markedly impaired leukemia reconstitution capacity in secondary recipients, indicating functional impairment of LSCs. In combination therapy settings, YL-5092 combined with Ven/Aza exerted stronger anti-leukemia efficacy and longer survival extension than either single agent in both CDX and PDX models.

References:

[1] Zhang H, Li Y, Zhao Y, et al. Small-molecule inhibition of YTHDC1 as a strategy against acute myeloid leukemia in mouse models. *Sci Transl Med.* 2026 Feb 4;18(835):eadu3137.

Background

YL-5092 is a novel, highly selective inhibitor of YTHDC1 (IC₅₀=7.4nM; K_D=29.6nM). YL-5092 competitively occupies the m⁶A-binding pocket of YTHDC1, thereby blocking the interaction between YTHDC1 and m⁶A-modified RNA. YL-5092 can be used for research related to acute myeloid leukemia (AML)^[1-4].

In vitro, YL-5092 (0.28–2.87μM) was applied to MOLM-13, MV4-11, U937 and other AML cell lines as well as primary AML specimens for 72h. YL-5092 disrupted the binding of YTHDC1 to its m⁶A substrates (e.g., MYC, FOXM1, GINS1, MCM2), reduced the stability and expression of target mRNAs, and induced G₀/G₁ cell cycle arrest, apoptosis, and myeloid differentiation^[1].

In vivo, YL-5092 (70mg/kg; twice daily) was administered intraperitoneally to MOLM-13 or U937 cell-derived xenograft mouse models for 18 days. YL-5092 reduced bone marrow leukemia burden and

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prolonged the survival of recipient mice. When combined with venetoclax/azacitidine, YL-5092 (50mg/kg; twice daily for 18 day) enhanced the anti-leukemic effect of venetoclax/azacitidine and further extended mouse survival^[1].

References:

- [1] Zhang H, Li Y, Zhao Y, et al. Small-molecule inhibition of YTHDC1 as a strategy against acute myeloid leukemia in mouse models. *Sci Transl Med*. 2026 Feb 4;18(835):eadu3137.
- [2] Cheng Y, Xie W, Pickering BF, et al. N6-Methyladenosine on mRNA facilitates a phase-separated nuclear body that suppresses myeloid leukemic differentiation. *Cancer Cell*. 2021 Jul 12;39(7):958-972.e8.
- [3] Li X, Zheng M, Ma S, et al. YTHDC1 is a therapeutic target for B-cell acute lymphoblastic leukemia by attenuating DNA damage response through the KMT2C-H3K4me1/me3 epigenetic axis. *Leukemia*. 2025 Feb;39(2):308-322.
- [4] Xiao W, Adhikari S, Dahal U, et al. Nuclear m(6)A Reader YTHDC1 Regulates mRNA Splicing. *Mol Cell*. 2016 Feb 18;61(4):507-519.

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