

Product Data Sheet

Product Name: A-485
Cat. No.: GC32677

Chemical Properties

Cas. No. 1889279-16-6

SMILES O=C(N1CC(N([C@@H](C)C(F)(F)F)CC2=CC=C(F)C=C2)=O)[C@]3(OC1=O)C4=CC=C(NC(NC)=O)C=C4CC3

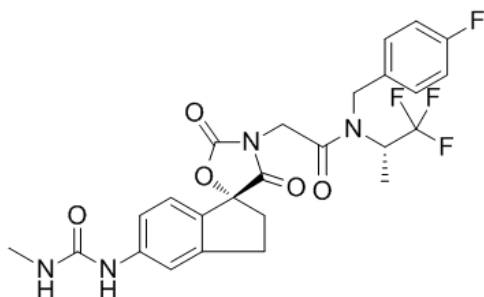
Formula $C_{25}H_{24}F_4N_4O_5$ M.Wt 536.48

Solubility DMSO : 100 mg/mL (186.40 mM) Storage Store at -20°C

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]:

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

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Cell lines Human T-ALL cell lines

Preparation Method TALL-1 cell lines were treated with 5μM A-485 or an equal volume of vehicle (DMSO), and 48 hours later, live TALL-1 cells were transiently transfected with an expression vector encoding human c-Myc. Cell viability was measured by MTS assay.

Reaction
Conditions 5μM, 48h

Applications A-485 inhibited the viability of TALL-1 cells, and the expression of exogenous c-Myc partially saved the viability of NotCH3-dependent TALL-1 cells exposed to A-485.

Animal experiment [2]:

Animal models LuCaP-77 CR xenograft model

Preparation Method LuCap-77 CR xenograft tumors were established in SCID mice, and A-485 was administered intraperitoneally (ip) at a dose of 100mg/kg twice daily for 21 days.

Dosage form 100mg/kg, twice daily for 21 days , i.p.

Applications After 21 days of administration, A-485 inhibited tumor growth by 54% compared to vehicle control.

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References:

- [1] Tottone L, Zhdanovskaya N, Carmona Pestaña Á, Zampieri M, Simeoni F, Lazzari S, Ruocco V, Pelullo M, Caiafa P, Felli MP, Checquolo S, Bellavia D, Talora C, Screpanti I, Palermo R. Histone Modifications Drive Aberrant Notch3 Expression/Activity and Growth in T-ALL. *Front Oncol.* 2019 Apr 3;9:198.
- [2] Lasko LM, et al. Discovery of a selective catalytic p300/CBP inhibitor that targets lineage-specific tumours. *Nature.* 2017 Oct 5;550(7674):128-132.

Background

A-485 is a potent and selective p300/CBP (histone acetyltransferase paralog/CREB binding protein) catalytic inhibitor with IC_{50} of 60nM for p300 HAT. A-485 inhibits the activity of p300-BHC (bromodomain HAT-C/H3) and CBP-BHC domains with IC_{50} of 9.8nM and 2.6nM, respectively. A-485 selectively inhibits the proliferation of lineage-specific tumor types, including several hematological malignancies and androgen receptor-positive prostate cancer [1-2].

A-485 reduces the level of acetylated histone H3 lysine 27 (H3K27Ac) in PC3 cells in a concentration-dependent manner with an EC_{50} of 73nM, but has little effect on H3K9Ac ($EC_{50} > 10\mu M$) [1]. A-485 has an inhibitory effect on H3K27Ac in three melanoma cell lines (WM2664, SKMEL5 and A375 cells) with IC_{50} of 0.59, 0.93 and 0.96 μM , respectively. A-485 significantly induces cell senescence in sensitive melanoma cell lines WM2664 and SKMEL5, but no similar effect was observed in resistant A375 cells [3].

A-485 reduced tumor volume (54%) in the LuCaP-77 CR mouse xenograft model of castration-resistant prostate cancer when administered at a dose of 100mg/kg for 21 days [1]. In the GH3 cell xenograft nude mouse model, A-485 can significantly inhibit tumor volume (50mg/kg group inhibited 32.37%, 100mg/kg group inhibited 54.15%) and tumor weight (50mg/kg group inhibited 43.83% , the 100mg/kg group inhibited 61.41%) [4].

References:

- [1] Lasko LM, et al. Discovery of a selective catalytic p300/CBP inhibitor that targets lineage-specific tumours. *Nature.* 2017 Oct 5;550(7674):128-132.

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- [2] Tottone L, Zhdanovskaya N, Carmona Pestaña A, Zampieri M, Simeoni F, Lazzari S, Ruocco V, Pelullo M, Caiafa P, Felli MP, Checquolo S, Bellavia D, Talora C, Screpanti I, Palermo R. Histone Modifications Drive Aberrant Notch3 Expression/Activity and Growth in T-ALL. *Front Oncol.* 2019 Apr 3;9:198.
- [3] Wang R, He Y, Robinson V, Yang Z, Hessler P, Lasko LM, Lu X, Bhathena A, Lai A, Uziel T, Lam LT. Targeting Lineage-specific MITF Pathway in Human Melanoma Cell Lines by A-485, the Selective Small-molecule Inhibitor of p300/CBP. *Mol Cancer Ther.* 2018 Dec;17(12):2543-2550.
- [4] Ji C, Xu W, Ding H, et al. The p300 inhibitor A-485 exerts antitumor activity in growth hormone pituitary adenoma[J]. *The Journal of Clinical Endocrinology & Metabolism*, 2022, 107(6): e2291-e2300.

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