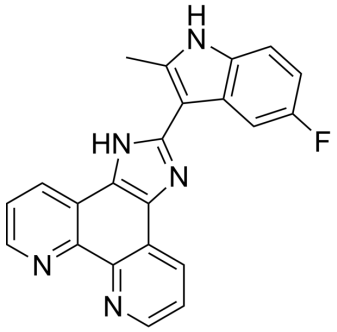
APTO-253

Cat. No.:	HY-16291
CAS No.:	916151-99-0
Molecular Formula:	$C_{22}H_{14}FN_5$
Molecular Weight:	367.38
Target:	c-Myc; KLF; Apoptosis
Pathway:	Apoptosis; MAPK/ERK Pathway
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 60 mg/mL (163.32 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7220 mL	13.6099 mL	27.2198 mL
	5 mM	0.5444 mL	2.7220 mL	5.4440 mL
	10 mM	0.2722 mL	1.3610 mL	2.7220 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.3 mg/mL (6.26 mM); Suspended solution; Need ultrasonic and warming
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (5.66 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

APTO-253 (LOR-253) is a small molecule that inhibits c-Myc expression, stabilizes G-quadruplex DNA, and induces cell cycle arrest and apoptosis in acute myeloid leukemia cells. APTO-253 mediates anticancer activity through induction of the Krüppel-like factor 4 (KLF4) tumor suppressor[1][2]. APTO-253 has antiarthritic activity[3].

IC_{50} & Target

c-Myc[1]; KLF4[2]

In Vitro

APTO-253 (LOR-253) is an inducer of KLF4. APTO-253 (5 μM) induces KLF4 expression, and enhances apoptosis induced by NSC 119875 in both SKOV3 and OVCAR3 cells. APTO-253 (5 μM) also leads to G1 phase arrest and reduces S and G2/M phase cells in SKOV3 and OVCAR3 cells[1].

APTO-253 is cytotoxic to Raji and Raji/253R cell lines, with IC_{50}s of 105 ± 2.4 nM and 1387 ± 94 nM, respectively. APTO-253 (0.5

μM) also causes DNA damage in Raji cells. BRCA1/2 deficient cells are hypersensitive to APTO-253. ABCG2 overexpressed HEK-293 cells are resistant to APTO-253 and inhibition of ABCG2 reverses resistance to APTO-253 in Raji/253R[2].
APTO-253 suppresses the proliferation of acute myeloid leukemia (AML) cell lines and various forms of lymphoma cell lines with IC_{50}s ranging from 57 nM to 1.75 μM. APTO-253 (500 nM) also causes G0/G1 cell cycle arrest, induces apoptosis, and down regulates MYC RNA and protein expression in AML lines. APTO-253 (500 nM) leads to DNA damage response pathways in MV4-11 cells. Futhermore, APTO-253 is a potent stabilizer of Gquadruplex (G4) motifs, and demonstrates the greatest propensity for stabilizing the MYC G4 sequences[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

APTO-253 (LOR-253; 15 mg/kg; IV; twice per day for 2 consecutive days per week for 14 days) has antiarthritic activity in a CIA model[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	DBA/1J male mice (6 weeks) with collagen induced arthritis (CIA)[3]
Dosage:	15 mg/kg
Administration:	IV; twice per day for 2 consecutive days per week for 14 days
Result:	Demonstrated significant preventive and therapeutic activity on arthritis formation.

CUSTOMER VALIDATION

- Ann Rheum Dis. 2020 Nov 2;annrheumdis-2020-218189.
- Nat Commun. 2023 Sep 2;14(1):5360.
- Nat Commun. 2019 Sep 25;10(1):4369.
- JCI Insight. 2022 Jul 19;e160688.
- Int Immunopharmacol. 2023 Jun 5;120:110425.

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REFERENCES

[1]. Local A, et al. APTO-253 Stabilizes G-quadruplex DNA, Inhibits MYC Expression, and Induces DNA Damage in Acute Myeloid Leukemia Cells. Mol Cancer Ther. 2018 Jun;17(6):1177-1186.

[2]. Hongying Zhang, et al. Inhibition of c-Myc By Apto-253 As an Innovative Therapeutic Approach to Induce Cell Cycle Arrest and Apoptosis in Acute Myeloid Leukemia. Blood 2016 128:1716.

[3]. Haruka Tsuchiya, et al. Parsing multiomics landscape of activated synovial fibroblasts highlights drug targets linked to genetic risk of rheumatoid arthritis. Ann Rheum Dis. 2020 Nov2;annrheumdis-2020-218189.

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