

MCB-36

Chemical Properties

CAS No. :

Formula:

Molecular Weight:

Keep away from direct sunlight

Storage:

Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Actual storage temperature shall be subject to the COA.

Biological Description

Description	MCB-36 is a versatile KRAS-targeting PROTAC degrader recruiting the VHL protein without affecting KRAS transcription. It exerts minimal impact on HRAS and NRAS protein levels. MCB-36 binds with high affinity ($K_d \approx 1 \text{ pM}$) to G12D, G12C, G12V, and wild-type KRAS in the GDP-loaded state. By reducing p-ERK levels, MCB-36 induces apoptosis (apoptosis). It effectively inhibits cancer cells resistant to KRASG12C and remodels the tumor immune microenvironment. MCB-36 is applicable in research on colorectal and lung cancer.
Targets(IC50)	Apoptosis,ERK,Caspase,p38 MAPK,PROTACs,TNF,Ras
In vitro	MCB-36 shows significant antiproliferative effects on KRAS-dependent cancer cells such as PC-1 (G12D), H358 (G12C), LS180 (G12V), and HCT116 (G13D) at concentrations ranging from 1 nM to 100 μM over 5 days, with an average IC50 of about 1 μM in 24 out of 30 cell lines tested, while having no impact on normal cells (hTERT-HPNE, NCM460) and KRAS-independent cells ($\text{IC}_{50} > 10 \text{ }\mu\text{M}$). At concentrations of 0-10 μM over 0-72 hours, MCB-36 effectively degrades KRAS protein, reduces p-ERK levels, and induces cell death in all tested cell lines, including MIA PaCa-2 cells expressing KRAS G12C, KRAS G12C/Y96C, and KRAS G12C/H95D. Additionally, MCB-36 (0-2.5 μM , 6 days) inhibits the growth of KRAS-mutant colorectal cancer organoids, accompanied by decreased abundance of MAPK signaling pathway components and increased apoptotic markers. Furthermore, MCB-36 significantly upregulates the TNF- α response pathway in CD45+ immune cells isolated from CT26 tumors and increases the abundance of effector CD8+ T cells.
In vivo	MCB-294 (10 mg/kg, i.p., single dose) demonstrates bioavailability in mice and can reduce KRAS and p-ERK levels 6 hours post-treatment. Additionally, MCB-294 (60 mg/kg, i.p., administered twice daily for 1-21 days) effectively inhibits KRAS G12C-resistant cancer cells and remodels the tumor immune microenvironment in mice.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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