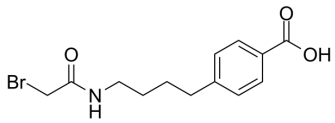
KRA-533

Cat. No.:	HY-138188
CAS No.:	10161-87-2
Molecular Formula:	$C_{13}H_{16}BrNO_3$
Molecular Weight:	314.18
Target:	Ras
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (795.72 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1829 mL	15.9144 mL	31.8289 mL
	5 mM	0.6366 mL	3.1829 mL	6.3658 mL
	10 mM	0.3183 mL	1.5914 mL	3.1829 mL

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

BIOLOGICAL ACTIVITY

Description

KRA-533 is a potent KRAS agonist. KRA-533 binds to the GTP/GDP binding pocket in the KRAS protein to prevent GTP cleavage, resulting in the accumulation of constitutively active GTP-bound KRAS that triggers both apoptotic and autophagic cell death pathways in cancer cells.

IC_{50} & Target

KRAS[1]

In Vitro

KRA-533 (10 μM; 48 hours; HCC827 cells) enhances KRAS activity to a greater extent[1].
KRA-533 (0~15 μM; 48 hours; H157 cells) enhances KRAS activity in a dose-dependent manner, which is associated increased levels of pERK, ratio of active caspase 3/procaspase 3 and PARP cleavage, leading to apoptotic cell death[1].
KRA-533 (10 μM; 10 days; H292 cells) mediates cell growth suppression than those without KRAS mutation. KRA-533 (5~15 μM) can directly bind to WT, G12C, G12D and G13D mutant KRAS proteins. KRA-533 activates WT KRAS to increase its activity in a dose-dependent manner. KRA-533 further enhances the activities of active KRAS mutants[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	HCC827 cells
Concentration:	10 μM
Incubation Time:	48 hours
Result:	Enhanced KRAS activity to a greater extent.

Apoptosis Analysis[1]

Cell Line:	H157 cells
Concentration:	0~15 μM
Incubation Time:	48 hours
Result:	Enhanced KRAS activity in a dose-dependent manner, which was associated increased levels of pERK, ratio of active caspase 3/procaspase 3 and PARP cleavage, leading to apoptotic cell death.

In Vivo

KRA-533 (0~30 mg/kg; i.p.; 28 days) suppresses tumor growth in a dose-dependent manner in lung cancer mutant KRAS xenografts and induces apoptosis and autophagy in tumor tissues in a dose-dependent manner[1].
KRA-533 shows optimal therapeutic index between 7.5 mg/kg and 30 mg/kg doses[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Nu/Nu nude mice (mutant KRAS xenografts)[1]
Dosage:	0~30 mg/kg
Administration:	i.p.; 28 days
Result:	Suppressed tumor growth in a dose-dependent manner in lung cancer mutant KRAS xenografts and induced apoptosis and autophagy in tumor tissues in a dose-dependent manner.

REFERENCES

[1]. Xu K, et al. Small Molecule KRAS Agonist for Mutant KRAS Cancer Therapy [published correction appears in Mol Cancer. 2020 May 20;19(1):93]. Mol Cancer. 2019;18(1):85. Published 2019 Apr 10.

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