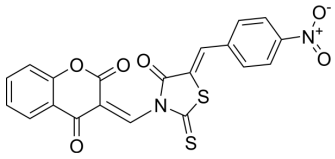
NSC-658497

Cat. No.:	HY-19539
CAS No.:	909197-38-2
Molecular Formula:	$C_{20}H_{10}N_2O_6S_2$
Molecular Weight:	438.43
Target:	Ras
Pathway:	GPCR/G Protein; MAPK/ERK Pathway
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

NSC-658497 is an effective inhibitor of Ras-GEF, SOS1. NSC-658497 binds to SOS1, competitively suppresses SOS1-Ras interaction, and dose-dependently inhibits SOS1 GEF activity. NSC-658497 showed dose-dependent efficacy in inhibiting Ras, downstream signaling activities, and associated cell proliferation[1].

In Vitro

NSC-658497 (0-20 μM; 2 hours; NIH/3T3 cells) dose-dependently inhibits EGF (50 ng/mL)-stimulated Ras, but not EGFR activation[1].

Concomitant to Ras inhibition, NSC-658497 (0-100 μM; 2 hours; NIH/3T3 cells) dose-dependently inhibited the EGF activated, Ras downstream targets ERK1/2 and AKT[1].

Consistent with these results, NSC-658497 dose-dependently suppressed Ras signaling mediated by the overexpression of an active SOS1 mutant (W729L), originally identified in Noonan's Syndrome, in human embryonic kidney cells[1].

NSC-658497 dose-dependently inhibits 50 nM SOS1-cat mediated GDP/GTP nucleotide exchange upon 2 μM H-Ras (aa. 1-166) in the BODIPYFL-GDP dissociation assay (IC_{50}=15.4μM)[1].

NSC-658497 (0-60 μM; 3 days; PC-3 and DU-145 cells) inhibits proliferation of prostate cancer cells[1].

NSC-658497 (0-60 μM; 2 hours; PC-3 and DU-145 cells) dose-dependently inhibits Ras-GTP activity and the downstream p-ERK1/2 and p-Akt activities[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	PC-3 and DU-145 cells
Concentration:	0-60 μM
Incubation Time:	3 days
Result:	Dose-dependently inhibited proliferation of PC-3 and DU-145 cells.

Western Blot Analysis[1]

Cell Line:	PC-3 and DU-145 cells
Concentration:	0-60 μM
Incubation Time:	2 hours
Result:	Dose-dependently inhibited Ras-GTP activity and the downstream p-ERK1/2 and p-Akt

	activities.

REFERENCES

[1]. Evelyn CR, et al. Rational design of small molecule inhibitors targeting the Ras GEF, SOS1. Chem Biol. 2014;21(12):1618-1628.

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