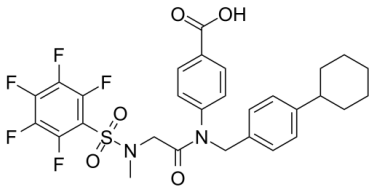
Data Sheet

Product Name:	SH-4-54
Cat. No.:	CS-4597
CAS No.:	1456632-40-8
Molecular Formula:	C29H27F5N2O5S
Molecular Weight:	610.59
Target:	STAT
Pathway:	JAK/STAT Signaling; Stem Cell/Wnt
Solubility:	DMSO : 100 mg/mL (163.78 mM; Need ultrasonic); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

SH-4-54 is a most potent, small molecule, nonphosphorylated **STAT** inhibitor, with **K_Ds** of 300, 464 nM for STAT3 and STAT5, respectively. IC50 & Target: KD: 300 nM (STAT3), 464 nM (STAT5)[1]. **In Vitro:** SH-4-54 potently kills glioblastoma brain cancer stem cells (BTSCs) and effectively suppresses STAT3 phosphorylation and its downstream transcriptional targets at low nM concentrations.SH-4-54 shows unprecedented cytotoxicity in human BTSCs, displays no toxicity in human fetal astrocytes, potently suppresses pSTAT3 with nanomolar IC_{50}s, inhibiting STAT3's downstream targets, and shows no discernible off-target effects at therapeutic doses[1]. **In Vivo:** SH-4-54 exhibits blood-brain barrier permeability potently controls glioma tumor growth, and inhibits pSTAT3 in vivo. SH-4-54 demonstrates the power of STAT3 inhibitors for the treatment of BTSCs and validates the therapeutic efficacy of a STAT3 inhibitor for GBM clinical application.SH-4-54 decreases pSTAT3 expression in tumor cells of treated mice. SH-4-54 appears to decrease proliferation and increase apoptosis of treated tumors[1].

PROTOCOL (Extracted from published papers and Only for reference)

Animal administration [1] SH-4-54 is given to three NOD-SCID mice at 10 mg/kg and 25 mg/kg dosing via intraperitoneal injection, and blood was collected at two time points (30 and 300 min). Brain was also collected from one mouse at each dose and concentrations of SH-4-54 determined by LCMS. We found that after 30 min at 10 mg/kg, SH-4-54 was found at a concentration of 700 nM. Following these studies, three mice per group were dosed for five consecutive days with 10 mg/kg. Blood was collected at 30 and 300 min post the last dose, and brain was collected from all animals at the 300 min time-point. Then, 313 nM of SH-4-54 was detected in the brains of treated animals. Encouragingly, these studies demonstrated that therapeutic doses of SH-4-54 could be achieved in vivo at values similar to the in vitro IC50s demonstrating efficacy against BTSCs.

References:

[1]. Haftchenary S, et al. Potent Targeting of the STAT3 Protein in Brain Cancer Stem Cells: A Promising Route for Treating Glioblastoma. ACS Med Chem Lett. 2013 Sep 8;4(11):1102-1107.

CAIndexNames:

Benzoic acid, 4-[[(4-cyclohexylphenyl)methyl][2-[methyl[(2,3,4,5,6-pentafluorophenyl)sulfonyl]amino]acetyl]amino]-

SMILES:

O=C(O)C1=CC=C(N(CC2=CC=C(C3CCCCC3)C=C2)C(CN(C)S(=O)(C4=C(F)C(F)=C(F)C(F)=C4F)=O)=O)C=C1

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

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