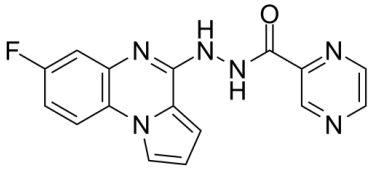
Data Sheet

Product Name:	SC144
Cat. No.:	CS-4440
CAS No.:	895158-95-9
Molecular Formula:	$C_{16}H_{11}FN_6O$
Molecular Weight:	322.30
Target:	Apoptosis; Interleukin Related
Pathway:	Apoptosis; Immunology/Inflammation
Solubility:	DMSO : 16.67 mg/mL (51.72 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

SC144 is a first-in-class, orally active **gp130 (IL6-beta)** inhibitor. SC144 binds gp130, induces gp130 phosphorylation (S782) and deglycosylation, abrogates Stat3 phosphorylation and nuclear translocation, and further inhibits the expression of downstream target genes. SC144 shows potent inhibition of gp130 ligand-triggered signaling. SC144 induces apoptosis in human ovarian cancer cells[1].
In Vitro: SC144 inhibits cell growth in a panel of human ovarian cancer cell lines with IC_{50}s in a submicromolar range (IC_{50}=OVCAR-8, OVCAR-5, OVCAR-3= 0.72, 0.49, 0.95 μM)[1].
The potency of SC144 toward NCI/ADR-RES (Paclitaxel- and Doxorubicin-resistant, IC_{50}=0.43 μM) and HEY (Cisplatin-resistant, IC_{50}=0.88 μM) suggests an ability to overcome drug resistance in ovarian cancer[1].
SC144 (2 μM; 24 hours) causes significantly more apoptosis in OVCAR-8 and Caov-3 than normal kidney epithelial and normal endometrial cells[1].
SC144 (0.5-2 μM; 0-6 hours) substantially increases the phosphorylation of gp130 (S782) in both OVCAR-8 and Caov-3 cells in a time- and dose-dependent manner[1].
SC144 is cytotoxic to ovarian cancer cells via a mechanism involving the inhibition of gp130 activity, leading to the inactivation of Akt and Stat3 as well as the suppression of Stat3-regulated gene expression. As are result, SC144 treatment eventually causes cell-cycle arrest, anti-angiogenesis, and apoptosis[1].
In Vivo: SC144 (10 mg/kg; i.p.; daily for 58 days) suppresses tumor growth in human ovariancancer xenografts[1].
SC144 (100 mg/kg;p.o.; daily for 35 days) treatment shows the average tumor volume in mice 82% smaller than that in the control group[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay [1] Cells were seeded in 96-well microtiter plates, allowed to attach 24 hours before siRNA transfections or the addition of corresponding compounds to the culture medium. After 72 hours, cells were incubated with 0.3 mg/mL MTT (Amresco) for an additional 3 hours at 37°C. After removal of the supernatant, DMSO was added to the wells and the absorbance was read at 570 nm. All assays were conducted in triplicate. Percentage of cell growth inhibition was expressed as: (1-A/C) × 100% (A and C were the absorbance values from experimental and control cells, respectively). Inhibitory concentration 50% (IC50) values were determined for each drug from a plot of log (drug concentration) versus percentage of cell growth inhibition. SDs were calculated on the basis of the IC50 values obtained from at least 3 independent experiments. Animal administration [1] To prepare SC144 solution for i.p. administration, 200 mg/mL DMSO stock solution of SC144 was diluted to 20 mg/mL in propylene glycol and further added to 0.9% NaCl with 40% propylene glycol. For oral administration, SC144 (100 mg/kg) was orally delivered every day to the treatment group. To prepare SC144 solution for oral administration, 300 mg/mL DMSO stock solution of SC144 was mixed with sesame oil. Mouse

body weight and tumor volume were measured twice a week.

References:

[1]. Xu S, et al. Discovery of a novel orally active small-molecule gp130 inhibitor for the treatment of ovarian cancer. Mol Cancer Ther. 2013 Jun;12(6):937-49.

CAIndexNames:

2-Pyrazinecarboxylic acid, 2-(7-fluoropyrrolo[1,2-a]quinoxalin-4-yl)hydrazide

SMILES:

O=C(C1=NC=CN=C1)NNC2=NC3=C(N4C2=CC=C4)C=CC(F)=C3

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