Product Data Sheet

Chemical Properties

- **Product Name:** RO4929097
- **Cas No.:** 847925-91-1
- **M.Wt:** 469.4
- **Formula:** C22H20F5N3O3
- **Synonyms:** N/A

- **Chemical Name:** 2,2-dimethyl-N-[(7S)-6-oxo-5,7-dihydrobenzo[d][1]benzazepin-7-yl]-N'-(2,2,3,3,3-pentafluoropropyl)propanediamide
- **Canonical SMILES:** CC(C)(C(=O)NCC(F)(F)(F)F)C(=O)NC1C2=CC=CC=CC2C3=CC=CC=C3NC1=O

- **Solubility:** ≥23.47mg/mL in DMSO
- **Storage:** Store at -20°C
- **General tips:** For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

- **Shopping Condition:** Evaluation sample solution: ship with blue ice
  All other available size: ship with RT, or blue ice upon request

Biological Activity

- **Targets:** Proteases
- **Pathways:** Gamma Secretase

**Description:**

RO4929097 is a small-molecule inhibitor of γ secretase with IC50 of 4 nM and EC50 of 5 nM [1]. It shows no in vitro inhibitory activity on the closely related proteases. It also has greater than 100-fold selectivity with respect to 75 other proteins of various types [1]. RO4929097 binds to γ
secretase and inhibits its protease activity, therefore blocking the cleavage of Notch and reducing Notch signaling. Up-regulation of this signaling pathway promotes tumorigenesis of multiple cancers. RO4929097 has shown potential antitumor activity both in vitro and in vivo. It impaired the growth of melanoma cell lines and tumor formation of human primary melanoma xenograft [2]. It slowed proliferation and reduces colony formation of breast cancer cell lines[1]. In addition, RO4929097 decreased tumor formation in xenograft models of colorectal, pancreatic, lung cancer and melanoma[1, 2]. RO4929097 has been tested in multiple phase I/II clinical trials in patients with advanced solid tumors, either as monotherapy or in combination with other anti-tumor agents[3-8].

Reference:

Protocol

Cell experiment:

Cell lines SUM190 and SUM149 cells

Preparation method The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting conditions 1 μM, 14 days for 2D cultures 7 days for 3D cultures
Applications

After treating with increasing doses of ionizing radiation in the presence or absence of the drug, 2D colonies were allowed to grow for 10–14 days, while the mammospheres were permitted to grow for 1 week. At 1 μM, RO4929097 was able to sensitize adherent cells to radiation with a more significant effect seen in SUM190 than in SUM149 cells. However, the same dose of inhibitor radioprotected cells grown under conditions that favor the enrichment of the cancer stem cells at higher doses of ionizing radiation. This discrepancy between 2D and 3D cultures suggested that cell contact may be needed for a Notch inhibitor to have a significant effect.

Animal experiment [3]:

Animal models
NOD/SCID/IL2gammaR-/- (NOG) mice injected with WM3248 cells

Dosage form
Oral administration, 10 mg/Kg/day for 30 days

Applications
There was a decrease in tumor growth with RO4929097 treatment, which was more appreciable after tumors were extracted for weight assessment. RO4929097-treated tumors also displayed lower expression of putative melanoma stem cell markers CD166, CD271 and JARID1B compared to vehicle-treated ones.

Other notes
Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:

Product Citations


Caution
Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short-term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.