产品名称：**GSK2256098**
产品别名：**GSK2256098**

## 生物活性：

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| **Description** | GSK2256098 is a selective FAK kinase inhibitor, which inhibits growth and survival of pancreatic ductal adenocarcinoma cells. |
| **$IC_{50}$ & Target** | FAK[1] |
| **In Vitro** | GSK2256098 is a thousand fold more selective for FAK compared to the nearest FAK family member, Pyk2. GSK2256098 inhibits FAK activity through targeting the phosphorylation site of FAK, tyrosine (Y) 397. GSK2256098 inhibits FAK activity or Y397 phosphorylation in cancer cell lines, OVCAR8 (ovary), U87MG (brain), and A549 (lung), at IC50s of 15, 8.5 and 12 nM, respectively. The responses of 6 PDAC cell lines in regards to FAK Y397 phosphorylation or activity to GSK2256098 treatments (0.1–10 μM) ranged from low (less than 20% inhibition) to high (more than 90% inhibition). The least and most sensitive cell lines (PANC-1 and L3.6P1) are selected for further analysis. GSK2256098 inhibition of FAK Y397 phosphorylation correlated with decreased levels of phosphorylated Akt and ERK in L3.6P1 cells. GSK2256098 decreases cell viability, anchorage-independent growth, and motility in a dose dependent manner[1]. |
| **In Vivo** | FAK is well-known to play an important role in angiogenesis, proliferation, and apoptosis, so the tumor samples harvested from the therapy experiments are examined. Evaluating CD31, significantly lower microvessel densities in tumors from mice treated with GSK2256098 and Paclitaxel is observed than in tumors from mice in the vehicle control group ($P<0.05$). This is consistent across both models, but Ishikawa tumors had the lowest microvessel density. All tumor models in mice treated with GSK2256098 exhibit less proliferation via Ki67 than control. Ishikawa tumors have the lowest Ki67 expression in response to therapy. Ishikawa tumors have higher apoptotic indices than Hec1A tumors after treatment with GSK2256098. Significant rates of apoptosis are seen in all models that had been treated with combination GSK2256098 and Paclitaxel[2]. |
| **Solvent&Solubility** | ***In Vitro:***<br>**DMSO : ≥ 30 mg/mL (72.31 mM)**<br>* "≥" means soluble, but saturation unknown. |

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
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| 1 mM | 2.4103 mL | 12.0514 mL | 24.1028 mL |
| 5 mM | 0.4821 mL | 2.4103 mL | 4.8206 mL |
| 10 mM | 0.2410 mL | 1.2051 mL | 2.4103 mL |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

***In Vivo:***

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出

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| | 现沉淀、析出现象，可以通过加热和/或超声的方式助溶<br>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline<br>Solubility: ≥ 2.5 mg/mL (6.03 mM); Clear solution<br>此方案可获得 ≥ 2.5 mg/mL (6.03 mM，饱和度未知) 的澄清溶液。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。<br><br>2.请依序添加每种溶剂： 10% DMSO →90% corn oil<br>Solubility: ≥ 2.5 mg/mL (6.03 mM); Clear solution<br>此方案可获得 ≥ 2.5 mg/mL (6.03 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **References** | [1]. Zhang J, et al. A small molecule FAK kinase inhibitor, GSK2256098, inhibits growth and survival of pancreatic ductal adenocarcinoma cells. Cell Cycle. 2014;13(19):3143-9.<br>[2]. Thanapprapasr D, et al. PTEN Expression as a Predictor of Response to Focal Adhesion Kinase Inhibition in Uterine Cancer. Mol Cancer Ther. 2015 Jun;14(6):1466-75. |

**实验参考：**

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| **Cell Assay** | PDAC cells are cultured on the wells of a 96-well plate. Ten microliters of MTS is added to the wells (total value: 100 μL). After the plate is kept in a 37°C incubator for 10-30 min, the absorbance at 450 nm wave length of reacted MTS is determined on a microplate reader. The Sigma plot program is used to calculate IC50 of GSK2256098 on cell viability. PDAC cells are cultured on a 6-well plate. When cell confluence reached about 70% in regular medium, the cells are incubated in the medium containing 0.1-10 μM GSK2256098 for 48 or 72 hr. At the end of treatments, cells are re-seeded and kept for 9 d Then, the cells are stained using Clonogenic Reagent, and the blue colonies are counted[1]. |
| **Animal Administration** | Mice[2]<br>Female 8- to 12-week-old athymic nude mice are used. For therapeutic experiments, $4\times10^6$ Ishikawa or Hec1A cells are inoculated into the uterine horn. Following tumor cell injection, the mice are randomized (n=10 mice per group) according to the following groups: 1) 100 μL of a vehicle control (oral, daily); 2) 75 mg/kg GSK2256098 in 100 μL of vehicle (oral, daily); 3) 2.5 mg/kg Paclitaxel in 200 μL of PBS (intraperitoneal, weekly); and 4) GSK2256098 and Paclitaxel (doses and frequencies given above). Therapy is initiated 10-14 days after tumor injection. The mice are monitored for adverse effects and sacrificed using cervical dislocation four to six weeks after initiation of treatment. At the completion of each experiment, each mouse's weight, aggregate tumor weight, location, and number of tumor nodules are recorded for each treatment group. Tumor samples are processed for further analysis via preservation in optimal cutting temperature medium for frozen section analysis as well as fixed in formalin for paraffin-embedded section analysis. |
| **References** | [1]. Zhang J, et al. A small molecule FAK kinase inhibitor, GSK2256098, inhibits growth and survival of pancreatic ductal adenocarcinoma cells. Cell Cycle. 2014;13(19):3143-9.<br>[2]. Thanapprapasr D, et al. PTEN Expression as a Predictor of Response to Focal Adhesion Kinase Inhibition in Uterine Cancer. Mol Cancer Ther. 2015 Jun;14(6):1466-75. |