产品名称：FH535
产品别名：FH535

生物活性：

Description	FH535 is an inhibitor of Wnt/β-catenin and PPAR, with anti-tumor activities.		
IC_{50} & Target	PPAR	Wnt	β-catenin
In Vitro	FH535 is an inhibitor of Wnt/β-catenin and PPAR. FH535 inhibits PPARγ and PPARδ transactivation in HCT116 cells. FH535 (15 μM) activities depend on functional PPARδ but does not require a cysteine residue in the PPAR ligand-binding domain. FH535 inhibits recruitment of the coactivators GRIP1 and β-catenin to PPARδ and PPARγ. FH535 shows toxic effects on 12 carcinoma cell lines expressing wnt/β-catenin pathway[1]. FH535 (20 μM) suppresses the β-catenin pathway in pancreatic cancer cells, and inhibits pancreatic cancer cell migration. Furthermore, FH535 (20, 40 μM) inhibits pancreatic cancer cell invasion and cell growth[2]. FH535 represses angiogenesis-related genes in pancreatic cancer cells[3].		
In Vivo	FH535 (25 mg/kg, i.p.) exhibits an anti-tumor effect on pancreatic cancer xenografts in mice. FH535 also represses angiogenesis in pancreatic cancer xenografts[2].		

Solvent&Solubility

In Vitro:

DMSO : 33.33 mg/mL (**92.28 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7685 mL	13.8427 mL	27.6855 mL
	5 mM	0.5537 mL	2.7685 mL	5.5371 mL
	10 mM	0.2769 mL	1.3843 mL	2.7685 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；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (6.92 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.92 mM，饱和度未知) 的澄清溶液。

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。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: 2.5 mg/mL (6.92 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (6.92 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

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 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。

References	[1]. Handeli S, et al. A small-molecule inhibitor of Tcf/beta-catenin signaling down-regulates PPARgamma and PPARdelta activities. Mol Cancer Ther. 2008 Mar;7(3):521-9. [2]. Wu MY, et al. FH535 inhibited metastasis and growth of pancreatic cancer cells. Onco Targets Ther. 2015 Jul 6;8:1651-70. [3]. Liu L, et al. FH535, a β-catenin pathway inhibitor, represses pancreatic cancer xenograft growth and angiogenesis. Oncotarget. 2016 Jul 26;7(30):47145-47162.

实验参考：

Cell Assay	Cell growth is evaluated using the MTT assay. Cells (5 × 10^4/well) are seeded in 24-well tissue culture plates. Blank control is treated with DMSO. After FH535 treatment, MTT is added to each well (final concentration, 0.5 mg/mL), followed by 4-hour incubation at 37°C. The medium is removed, and 800 μL of DMSO is added to each well. The absorbance of the mixture is measured at 490 nm using a microplate enzyme-linked immunosorbent assay reader. The relative cell viability is calculated as follows: relative cell viability = (mean experimental absorbance/mean control absorbance) ×100%[2].
Animal Administration	Four-week-old female BALB/c athymic nude mice receive humane care. PANC-1 cells stably expressing firefly luciferase are injected into the left flanks of the mice in a total volume of 100 μL (0.5 × 10^7 cells), and the mice are randomly assigned to a DMSO [intraperitoneally injected with 100 μL DMSO/DMEM (1:1)] or FH535 group [intraperitoneally injected with 25 mg/kg FH535 dissolved in 100 μL DMSO/DMEM (1:1)]. Treatment is conducted every 2 days for 20 days; tumor volume is measured with a caliper using the formula: volume = length × $width^2$/2. At the end of the experiment, the mice are anaesthetized and given D-luciferin in PBS. Twenty minutes after the injection, bioluminescence is imaged with a charge-coupled device camera. Then, the tumor tissue is stripped and formalin-fixed, paraffin-embedded, cut into 4-μm sections, and immunohistochemically stained [3].
References	[1]. Handeli S, et al. A small-molecule inhibitor of Tcf/beta-catenin signaling down-regulates PPARgamma and PPARdelta activities. Mol Cancer Ther. 2008 Mar;7(3):521-9. [2]. Wu MY, et al. FH535 inhibited metastasis and growth of pancreatic cancer cells. Onco Targets Ther. 2015 Jul 6;8:1651-70. [3]. Liu L, et al. FH535, a β-catenin pathway inhibitor, represses pancreatic cancer xenograft growth and angiogenesis. Oncotarget. 2016 Jul 26;7(30):47145-47162.