

产品名称：**GSK1838705A**
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生物活性：				
Description	GSK1838705A is a potent and reversible IGF-IR and the insulin receptor inhibitor with IC ₅₀ s of 2.0 and 1.6 nM, respectively. It also inhibits ALKwith an IC ₅₀ of 0.5 nM.			
IC ₅₀ & Target	IC50: 2.0 nM (IGF-IR), 1.6 nM (insulin receptor), 0.5 nM (ALK)[1]			
In Vitro	In cellular phosphorylation assays, GSK1838705A potently inhibits IGF-IR and insulin receptor phosphorylation with IC50s of 85 and 79 nM, respectively. appKi values are 0.7 nM for IGF-IR and 1.1 nM for insulin receptor using the filter binding assay. GSK1838705A inhibits the proliferation in a panel of cell lines derived from solid and hematologic tumors. The EC50s of GSK1838705A range from 20 nM to >8 μM, but are <1 μM in most multiple myeloma and Ewing's sarcoma cell lines[1].			
In Vivo	GSK1838705A shows robust antitumor activity in animal xenograft models. Tumor types likely to respond to GSK1838705A include multiple myeloma and Ewing's sarcoma, as well as ALK-driven tumors (e.g., ALCL, NSCLC, and neuroblastoma). A single oral dose of GSK1838705A at 0.1 and 0.3 mg/kg results in 35% and 65% inhibition of IGF-IR phosphorylation, respectively, whereas doses ≥ 1 mg/kg results in complete inhibition of ligand-induced IGF-IR phosphorylation[1].			
Solvent&Solubility	In Vitro: DMSO : ≥ 100 mg/mL (187.77 mM) * "≥" means soluble, but saturation unknown.			
	<div>Preparing Stock Solutions</div>	<div>Solvent Concentration</div> <div>Mass</div>	1 mg	5 mg
		1 mM	1.8777 mL	9.3884 mL
		5 mM	0.3755 mL	1.8777 mL
		10 mM	0.1878 mL	0.9388 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℃，6 months；-20℃，1 month。-80℃ 储存时，请在 6 个月内使用，-20℃ 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: 3 mg/mL (5.63 mM); Suspended solution; Need ultrasonic 此方案可获得 3 mg/mL (5.63 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 30.0 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。			
References	[1]. Sabbatini P, et al. GSK1838705A inhibits the insulin-like growth factor-1 receptor and anaplastic lymphoma kinase and shows antitumor activity in experimental models of human cancers. Mol Cancer			

实验参考:

Cell Assay	Cells are seeded in 96-well dishes, incubated overnight at 37°C, and treated with DMSO or GSK1838705A for 72 h. For the NIH-3T3/LISN proliferation assays, cells are seeded on collagen-coated 96-well tissue culture plates and allowed to adhere for 24 h. The medium is replaced with serum-free medium and the cells are treated with GSK1838705A for 2 h. Cells are incubated for 72 h after addition of IGF-I (30 ng/mL). Cell proliferation is quantified using the CellTiter-Glo Luminescent Cell Viability Assay. IC50s are determined from cytotoxicity curves using a four-parameter curve fit software package[1].
Animal Administration	Mice: Exponentially growing cells are implanted s.c. into the right flank of 8- to 12-wk-old female nu/nu CD-1 or SCID mice. Mice are dosed p.o. with the formulating vehicle or GSK1838705A. Mice are weighed and tumors measured by calipers twice weekly. Tumor volumes are calculated[1]
Kinase Assay	Baculovirus-expressed glutathione S-transferase-tagged proteins encoding the intracellular domain of IGF-IR (amino acids 957–1367) and IR (amino acids 979–1382) are used for determinations of IC50s by a homogeneous time-resolved fluorescence assay. A filter binding assay is used for appKi determinations using activated IGF-IR and IR kinases. Expanded kinase-selectivity profiling of GSK1838705A is carried out by screening the compound in the KinaseProfiler panel[1].
References	[1]. Sabbatini P, et al. GSK1838705A inhibits the insulin-like growth factor-1 receptor and anaplastic lymphoma kinase and shows antitumor activity in experimental models of human cancers. Mol Cancer Ther. 2009 Oct;8(10):2811-20.

源叶生物