产品名称：SU11274
产品别名：SU11274

生物活性：

Description	SU11274 is a selective Met inhibitor with IC_{50} of 10 nM, but has no effects on PGDFRβ, EGFR or Tie2.
IC_{50} & Target	IC50: 10 nM (Met)[1]
In Vitro	SU11274 exhibits greater than 50-fold selectivity for Met versus Flk and more than 500 times selectivity versus other tyrosine kinases such as FGFR-1, c-src, PDGFbR, and EGFR. SU11274 inhibits the phosphorylation of key regulators of the PI3K pathway, including AKT, FKHR, or GSK3β. SU11274 treatment inhibits the growth of TPR-MET-transformed BaF3 cells in a dose-dependent manner with IC50 of < 3 μM in the absence of interleukin 3, without growth inhibition of BaF3 cells transformed by other oncogenic tyrosine kinases, including BCR-ABL, TEL-JAK2, TEL-ABL, and TEL-PDGFβR. In addition to cell growth, SU11274 treatment significantly inhibits the migration of BaF3. TPR-MET cells by 44.8% and 80% at 1 μM and 5 μM, respectively. SU11274 inhibits HGF-dependent phosphorylation of Met as well as HGF-dependent cell proliferation and motility with an IC50 of 1-1.5 μM. In H69 and H345 cells which have functional Met receptor, SU11274 inhibits the HGF-induced cell growth with IC50 of 3.4 μM and 6.5 μM, respectively. SU11274 induces G1 cell cycle arrest with cells in G1 phase increased from 42.4% to 70.6% at 5 μM, and induces caspase-dependent apoptosis by 24% at 1 μM[2]. SU11274 inhibits cell viability in c-Met-expressing non-small cell lung cancer (NSCLC) cells with IC50 values of 0.8-4.4 μM, and abrogates hepatocyte growth factor-induced phosphorylation of c-Met and its downstream signaling[3].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (176.03 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7603 mL	8.8014 mL	17.6028 mL
5 mM	0.3521 mL	1.7603 mL	3.5206 mL
10 mM	0.1760 mL	0.8801 mL	1.7603 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 (4.40 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.40 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。

References	[1]. Wang X, et al. Potent and selective inhibitors of the Met [hepatocyte growth factor/scatter factor (HGF/SF) receptor] tyrosine kinase block HGF/SF-induced tumor cell growth and invasion. Mol Cancer Ther, 2003, 2(11):1085-1092. [2]. Sattler M, et al. A novel small molecule met inhibitor induces apoptosis in cells transformed by the oncogenic TPR-MET tyrosine kinase. Cancer Res, 2003, 63(17), 5462-5469. [3]. Ma PC, et al. Functional expression and mutations of c-Met and its therapeutic inhibition with SU11274 and small interfering RNA in non-small cell lung cancer. Cancer Res, 2005, 65(4), 1479-1488.

实验参考：

Cell Assay	Cells are exposed to various concentrations of SU11274 in the presence or absence of HGF for 24, 48, and 72 hours. The number of viable cells is determined using the MTT assay or trypan blue exclusion. Cell Cycle and apoptosis are measured by fluorescence-activated cell sorter analysis via propidium iodide staining and Annexin V-positive staining, respectively. [2]
Kinase Assay	A chimeric protein is constructed containing the cytoplasmic domain of human c-Met fused to Glutathione S-transferase (GST) and expressed in SF9 cells. The c-Met kinase GST-fusion protein is used for an ELISA-based Met biochemical assay using the random copolymer poly(Glu:Tyr) (4:1) immobilized on microtiter plates as a substrate. IC_{50} value is determined with various concentrations of SU11274 in a buffer containing 5 μM ATP and 10 mM $MnCl_2$, 50 mM HEPES (pH 7.5), 25 mM NaCl, 0.01% BSA, and 0.1 mM Na orthovanadate. The kinase reaction is performed for 5 minutes at room temperature. The extent of substrate phosphorylation is measured using horseradish peroxidase-conjugated anti-pTyr antibodies. [1]
References	[1]. Wang X, et al. Potent and selective inhibitors of the Met [hepatocyte growth factor/scatter factor (HGF/SF) receptor] tyrosine kinase block HGF/SF-induced tumor cell growth and invasion. Mol Cancer Ther, 2003, 2(11):1085-1092. [2]. Sattler M, et al. A novel small molecule met inhibitor induces apoptosis in cells transformed by the oncogenic TPR-MET tyrosine kinase. Cancer Res, 2003, 63(17), 5462-5469. [3]. Ma PC, et al. Functional expression and mutations of c-Met and its therapeutic inhibition with SU11274 and small interfering RNA in non-small cell lung cancer. Cancer Res, 2005, 65(4), 1479-1488.