产品名称：SR3335
产品别名：SR3335

生物活性：

Description	SR3335 is a selective RORα inverse agonist that directly binds to RORα with a K_i of 220 nM.
IC_{50} & Target	Ki: 220 nM (RORα)[1]
In Vitro	SR3335 is a selective RORα partial inverse agonist. In a biochemical radioligand binding assay using [^{3}H]25-hydroxycholesterol as a label it is clear that unlabeled SR3335 dose-dependently competes for binding to the RORα LBD. The Ki is calculated as 220 nM using the Cheng-Prusoff equation. In a cell-based chimeric receptor Gal4 DNA-binding domain-NR ligand binding domain cotransfection assay, SR3335 significantly inhibits the constitutive transactivation activity of RORα (IC50=480 nM)(partial inverse agonist activity), but has no effect on the activity of LXRα and RORγ[1].
In Vivo	Pharmacokinetic studies indicate that SR3335 displays reasonable exposure following an i.p. injection into mice. The ability of SR3335 is assessed to suppress gluconeogenesis using a diet induced obesity (DIO) mouse model where the mice where treated with 15 mg/kg b.i.d., i.p. for 6-days followed by a pyruvate tolerance test. SR3335 treated mice displays lower plasma glucose levels following the pyruvate challenge consistent with suppression of gluconeogenesis. Importantly, mice treated with SR3335 displayed no difference in body weight or food intake after 7-days of treatment with SR3335[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (246.71 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4671 mL	12.3353 mL	24.6706 mL
5 mM	0.4934 mL	2.4671 mL	4.9341 mL
10 mM	0.2467 mL	1.2335 mL	2.4671 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 (6.17 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.17 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 (6.17 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.17 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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.17 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.17 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。 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]. Kumar N, et al. Identification of SR3335 (ML-176): a synthetic RORα selective inverse agonist. ACS Chem Biol. 2011 Mar 18;6(3):218-22.

实验参考：

Cell Assay	HEK293 cells are maintained in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum at 37°C under 5% CO_2. HepG2 cells are maintained and routinely propagated in minimum essential medium supplemented with 10% fetal bovine serum at 37°C under 5% CO_2. 24 h prior to transfection, cells are plated in 96-well plates at a density of 15×10^3 cells/well. Transfections are performed using LipofectamineTM 2000. 16 h post-transfection, the cells are treated with vehicle or SR3335. 24 h post-treatment, the luciferase activity is measured using the Dual-GloTM luciferase assay system. The values indicated represent the means±S.E. from four independently transfected wells. The experiments are repeated at least three times[1].
Animal Administration	Mice[1] 30 week old Diet induced obese (DIO) C57BL/6 male mice are purchased from Jackson Laboratories that are maintained on a 65% Kcal high-fat diet from weaning. DIO mice are treated twice per day (07:00h and 18:00h) with 15 mg/kg SR3335 or vehicle for 6 days i.p. Pyruvate tolerance test is conducted on day 6 of the treatment. Food is removed from mice in the morning after SR3335 injection, fasted for 6 hours and the pyruvate tolerance test is conducted at 13:00h. Time 0 blood glucose is measured taken from the tail nip and the pyruvate challenge is initiated by injection of 2g/kg of pyruvate i.p. followed by measuring blood glucose at 15, 30 and 60 min following the injection. Blood glucose is measured by one touch ultra glucose-meter.
References	[1]. Kumar N, et al. Identification of SR3335 (ML-176): a synthetic RORα selective inverse agonist. ACS Chem Biol. 2011 Mar 18;6(3):218-22.