产品名称：**2-氰基-3-[5-(2,5-二氯苯基)-2-呋喃基]-N-5-喹啉基-2-丙烯酰胺**
产品别名：**AGK2**

生物活性：

Description	AGK2 is a selective SIRT2 inhibitor with IC50 of 3.5 μM. AGK2 can also inhibit SIRT1 and SIRT3 with IC50 of 30 and 91 μM, respectively.		
IC_{50} & Target	SIRT2	SIRT1	SIRT3
	3.5 μM (IC_{50})	30 μM (IC_{50})	91 μM (IC_{50})
In Vitro	AGK2 significantly inhibits cell proliferation in a dose-dependent manner. AGK2 also significantly inhibits cell growth in a dose-dependent manner without inducing cytotoxicity at low doses. Twelve days after AGK2 (5 μM) treatment, cells show a significantly reducing colony forming ability in soft agar to 46% of the control cells. Western blot analysis shows that the levels of CDK4 or CDK6 and cyclin D1 are decreased after AGK2 treatment in a dose-dependent manner. In addition, AGK2 inhibits the expression of p53 protein[2]. Treatment of microglial BV2 cells with 10 μM AGK2 leads to a significant increase in PAR signals. Treatment of microglial BV2 cells with 10 μM AGK2 also leads to a significant decrease in the intracellular ATP and significant increases in both late-stage apoptosis and necrosis of the cells[3].		
In Vivo	AGK2 significantly reduces mortality and decreases levels of cytokines in blood (TNF-α: 298.3±24.6 vs 26.8±2.8 pg/mL, p=0.0034; IL-6: 633.4±82.8 vs 232.6±133.0 pg/mL, p=0.0344) and peritoneal fluid (IL-6: 704.8±67.7 vs 391.4±98.5 pg/mL, p=0.033) compare to vehicle control. AGK2 also suppresses the TNF-α and IL-6 production in the culturing splenocytes (TNF-α: 68.1±6.4 vs 23.9±2.8 pg/mL, p=0.0009; IL-6: 73.1±4.2 vs 49.6±3.0 pg/mL; p=0.0051)[4].		

Solvent&Solubility

In Vitro:

DMSO : 6 mg/mL (**13.82 mM;** Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3027 mL	11.5136 mL	23.0271 mL
	5 mM	0.4605 mL	2.3027 mL	4.6054 mL
	10 mM	0.2303 mL	1.1514 mL	2.3027 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: ≥ 0.5 mg/mL (1.15 mM); Clear solution

此方案可获得 ≥ 0.5 mg/mL (1.15 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 5.0 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: ≥ 0.5 mg/mL (1.15 mM); Clear solution 此方案可获得 ≥ 0.5 mg/mL (1.15 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 5.0 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: ≥ 0.5 mg/mL (1.15 mM); Clear solution 此方案可获得 ≥ 0.5 mg/mL (1.15 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 5.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Tatum PR, et al. Identification of novel SIRT2-selective inhibitors using a click chemistry approach. Bioorg Med Chem Lett. 2014 Apr 15;24(8):1871-4. [2]. Kim HW, et al. Sirtuin inhibitors, EX527 and AGK2, suppress cell migration by inhibiting HSF1 protein stability. Oncol Rep. 2016 Jan;35(1):235-42. [3]. Li Y, et al. Poly(ADP-ribose) polymerase mediates both cell death and ATP decreases in SIRT2 inhibitor AGK2-treated microglial BV2 cells. Neurosci Lett. 2013 Jun 7;544:36-40. [4]. Zhao T, et al. Selective Inhibition of SIRT2 Improves Outcomes in a Lethal Septic Model. Curr Mol Med. 2015;15(7):634-41.

实验参考：

Cell Assay	Cells are exposed to different concentrations of AGK2 in 1 mL of 0.3% basal medium agar containing 10% FBS. The cultures are maintained at 37°C in a 5% CO2 incubator for 10-15 days, and the cell colonies are scored using an inverted microscope[2].
Animal Administration	Mice are intraperitoneally given either AGK2 (82 mg/kg) in dimethyl sulfoxide (DMSO) or DMSO alone, and 2 h later subjects to CLP. Survival is monitored for 240 hours. AGK2-treating mice are grouped into (i) DMSO vehicle, and (ii) AGK2, with sham mice (operating but without any treatment) serving as controls. Peritoneal fluid and peripheral blood are examined at 24 and 48 hours for cytokine production[4].
References	[1]. Tatum PR, et al. Identification of novel SIRT2-selective inhibitors using a click chemistry approach. Bioorg Med Chem Lett. 2014 Apr 15;24(8):1871-4. [2]. Kim HW, et al. Sirtuin inhibitors, EX527 and AGK2, suppress cell migration by inhibiting HSF1 protein stability. Oncol Rep. 2016 Jan;35(1):235-42. [3]. Li Y, et al. Poly(ADP-ribose) polymerase mediates both cell death and ATP decreases in SIRT2 inhibitor AGK2-treated microglial BV2 cells. Neurosci Lett. 2013 Jun 7;544:36-40. [4]. Zhao T, et al. Selective Inhibition of SIRT2 Improves Outcomes in a Lethal Septic Model. Curr Mol Med. 2015;15(7):634-41.