产品名称：Akti-1/2
产品别名：AKT inhibitor VIII

生物活性：

Description

AKT inhibitor VIII (AKTi-1/2) is a cell-permeable quinoxaline compound that has been shown to potently, selectively, allosterically, and reversibly inhibit Akt1, Akt2, and Akt3 activity with IC_{50}s of 58 nM, 210 nM, and 2119 nM, respectively.

IC_{50} & Target

Akt1	Akt2	Akt3
58 nM (IC_{50})	210 nM (IC_{50})	2119 nM (IC_{50})

In Vitro

When LnCaP cells are pretreated with AKT inhibitor VIII and then incubated with TRAIL, a dramatic increase in caspase-3 activity (6-10-fold relative to control or TRAIL alone) is observed. This sensitization of tumor cell lines with AKT inhibitor VIII is not limited to LnCaP cells as similar apoptosis induction is observed in HT29, MCF7, and A2780 cells, among others, with chemosensitizers such as camptothecin, herceptin, and doxorubicin[1]. The furanodiene-induced decrease of p-Akt and Akt expressions is enhanced by the Akt inhibitor VIII pretreatment. Furthermore, the furanodiene-induced PARP cleavage is enhanced by Akt inhibitor VIII pretreatment. The Akt inhibitor VIII shows no effect on cleaved PARP expression but decreases the p-Akt and Akt expressions[2]. AKT inhibitor VIII decreases cell viability and increases phosphatidylserine (PS) translocation to the outer leaflet of the plasma membrane, DNA fragmentation, Caspase-9 cleavage, Caspase-3 activation and PARP proteolysis in hESC lines WA01 (H1) and WA09 (H9) and in a hiPSCs cell line generated in our laboratory (FN2.1)[3].

In Vivo

Mice are dosed with AKT inhibitor VIII (50 mpk, 3 doses, ip, every 90 min) achieving plasma concentrations of 1.5-2.0 μM, and then the animals are tail vein injected with IGF to stimulate Akt phosphorylation. By IP Western, both basal and IGF stimulated Akt1 and Akt2 phosphorylation are inhibited in mouse lung, with no effect on Akt3 phosphorylation[1].

Solvent&Solubility

In Vitro:

DMSO : 20 mg/mL (36.26 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8128 mL	9.0639 mL	18.1278 mL
5 mM	0.3626 mL	1.8128 mL	3.6256 mL
10 mM	0.1813 mL	0.9064 mL	1.8128 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 mg/mL (3.63 mM); Clear solution

	此方案可获得 ≥ 2 mg/mL (3.63 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.0 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% corn oil Solubility: ≥ 2 mg/mL (3.63 mM); Clear solution 此方案可获得 ≥ 2 mg/mL (3.63 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 20.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Lindsley, et al. Allosteric Akt (PKB) inhibitors: discovery and SAR of isozyme selective inhibitors. Bioorg. Med. Chem. Lett. (2005), 15(3), 761-764. [2]. Zhong Z, et al. Furanodiene, a Natural Product, Inhibits Breast Cancer Growth Both in vitro and in vivo. Cell Physiol Biochem. 2012;30(3):778-90. Epub 2012 Aug 2. [3]. Leonardo Romorini, et al. AKT/GSK3β signaling pathway is critically involved in human pluripotent stem cell survival. Sci Rep. 2016; 6: 35660

实验参考：

Cell Assay	PSC are plated onto Matrigel coated 96-well plates at densities between 1×10^3-3×10^5 cells per well and grown until confluence. 24 hours post-treatments, 50 μg/well of activated 2,3-bis (2-methoxy-4-nitro-5-sulfophenyl)-5 [(phenylamino) carbonyl]-2 H-tetrazolium hydroxide(XTT) in PBS containing 0.3 μg/well of N-methyl dibenzopyrazine methyl sulfate (PMS) are added (final volume 100 μL) and incubated for 1-2 hours at 37°C. Cellular metabolic activity is determined spectrophotometrically at 450 nm. [3]
References	[1]. Lindsley, et al. Allosteric Akt (PKB) inhibitors: discovery and SAR of isozyme selective inhibitors. Bioorg. Med. Chem. Lett. (2005), 15(3), 761-764. [2]. Zhong Z, et al. Furanodiene, a Natural Product, Inhibits Breast Cancer Growth Both in vitro and in vivo. Cell Physiol Biochem. 2012;30(3):778-90. Epub 2012 Aug 2. [3]. Leonardo Romorini, et al. AKT/GSK3β signaling pathway is critically involved in human pluripotent stem cell survival. Sci Rep. 2016; 6: 35660