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产品名称：KHS101 hydrochloride
CAS 号：1784282-12-7
产品货号：T23329

生物活性：

Description	KHS101 is a blood-brain barrier-penetrant anticancer agent that primarily functions by inhibiting HSPD1 (IC50 = 14.4 μM) and TACC3 across different cellular backgrounds. KHS101 promotes the aggregation of HSPD1 with client proteins, destabilizes TACC3, and reduces the levels of TACC3, Aurora A and PLK1. KHS101 induces autophagy, apoptosis, cell cycle exit and neuronal differentiation; it suppresses cancer cell growth, motility, EMT and stemness; it also impairs mitochondrial bioenergetics and glycolysis in glioblastoma cells. KHS101 can be used in research related to glioblastoma multiforme and breast cancer[1][2][3].
IC50 & Target	TACC3[1]
In Vitro	KHS101 (0-20 μM; 5 days) 可在全部 6 株患者来源 GBM 细胞系以及 U251/U87 细胞中诱导剂量依赖性细胞毒性，作用 5 天后的 IC50 值分别为：GBM1 细胞 2.23 μM、GBM4 细胞 0.97 μM、GBM11 细胞 5.05 μM、GBM13 细胞 3.28 μM、GBM14 细胞 1.98 μM、GBM20 细胞 1.87 μM[1]。 KHS101 (1-7.5 μM; 12 h) 处理 12 小时后，可在患者来源的人胶质母细胞瘤 (GBM) 细胞系 (GBM1、GBM4、GBM11、GBM13、GBM14、GBM20) 中选择性诱导浓度依赖性自噬，而在非癌性 NP1 神经祖细胞中无可见作用[1]。 KHS101 (7.5 μM; 48 h) 选择性地在患者来源的人 GBM 细胞系 (GBM1、GBM11、GBM20) 中诱导时间依赖性凋亡，而对非癌变的 NP1 神经前体细胞的影响极小，且该凋亡不依赖于晚期自噬[1]。 KHS101 (7.5 μM) 可选择性破坏患者来源的人 GBM 细胞系的代谢表型，诱导代谢活性发生显著的缺氧转变，而在以 7.5 μM 进行急性处理后，对非癌细胞系 (NP1, NP2, NHAs) 仅造成极微小的糖酵解变化[1]。 KHS101 (7.5 μM; 4-24 h) 选择性地损伤患者来源的人 GBM1 细胞的有氧糖酵解与三羧酸 (TCA) 循环活性，减少葡萄糖来源的碳向关键代谢中间产物的掺入，并在 24 小时后使细胞总 ATP 水平降低 ≥ 50%；而该药物在非癌细胞 NP1 神经祖细胞中无此类作用[1]。 KHS101 (7.5 μM; 1 h) 选择性诱导患者来源的人 GBM1 细胞中 HSPD1 和关键代谢酶发生聚集，而在非癌性 NP1 神经祖细胞中仅观察到极少量聚集[1]。 KHS101 (10-100 μM; 24 h) 以与 TACC3 表达相关的方式抑制 MDA-MB-231、MDA-MB-468 和 MCF7 乳腺癌细胞的增殖，其中 20 μM 可选择性抑制乳腺癌细胞生长，且不影响非致瘤性乳腺上皮细胞 MCF10A[2]。 KHS101 (5-20 μM; 24 h) 在 20 μM 浓度下可降低 MDA-MB-231 和 SKBR3 乳腺癌细胞中的 TACC3 蛋白水平，但处理 24 h 后不会改变 MDA-MB-468 和 BT549 乳腺癌细胞中的 TACC3 水平[2]。 KHS101 (5-20 μM; 7 days) 可抑制 MDA-MB-468 和 SKBR3 乳腺癌细胞的乳腺球形成，并降低其乳腺球形成效率[2]。 KHS101 (5-20 μM; 24 h) 可降低 MDA-MB-231 乳腺癌细胞中 Oct4、Sox2 和 Nanog 干细胞标志物的 mRNA 表达水平[2]。 KHS101 (20 μM; 24 h) 可降低 MDA-MB-231 乳腺癌细胞中间质标志物 (N-cadherin、Vimentin) 以及干性标志物 CD44 的蛋白表达水平[2]。 KHS101 (20 μM; 24 h) 可降低 MDA-MB-231 乳腺癌细胞中 Snail、Slug 和 Twist 这些 EMT 转录因子的 mRNA 表达水平[2]。 KHS101 (20-60 μM; 16 h) 抑制 MDA-MB-231 和 MDA-MB-468 乳腺癌细胞的迁移[2]。 KHS101 (20 μM; 24 h) 可在 20 μM 处理 24 h 后抑制 MDA-MB-231 和 MDA-MB-468 乳腺癌细胞

的侵袭[2]。

KHS101 (20 μM; 24-72 h) 可在 20 μM 处理 24、48 和 72 h 后增加 MDA-MB-231 和 MDA-MB-468 乳腺癌细胞中的亚 G1 期凋亡细胞群，且对整体细胞周期分布具有细胞类型特异性作用[2]。

KHS101 (20 μM; 24-72 h) 可在 20 μM 浓度下处理 24、48 和 72 h 后，诱导 MDA-MB-231 和 MDA-MB-468 乳腺癌细胞发生时间依赖性凋亡，且对 MDA-MB-468 细胞的作用更强[2]。

KHS101 (20 μM) 可改变 MDA-MB-468 乳腺癌细胞的全局蛋白质组谱，参与催化活性、结合作用、代谢过程、细胞过程以及多种癌症相关信号通路的蛋白质发生显著变化[2]。

KHS101 (20 μM; 24 h) 可降低 MDA-MB-468、SKBR3 和 MCF7 乳腺癌细胞中 Aurora A 和 PLK1 有丝分裂激酶的蛋白表达[2]。

KHS101 (0.6-5 μM; 1-12 d) 可剂量依赖性地诱导贴壁培养的成年大鼠海马神经前体细胞 (NPCs) 发生神经元分化，其 EC50 约为 1 μM；在 5 μM 浓度下作用 12 天可生成功能性成熟神经元[3]。

KHS101 (1.5-5 μM; 4 d) 可诱导成年大鼠海马体和 SVZ 神经前体细胞 (NPCs) 来源的次级神经球发生神经元分化，在 1.5-5 μM 作用 4 天的条件下，有 40%-60% 的细胞成为 TuJ1 阳性神经元[3]。

KHS101 (0.6-5 μM; 4 d) 可剂量依赖性地抑制 BMP4 诱导的成年大鼠海马神经前体细胞 (NPCs) 向星形胶质细胞分化，并促进其向神经元分化[3]。

KHS101 (0.6-5 μM; 24 h-72 h) 呈剂量依赖性上调 Cdkn1 的表达，并抑制成年大鼠海马神经前体细胞 (NPCs) 的增殖及有丝分裂活性；在 5 μM 作用 72 小时后，Ki67 阳性细胞数量显著降低[3]。

KHS101 (5-15 μM; 12-24 h) 可在异位表达的 293T 细胞及成年大鼠海马神经前体细胞 (NPCs) 中增强 ARNT2 的核定位[3]。

Cell Autophagy Assay[1]

Cell Line:	Patient-derived human GBM cell lines (GBM1, GBM4, GBM11, GBM13, GBM14, GBM20), noncancerous adult brain neural progenitor (NP1) cell line
Concentration:	1 μM, 2.5 μM, 7.5 μM
Incubation Time:	12 h
Result:	Induced pronounced intracellular vacuole development and increased LC3B-positive autophagosomal compartments in GBM1 cells compared to NP1 cells and vehicle-treated controls after 12 hours of treatment with 7.5 μM. Increased LC3B staining in all tested GBM cell lines, while NP1 cells showed no such increase. Caused concentration-dependent increase in LC3B-positive cytoplasmic area in GBM1, GBM11, and GBM20 cells after 12 hours, with the highest response at 7.5 μM. Increased CYTO-ID positive cells in GBM1 cells in a concentration-dependent manner, with > 80% of cells positive after 12 hours of treatment with 7.5 μM.

Apoptosis Analysis[1]

Cell Line:	Patient-derived human GBM cell lines (GBM1, GBM4, GBM11, GBM13, GBM14, GBM20), noncancerous adult brain neural progenitor (NP1) cell line
Concentration:	7.5 μM
Incubation Time:	48 h

Result:	Induced a time-dependent increase in caspase 3/7 activation in GBM1 cells over 50 hours, with significantly higher activation than vehicle controls at the 48-hour time point. Caused marked increases in relative caspase 3/7 activation in GBM1, GBM11, and GBM20 cells compared to NP1 cells after 48 hours of treatment with 7.5 μM. Induced significant accumulation of annexin V-positive apoptotic cells in GBM1 cells 48 hours after treatment, and this apoptotic cell death was not prevented by chemical inhibition of late-stage autophagy.
Cell Proliferation Assay[1]	
Cell Line:	MCF10A non-tumorigenic human mammary epithelial cells, MDA-MB-231, MDA-MB-468, and MCF7 breast cancer cells
Concentration:	10, 20, 40, 60, 80, 100 μM
Incubation Time:	24 h
Result:	Showed breast cancer cells (MDA-MB-231, MDA-MB-468, MCF7) were more sensitive to KHS101 than MCF10A cells, with proliferation inhibition correlated to endogenous TACC3 expression. Revealed MDA-MB-231 and MDA-MB-468 (high TACC3) showed greater sensitivity than MCF7 (low/undetectable TACC3). Suppressed breast cancer cell growth at 20 μM but did not affect MCF10A cell growth.
Western Blot Analysis[2]	
Cell Line:	MDA-MB-231, MDA-MB-468, SKBR3, and BT549 breast cancer cells
Concentration:	5, 10, 20 μM
Incubation Time:	24 h
Result:	Significantly reduced TACC3 protein levels at 20 μM in MDA-MB-231 and SKBR3 cells. Showed no significant change in TACC3 levels in MDA-MB-468 and BT549 cells.
Real Time qPCR[2]	
Cell Line:	MDA-MB-231 breast cancer cells
Concentration:	5, 10, 20 μM
Incubation Time:	24 h
Result:	Reduced mRNA expression of stem cell markers Oct4, Sox2, and Nanog in a concentration-dependent manner. Showed all tested concentrations significantly decreased marker expression relative to control.
Western Blot Analysis[2]	
Cell Line:	MDA-MB-468 and MDA-MB-231 breast cancer cells
Concentration:	20 μM

Incubation Time:	24 h
Result:	Reduced protein expression of mesenchymal markers N-cadherin and Vimentin, and stemness marker CD44 in MDA-MB-231 cells. Found MDA-MB-468 cells showed undetectable N-cadherin and CD44 levels, and reduced TACC3 expression.
Real Time qPCR[2]	
Cell Line:	MDA-MB-231 breast cancer cells
Concentration:	20 μM
Incubation Time:	24 h
Result:	Significantly reduced mRNA expression of EMT transcription factors Snail, Slug, and Twist relative to control.
Cell Migration Assay[2]	
Cell Line:	MDA-MB-231 and MDA-MB-468 breast cancer cells
Concentration:	20, 40, 60 μM
Incubation Time:	16 h
Result:	Reduced relative migration of MDA-MB-231 and MDA-MB-468 cells in a concentration-dependent manner. Showed all tested concentrations significantly decreased migration relative to control.
Cell Invasion Assay[2]	
Cell Line:	MDA-MB-231 and MDA-MB-468 breast cancer cells
Concentration:	20 μM
Incubation Time:	24 h
Result:	Significantly reduced relative invasion of MDA-MB-231 and MDA-MB-468 cells relative to control.
Cell Cycle Analysis[2]	
Cell Line:	MDA-MB-231 and MDA-MB-468 breast cancer cells
Concentration:	20 μM
Incubation Time:	24, 48, 72 h
Result:	Induced cell cycle distribution changes in a cell type-dependent manner. Significantly increased the sub-G1 population (a marker of apoptotic cells) in both MDA-MB-231 and MDA-MB-468 cells in a time-dependent manner.
Apoptosis Analysis[2]	
Cell Line:	MDA-MB-231 and MDA-MB-468 breast cancer cells
Concentration:	20 μM
Incubation Time:	24, 48, 72 h
Result:	Increased the percentage of apoptotic cells in both MDA-MB-231 and MDA-MB-468 cells in a time-dependent manner.

		Found MDA-MB-468 cells showed a greater magnitude of apoptotic induction than MDA-MB-231 cells.
	Western Blot Analysis[2]	
	Cell Line:	MDA-MB-468 and MDA-MB-231 breast cancer cells
	Concentration:	20 μM
	Incubation Time:	24 h
	Result:	Significantly reduced protein expression of mitotic kinases Aurora A and PLK1 in MDA-MB-468, SKBR3, and MCF7 cells, regardless of endogenous TACC3 expression levels.
In Vivo	KHS101 (6 mg/kg；皮下注射；每日 2 次；共 10 天) 可降低颅内患者来源异种移植小鼠模型中 GBM 肿瘤的增殖、侵袭与扩散，且无明显毒性[1]。 KHS101 (6 mg/kg；皮下注射；每日 2 次；每周交替给药 3 或 5 次，共 10 周) 可显著提高 GBMX1 颅内异种移植小鼠模型的存活率并缩小肿瘤体积，且无明显毒性[1]。 KHS101 (6 mg/kg；皮下注射；每日 2 次；连续 14 天) 可显著提高成年大鼠内源性神经祖细胞的神经元分化水平，将 BrdU/NeuN 双阳性细胞的比例从约 20%提升至约 40%，同时可降低神经祖细胞的增殖能力，且不会诱导细胞凋亡或产生明显毒性[3]。	
	Animal Model:	Immunodeficient mice[1]
	Dosage:	6 mg/kg
	Administration:	s.c.; twice daily; 10 days
	Result:	Increased NAD(P)H autofluorescence signal area in tumor tissue. Increased HK2-positive tumor area. Reduced tumor cell proliferation by ~2-fold (assessed by MKI67 staining). Increased acellular/pyknotic areas in tumor sections. Reduced frontal-to-caudal tumor expansion across sequential brain sections. Reduced vimentin-positive tumor cell invasion across the corpus callosum by ≥ 2-fold. Showed no discernible hepatic toxicity.
	Animal Model:	Immunodeficient mice[1]
	Dosage:	6 mg/kg
	Administration:	s.c.; twice daily; biweekly alternating 5 and 3 treatment days per week for 10 weeks
	Result:	Increased survival of GBMX1 tumor-bearing mice in both cohorts. Reduced tumor size by ~2-fold compared with vehicle-treated mice. Showed no treatment-related adverse effects leading to study removal.
	Animal Model:	Fisher 344 (adult, ~10 weeks old)[3]
	Dosage:	6 mg/kg
	Administration:	s.c.; twice daily; 14 days
	Result:	Increased the percentage of BrdU/NeuN double-positive cells from ~20% to ~40% in the hippocampal dentate gyrus.

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		Significantly reduced the number of Ki67-positive cells and BrdU-positive cells in the subgranular layer of the dentate gyrus. Showed no significant difference in the percentage of BrdU/GFAP double-positive cells. Left apoptosis (assessed via cleaved caspase 3 staining) in the dentate gyrus unchanged compared to vehicle controls. Caused no signs of lethargy, weight loss, or sickness in treated animals.

Solvent&Solubility

细胞实验:

DMSO 中的溶解度 ：160 mg/mL (425.62 mM; 超声助溶; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO)

H2O 中的溶解度 ：10 mg/mL (26.60 mM; 超声助溶 (<60° C))

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6601 mL	13.3007 mL	26.6014 mL
	5 mM	0.5320 mL	2.6601 mL	5.3203 mL
	10 mM	0.2660 mL	1.3301 mL	2.6601 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 (sealed storage, away from moisture)。-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。

动物实验:

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

方案 一

请依序添加每种溶剂： 10% DMSO → 40% PEG300 → 5% Tween-80 → 45% Saline

Solubility: ≥ 2.67 mg/mL (7.10 mM); 澄清溶液

此方案可获得 ≥ 2.67 mg/mL（饱和度未知）的澄清溶液。

以 1 mL 工作液为例，取 100 μL 26.7 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；再向上述体系中加入 50 μL Tween-80，混合均匀；然后再继续加入 450 μL 生理盐水 定容至 1 mL。

生理盐水的配制：将 0.9 g 氯化钠，溶解于 ddH₂ O 并定容至 100 mL，可以得到澄清透明的生理盐水溶液。

方案 二

请依序添加每种溶剂： 10% DMSO → 90% (20% SBE-β-CD in Saline)

Solubility: ≥ 2.67 mg/mL (7.10 mM); 澄清溶液

此方案可获得 ≥ 2.67 mg/mL（饱和度未知）的澄清溶液。

以 1 mL 工作液为例，取 100 μL 26.7 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。

2 g SBE-β-CD（磺丁基醚 β-环糊精）粉末定容于 10 mL 的生理盐水中，完全溶解至澄清透明。

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	方案 三 请依序添加每种溶剂： 10% DMSO → 90% Corn Oil Solubility: ≥ 2.67 mg/mL (7.10 mM); 澄清溶液 此方案可获得 ≥ 2.67 mg/mL（饱和度未知）的澄清溶液，此方案实验周期在半个月以上的动物实验酌情使用。 以 1 mL 工作液为例，取 100 μL 26.7 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
参考文献	[1]. Polson ES, et al. KHS101 disrupts energy metabolism in human glioblastoma cells and reduces tumor growth in mice. Sci Transl Med. 2018;10(454):eaar2718. [2]. Campo L, et al. Inhibition of TACC3 by a small molecule inhibitor in breast cancer. Biochem Biophys Res Commun. 2018;498(4):1085-1092. [3]. Wurdak H, et al. A small molecule accelerates neuronal differentiation in the adult rat. Proc Natl Acad Sci U S A. 2010;107(38):16542-16547.

完整储备液配制表：

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 (sealed storage, away from moisture)。-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。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
H2O / DMSO	**1 mM**	2.6601 mL	13.3007 mL	26.6014 mL	66.5035 mL
	5 mM	0.5320 mL	2.6601 mL	5.3203 mL	13.3007 mL
	10 mM	0.2660 mL	1.3301 mL	2.6601 mL	6.6504 mL
	15 mM	0.1773 mL	0.8867 mL	1.7734 mL	4.4336 mL
	20 mM	0.1330 mL	0.6650 mL	1.3301 mL	3.3252 mL
	25 mM	0.1064 mL	0.5320 mL	1.0641 mL	2.6601 mL
DMSO	**30 mM**	0.0887 mL	0.4434 mL	0.8867 mL	2.2168 mL
	40 mM	0.0665 mL	0.3325 mL	0.6650 mL	1.6626 mL
	50 mM	0.0532 mL	0.2660 mL	0.5320 mL	1.3301 mL
	60 mM	0.0443 mL	0.2217 mL	0.4434 mL	1.1084 mL
	80 mM	0.0333 mL	0.1663 mL	0.3325 mL	0.8313 mL
	100 mM	0.0266 mL	0.1330 mL	0.2660 mL	0.6650 mL

* 备注：如您选择水作为储备液，请稀释至工作液后，再用 0.22 μm 的滤膜过滤除菌后使用。