上海源叶生物科技有限公司
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产品名称：Fer and FerT inhibitor；E260

CAS 号：1241537-79-0

产品货号：S88321

生物活性：

Description	E260 是一种 Fer/FerT 激酶抑制剂。
IC50 & Target	Fer/FerT kinase[1]
In Vitro	E260 is a Fer and FerT inhibitor, which selectively evokes metabolic stress in cancer cells by imposing mitochondrial dysfunction and deformation, and onset of energy-consuming autophagy which decreases the cellular ATP level. To demonstrate that E260 directly targets Fer and FerT, an in vitro kinase assay is performed using a purified kinase domain (KD)-containing fragment of these enzymes. This analysis demonstrates the direct inhibitory effect of E260 on this domain as reflected by the significantly decreased auto-phosphorylation level of the Fer/FerT KD when incubated with ATP and increasing concentrations of E260. Moreover, computational analysis of E260 docking in the modeled whole Fer protein reveals that the highest scored binding mode of E260 to Fer falls in the ATP-binding pocket of the enzyme ’ s KD. To measure the dissociation constant (Kd) of E260 from Fer/FerT KD, a microscale thermophoresis (MST) test is performed using ascending concentrations of E260. This analysis corroborates the direct binding of E260 to Fer/FerT KD and determines a Kd of 0.85 μ M. To examine the effect of the E260 micellar formulation on Fer in malignant cells, the kinase is immunoprecipitated from untreated and from E260-treated SW620 CC cells. When applied to metastatic grade IV SW620 CC cells, which are serum starved for 16 h and treated with 3 mM H2O2 to activate Fer, E260 exhibits inhibitory effects on the Fer-kinase activity as is reflected by suppressed auto-phosphorylation activity of the enzyme. To characterize the effect of E260 on malignant cells, metastatic SW620 cells are treated with E260 followed by analysis of viability. Onset of death is observed in the E260-treated cells, with an EC50 value of 400 nM after 24 h of treatment and an EC50 of 300 nM after 48 h. E260 exhibits an EC50 of 3.2 μ M after 72 h treatment of non-metastatic PANC-1 cells, which are derived from a primary pancreatic ductal carcinoma. Moreover, the maximum death level of these cells after 72 h of treatment with E260 is about 70% following treatment with 4 μ M E260. In comparison, SU.86.86 which are metastatic ductal carcinoma cells, prove to be more susceptible to E260 with an EC50 of 1.1 μ M after 72 h of treatment and 100% death level imposed by 2 μ M E260[1]。
In Vivo	E260 suppresses xenografts progression in vivo. The pharmacokinetic (PK) profile of E260 is determined in mice. E260 exhibits a T1/2 of 175 min in the blood, and a volume of distribution of 4244 mL/kg suggesting an efficient distribution of the compound in the animal tissues. To evaluate the efficacy of E260 on tumor growth, SW620 cells are subcutaneously introduced into immuno-compromised "Nude" mice. Administration of E260 leads to a significant attenuation of tumor progression throughout the experiment, and to a 10-fold decrease in average tumor volume after 22 days of treatment. To further demonstrate the anti-cancer activity of E260 in vivo, mice bearing SW48 cells derived xenografts are treated with E260 and the tumor progression profiles are determined. Mice treated with E260 demonstrate a 5-6-fold attenuation in tumors progression when compared to the control treated group[1].
Solvent&Solubility	**细胞实验:** DMSO 中的溶解度 ：1 mg/mL (2.28 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)

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.2798 mL	11.3991 mL	22.7983 mL
	5 mM	---	---	---

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		10 mM	---	---	---

*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, 2 years; -20°C, 1 year。-80°C 储存时，请在 2 年内使用， -20°C 储存时，请在 1 年内使用。

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: ≥ 0.1 mg/mL (0.23 mM); 澄清溶液

此方案可获得 ≥ 0.1 mg/mL（饱和度未知）的澄清溶液。

以 1 mL 工作液为例，取 100 μL 1.0 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 ddH_2O 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: ≥ 0.1 mg/mL (0.23 mM); 澄清溶液

此方案可获得 ≥ 0.1 mg/mL（饱和度未知）的澄清溶液。

以 1 mL 工作液为例，取 100 μL 1.0 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。

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。

方案 三

请依序添加每种溶剂： 10% DMSO → 90% Corn Oil

Solubility: ≥ 0.1 mg/mL (0.23 mM); 澄清溶液

此方案可获得 ≥ 0.1 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 1.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。

以下溶解方案，请直接配制工作液。建议现用现配，在短期内尽快用完。 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： 0.5% CMC-Na/saline water

Solubility: 22 mg/mL (50.16 mM); 悬浊液; 超声助溶。

参考文献

[1]. Elkis Y, et al. A novel Fer/FerT targeting compound selectively evokes metabolic stress and necrotic death in malignant cells. Nat Commun. 2017 Oct 16;8(1):940.

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

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效。

储备液的保存方式和期限：-80°C, 2 years; -20°C, 1 year。-80°C 储存时，请在 2 年内使用， -20°C 储存时，请在 1 年内使用。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	2.2798 mL	11.3991 mL	22.7983 mL	56.9956 mL