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产品名称：D8-MMAE
产品别名：D8-Monomethyl auristatin E

生物活性：

Description	D8-MMAE (D8-Monomethyl auristatin E) is a deuterated labeled MMAE, a potent mitotic inhibitor and a tubulin inhibitor.
IC_{50} & Target	Auristatin
In Vitro	Antibody-drug conjugates (ADC) comprise targeting antibodies armed with potent small-molecule payloads. ADCs are generated to target different receptors on the anaplastic large cell lymphoma line L-82, but delivered the same cytotoxic payload (monomethyl auristatin E, MMAE), and the intracellular concentration of released MMAE correlated with in vitro ADC-mediated cytotoxicity independent of target expression or drug:antibody ratios. LC-MS is used to measure the concentration of MMAE in a parallel cohort of L-82 tumors with an identical treatment regimen. Although tumor volume is not different among treatment groups 3 days after dose, the intratumoral MMAE measurement reveals two patterns. First, intratumoral MMAE concentration increases proportionally to the ADC dose, which correspondes to stronger antitumor activity. Second, the intratumoral MMAE concentration obtained from treatment with both cOKT9-vcMMAE and cAC10-vcMMAE is similar at each dose, consistent with the observation that tumor responded similarly to these two ADCs[1].
In Vivo	Intratumoral MMAE concentrations consistently correlates with the extent of tumor growth inhibition in tumor xenograft models. IHC analysis reveals that nonbinding control-treated tumors consist of both $CD30^+$ and $CD30^-$cells, presumably because they do not kill either $CD30^+$ or $CD30^-$ Karpas 299 cells. Only $CD30^-$ cells are found in cAC10-vcMMAF-treated tumors, illustrating that cAC10-vcMMAF eliminates most $CD30^+$ cells. Interestingly, the two tumors that relapses from cAC10-vcMMAE treatment are also found to be $CD30^-$ by the end of study, indicating a small fraction of $CD30^-$ cells might have escaped from bystander killing in these two remaining tumors[1].
Solvent&Solubility	***In Vitro:*** **DMSO : 100 mg/mL** (**137.74 mM;** Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.3774 mL	6.8868 mL	13.7735 mL
5 mM	0.2755 mL	1.3774 mL	2.7547 mL
10 mM	0.1377 mL	0.6887 mL	1.3774 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；该产品在溶液状态不稳定，建议您现用现配，即刻使用。

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 (3.44 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.44 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 (3.44 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.44 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 (3.44 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (3.44 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]. Li F, et al. Intracellular Released Payload Influences Potency and Bystander-Killing Effects of Antibody-Drug Conjugates in Preclinical Models. Cancer Res. 2016 May 1;76(9):2710-9.
实验参考：	
Kinase Assay	Cell pellets are collected 24 hours after ADC treatment. Cell count, diameter, and circularity are determined on Vi-Cell Counter. MMAE extraction and quantification method is performed. Briefly, tumors or cell pellets are homogenized with methanol and acetonitrile containing internal standard (d^8-MMAE for MMAE detection and ^{13}C-MMAF for MMAF detection). The homogenates are centrifuged at 10,000 rpm to precipitate protein and protein-bound payloads. The supernatant is then subjected to solid phase extraction, and signals of MMAE and MMAF are detected by LC-MS[1].
References	[1]. Li F, et al. Intracellular Released Payload Influences Potency and Bystander-Killing Effects of Antibody-Drug Conjugates in Preclinical Models. Cancer Res. 2016 May 1;76(9):2710-9.