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产品名称: **17-(3-pyridyl)androsta-5,16-dien-3-one**
产品别名: **D4-abiraterone; Δ4-Abiraterone; CB-7627; Abiraterone D4A metabolite**

生物活性:				
Description	D4-abiraterone is a major metabolite of abiraterone. D4-abiraterone is an inhibitor of CYP17A1, 3b-hydroxysteroid dehydrogenase (3βHSD) and steroid-5a-reductase (SRD5A) and also an antagonist of androgen receptor.			
IC ₅₀ & Target	CYP17A1, 3βHSD, SRD5A, androgen receptor ^[1]			
In Vitro	D4-abiraterone (D4A) (10 mM) nearly completely blocks conversion from D4-androstenedione (AD) to 5α-androstenedione and other 5α-reduced androgens. The affinity of D4-abiraterone for mutant (expressed in LNCaP, half-maximum inhibitory concentration (IC ₅₀ =5.3 nM)) and wild type (expressed in LAPC4, IC ₅₀ =7.9 nM) androgen receptor (AR) is greater than that of abiraterone (Abi) (IC ₅₀ =418 and >500 nM, respectively). Compare with Abi, D4-abiraterone clearly better suppresses PSA, TMPRSS2 and FKBP5 expression in LNCAP, LAPC4 and C4-2 cell lines. D4-abiraterone also inhibits AR target gene expression in a dose-dependent manner ^[1] .			
In Vivo	D4-abiraterone (D4A) is tenfold more potent than abiraterone (Abi) in blocking conversion from dehydroepiandrosterone (DHEA) by 3β-hydroxysteroid dehydrogenase (3βHSD) to D4-androstenedione (AD) in LNCaP and VCaP xenografts. 0.1 μM D4-abiraterone is equivalent to 1 μM Abi for blocking AD accumulation at 48 h in both LNCaP and VCaP xenografts. Progression is significantly delayed in the D4-abiraterone group compare with the Abi acetate group (P=0.011). D4-abiraterone treatment increases progression-free survival compare with Abi acetate ^[1] .			
Solvent&Solubility	In Vitro: DMSO : 50 mg/mL (143.89 mM; Need ultrasonic)			
		Solvent Mass Concentration	1 mg	5 mg
	Preparing	1 mM	2.8778 mL	14.3889 mL
	Stock Solutions	5 mM	0.5756 mL	2.8778 mL
		10 mM	0.2878 mL	1.4389 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 (stored under nitrogen)。-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→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (7.19 mM); Clear solution				



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	<p>此方案可获得 ≥ 2.5 mg/mL (7.19 mM, 饱和度未知) 的澄清溶液。</p> <p>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 生理盐水溶液中, 混合均匀。</p> <p>2.请依序添加每种溶剂: 10% DMSO \rightarrow 90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (7.19 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (7.19 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。</p> <p>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。</p>
References	[1]. Li Z, et al. Conversion of abiraterone to D4A drives anti-tumour activity in prostate cancer. <i>Nature</i> . 2015 Jul 16;523(7560):347-51.
实验参考:	
Cell Assay	Cells are cultured in serum-free medium for 48 h and then treated with the indicated concentrations of D4-abiraterone (D4A) for 30 min. Cells are washed with 1 \times PBS four times and 0.9% NaCl solution twice before lysis with RIPA buffer. Intracellular radioactivity is measured with a liquid scintillation counter and normalized to the protein concentration as detected with a Multilabel counter ^[1] .
Animal Administration	Male NSG mice, 6 to 8 weeks of age are used in this study. Mice are surgically orchietomized and implanted with a 5 mg 90-day sustained-release dehydroepiandrosterone (DHEA) pellet to mimic castration-resistant prostate cancer (CRPC) in the context of human adrenal physiology. Two days later, 10 ⁷ VCaP or C4-2 cells are injected subcutaneously with matrigel. Once tumours reach 300mm ³ , mice are arbitrarily (but not strictly randomized) assigned to vehicle (n=9 or 10 mice for VCaP and C4-2 respectively), D4-abiraterone (D4A) (n=10 mice for both cell lines) treatment groups. D4-abiraterone (0.5 mmol per kg per day in 0.1 mL 5% benzyl alcohol and 95% safflower oil solution) is administered via 5 mL per kg intraperitoneal injection every day for up to 15 days. Control groups are administered 0.1 mL 5% benzyl alcohol and 95% safflower oil solution via intraperitoneal injection every day. Tumour volume is measured daily, and time to increase in tumour volume by 20% is determined. Mice are killed at treatment day 15 or when the tumour size is twofold greater than baseline ^[1] .
Kinase Assay	To test D4-abiraterone (D4A) as an inhibitor of 3 β HSD, enzyme assays are performed. Briefly, incubations are prepared with recombinant human 3 β HSD1 or 3 β HSD2 (in yeast microsomes, 45 or 2.5 μ g protein per incubation, respectively), D4-abiraterone (5 to 20 μ M) or ethanol vehicle in 0.5 mL of potassium phosphate buffer (pH 7.4). After a pre-incubation at 37°C for 1 to 3 min, NAD ⁺ (1 mM) is added, and the incubation is conducted at 37°C for 20 min. The reaction is stopped by addition of 1 mL ethyl acetate:isooctane (1:1), and the steroids are then extracted into the organic phase and dried. The steroids in the dried extracts are resolved by HPLC and quantitated by in-line scintillation counting ^[1] .
References	[1]. Li Z, et al. Conversion of abiraterone to D4A drives anti-tumour activity in prostate cancer. <i>Nature</i> . 2015 Jul 16;523(7560):347-51.