

产品名称: **RTA-408**  
 产品别名: **Omaveloxolone**

生物活性:					
Description	RTA-408 is an antioxidant inflammation modulator (AIM), which activates Nrf2 and suppresses nitric oxide (NO). RTA-408 attenuates osteoclastogenesis by inhibiting STING dependent NF-kb signaling.				
IC <sub>50</sub> & Target	Nrf2[1]				
In Vitro	To evaluate the anti-inflammatory activity of RTA-408, RAW 264.7 mouse macrophage cells are treated with RTA-408 for two hours and then IFNγ is added to stimulate NO production and release into the media. RTA-408 dose-dependently reduces NO concentrations in the media with an IC <sub>50</sub> value of 4.4±1.8 nM. The potency of RTA-408 in this assay is similar to that of Bardoxolone methyl, which has an IC <sub>50</sub> value of 1.9±0.8 nM. Nrf2 activation is required for AIM-mediated NO suppression. A decrease in nitric oxide synthase 2 (Nos2) protein levels is observed in bardoxolone methyl-treated RAW 264.7 cells, which is attenuated when Nrf2 mRNA levels are reduced by siRNA. To evaluate the anticancer activity of RTA-408, a panel of eight human cell lines derived from tumors of different origin are treated with RTA-408 and measured cell growth 72 hours later using the sulforhodamine B (SRB) assay. RTA-408 inhibits the growth of all tumor lines with an average GI <sub>50</sub> value of 260±74 nM. To determine whether RTA-408 induces apoptosis, the panel of tumor cells are treated with RTA-408 and the caspase substrate, DEVD-AFC, for 24 hours. RTA-408 dose-dependently increases DEVD-AFC cleavage, indicating that RTA-408 treatment triggers caspase activation in cancer cells. Caspase-3 and caspase-9 cleavage is also observed by western blot at the same concentrations of RTA-408 that increases DEVD-AFC cleavage[1].				
In Vivo	To determine whether RTA-408 is an effective mitigator of hematopoietic acute radiation syndrome after bone marrow-lethal doses of total-body irradiation (TBI), mice are administered 3 daily injections of 17.5 mg/kg RTA-408 beginning 24 h after TBI. Treatment with RTA-408 results in the 35 day survival of 100% of 7 Gy (LD <sub>40/35</sub> ) TBI mice (P<0.05) and 60% of 7.5 Gy (LD <sub>100/13</sub> ) TBI mice (P<0.0001)[2].				
Solvent&Solubility	<b>In Vitro:</b>				
	<b>DMSO : ≥ 100 mg/mL (180.27 mM)</b>				
	* "≥" means soluble, but saturation unknown.				
	<div><div>Solvent</div><div>Concentration</div><div>Mass</div></div>	1 mg	5 mg	10 mg	
	Preparing	1 mM	1.8027 mL	9.0137 mL	18.0274 mL
	Stock Solutions	5 mM	0.3605 mL	1.8027 mL	3.6055 mL
	10 mM	0.1803 mL	0.9014 mL	1.8027 mL	
<b>*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。</b>					
储备液的保存方式和期限：-80℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。					
<b>In Vivo:</b>					
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 <b>In Vitro</b> 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					

	<p>1.请依序添加每种溶剂： 10% DMSO →90% corn oil</p> <p>Solubility: <math>\geq 2.5</math> mg/mL (4.51 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.5</math> mg/mL (4.51 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 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中, 混合均匀。</p>
References	<p>[1]. <a href="#">Probst BL, et al. RTA 408, A Novel Synthetic Triterpenoid with Broad Anticancer and Anti-Inflammatory Activity. PLoS One. 2015 Apr 21;10(4):e0122942.</a></p> <p>[2]. <a href="#">Peng Han, et al. RTA-408 Protects Kidney from Ischemia-Reperfusion Injury in Mice via Activating Nrf2 and Downstream GSH Biosynthesis Gene. Oxid Med Cell Longev. 24 December 2017.</a></p> <p>[3]. <a href="#">Goldman DC, et al. The triterpenoid RTA 408 is a robust mitigator of hematopoietic acute radiation syndrome in mice. Radiat Res. 2015 Mar;183(3):338-44</a></p>
实验参考:	
Cell Assay	<p>MEFs, PANC-1, A549, A375, A549/NF-<math>\kappa</math>B-Luc and HeLa/NF-<math>\kappa</math>B-Luc cells are cultured in Gibco high glucose DMEM with 10% FBS. G-361 cells are cultured in McCoy's 5A medium with 10% FBS. All other cell lines are cultured in RPMI 1640 medium with 10% FBS. For growth inhibition assays, cells are plated in duplicate 96-well culture dishes at <math>3 \times 10^3</math> cells per well. The following day, one plate is treated with RTA-408 (200, 400, 600, 800 and 1000 nM) and the other is immediately processed for the sulforhodamine B (SRB) assay (time 0). Cells in the RTA-408-treated plate are processed for the SRB assay 72 hours after the start of treatment. Percentage of growth relative to vehicle-treated cells is calculated. Dose-response curves are plotted in GraphPad Prism and <math>GI_{50}</math> values are calculated. For cell counting experiments, MEFs are plated in 6-well culture dishes at <math>5 \times 10^4</math> cells per well and treated with RTA-408 the following day. Following treatment, cells are counted using a Vi-CELL XR cell analyzer. For clonogenic assays, wild-type (<math>1 \times 10^3</math> cells per well) and <i>Keap1</i><sup>-/-</sup> (<math>0.5 \times 10^3</math> cells per well) MEFs are seeded in 6-well dishes. Six hours later, MEFs are treated with RTA-408. After seven days, colonies are fixed with a 1:7 solution of acetic acid:MeOH and stained with 0.5% crystal violet in MeOH. Colonies consisting of <math>\geq 50</math> cells are counted[1].</p>
Animal Administration	<p>Mice[2]</p> <p>For radiation survival experiments, wild-type C57Bl/6 CD45.2 mice (6-8 weeks old) are used. Congenic wild-type C57Bl/6 CD45.1 and C57Bl/6 CD45.1/CD45.2 hybrid host mice are used as recipients in transplantation experiments. RTA-408 stock solutions for vehicle control (DMSO) are prepared within 1 h before injection. RTA-408 (17.5 mg/kg) or DMSO is administered intraperitoneally at 24, 48 and 72 h after irradiation. Whole-body irradiation (7-8 Gy) is performed using a 250-kVp X-ray machine with 50 cm source-to-skin distance and a 2 mm copper filter. The dose rate is approximately 1.4 Gy/min.</p>
References	<p>[1]. <a href="#">Probst BL, et al. RTA 408, A Novel Synthetic Triterpenoid with Broad Anticancer and Anti-Inflammatory Activity. PLoS One. 2015 Apr 21;10(4):e0122942.</a></p> <p>[2]. <a href="#">Peng Han, et al. RTA-408 Protects Kidney from Ischemia-Reperfusion Injury in Mice via Activating Nrf2 and Downstream GSH Biosynthesis Gene. Oxid Med Cell Longev. 24 December 2017.</a></p> <p>[3]. <a href="#">Goldman DC, et al. The triterpenoid RTA 408 is a robust mitigator of hematopoietic acute radiation syndrome in mice. Radiat Res. 2015 Mar;183(3):338-44</a></p>