产品名称：**PYR-41**
产品别名：**PYR-41**

生物活性：

Description	PYR-41 is a selective and cell permeable inhibitor of ubiquitin-activating enzyme E1 with an IC_{50} of < 10 μM, with little activity at E2 and E3.
IC_{50} & Target	IC50: < 10 μM (E1)
In Vitro	PYR-41 increases total sumoylation in cells in addition to blocking ubiquitylation. PYR-41 attenuates cytokine-mediated nuclear factor-κB activation. PYR-41 also prevents the downstream ubiquitylation and proteasomal degradation of IκBα. Furthermore, PYR-41 inhibits degradation of p53 and activates the transcriptional activity of this tumor suppressor[1]. PYR-41 (50 μM) promotes accumulation of ubiquitinated proteins. PYR-41 causes a concentration-dependent (10-50 μM) decline in DUB activity in Z138 cells after 4 h. PYR-41 potently inhibits USP5 DUB activity, even at the lowest concentration (10 μM). PYR-41 potently (10-50 μM) inhibits the activity of various DUBs, determined to represent USP9x, USP5, USP14, UCH37 and UCH-L3. Co-treatment of Z138 cells with DTT and PYR-41 completely abolishes the accumulation of ubiquitinated proteins[2].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 46 mg/mL (123.89 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6932 mL	13.4662 mL	26.9324 mL
	5 mM	0.5386 mL	2.6932 mL	5.3865 mL
	10 mM	0.2693 mL	1.3466 mL	2.6932 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。-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→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (6.73 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.73 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。

References	[1]. Yang Y, et al. Inhibitors of ubiquitin-activating enzyme (E1), a new class of potential cancer therapeutics. Cancer Res. 2007 Oct 1;67(19):9472-81. [2]. Kapuria V, et al. Protein cross-linking as a novel mechanism of action of a ubiquitin-activating enzyme

	inhibitor with anti-tumor activity. Biochem Pharmacol. 2011 Aug 15;82(4):341-9.
实验参考：	
Kinase Assay	Rabbit or mouse E1 (apper 250 ng) is incubated with ^{32}P-ubiquitin in 1× reaction buffer [50 mM Tris (pH 7.4), 0.2 mM ATP, 0.5 mM $MgCl_2$] at room temperature for 15 min. In some experiments, the His-tagged mouse E1 is bound to TALON cobalt affinity resin before carrying out incubations and reactions. Mouse E1 and ^{32}P-ubiquitin are added to the beads in 1× reaction buffer and incubated as for E1 reactions. Samples are heated in nonreducing SDS-PAGE sample buffer and resolved by SDS-PAGE. Thioesters with ubiquitin are visualized by Storm PhosphoImager. [1]
References	[1]. Yang Y, et al. Inhibitors of ubiquitin-activating enzyme (E1), a new class of potential cancer therapeutics. Cancer Res. 2007 Oct 1;67(19):9472-81. [2]. Kapuria V, et al. Protein cross-linking as a novel mechanism of action of a ubiquitin-activating enzyme inhibitor with anti-tumor activity. Biochem Pharmacol. 2011 Aug 15;82(4):341-9.