

产品名称：**Ruxolitinib(INCB018424)**  
产品别名：**Ruxolitinib；索利替尼**

生物活性：				
Description	Ruxolitinib (INCB18424) is a potent and selective JAK1/2 inhibitor with IC <sub>50</sub> s of 3.3 nM and 2.8 nM in cell-free assays, and has 130-fold selectivity for JAK1/2 over JAK3.			
IC <sub>50</sub> & Target	JAK2	JAK1	Tyk2	JAK3
	2.8 nM (IC <sub>50</sub> )	3.3 nM (IC <sub>50</sub> )	19 nM (IC <sub>50</sub> )	428 nM (IC <sub>50</sub> )
In Vitro	Ruxolitinib potently and selectively inhibits JAK2V617F-mediated signaling and proliferation, markedly increases apoptosis in a dose dependent manner, and at 64 nM results in a doubling of cells with depolarized mitochondria in Ba/F3 cells. Ruxolitinib demonstrates remarkable potency against erythroid colony formation with IC50 of 67 nM, and inhibits proliferating of erythroid progenitors from normal donors and polycythemia vera patients with IC50 values of 407 nM and 223 nM, respectively[1].			
In Vivo	Ruxolitinib (180 mg/kg, orally, twice a day) results in survive rate of greater than 90% by day 22 and markedly reduces splenomegaly and circulating levels of inflammatory cytokines, and preferentially eliminated neoplastic cells, resulting in significantly prolonged survival without myelosuppressive or immunosuppressive effects in a JAK2V617F-driven mouse model[1]. In the Ruxolitinib group, the primary end point is reached in 41.9% of patients, as compared with 0.7% in the placebo group in the double-blind trial of myelofibrosis. Ruxolitinib results in maintaining of reduction in spleen volume and improvement of 50% or more in the total symptom score[2]. Ruxolitinib (15 mg twice daily) treatment leads a total of 28% of the patients to have at least a 35% reduction in spleen volume at week 48 in patients with myelofibrosis, as compared with 0% in the group receiving the best available therapy. The mean palpable spleen length has decreased by 56% with Ruxolitinib but has increased by 4% with the best available therapy at week 48. Patients in the ruxolitinib group has an improvement in overall quality-of-life measures and a reduction in symptoms associated with myelofibrosis[3].			
Solvent&Solubility	<b>In Vitro:</b> <b>DMSO : ≥ 100 mg/mL (326.40 mM)</b> <b>H<sub>2</sub>O : &lt; 0.1 mg/mL (insoluble)</b>  * "≥" means soluble, but saturation unknown.			
	<div><div></div><div>Solvent</div><div>Mass</div><div>Concentration</div></div>	1 mg		5 mg
		10 mg		
		1 mM	3.2640 mL	16.3201 mL
		5 mM	0.6528 mL	3.2640 mL
	Stock Solutions	10 mM	0.3264 mL	1.6320 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℃, 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			

	<p>现沉淀、析出现象，可以通过加热和/或超声的方式助溶</p> <p>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (8.16 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (8.16 mM, 饱和度未知) 的澄清溶液。</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 400 <math>\mu</math>L PEG300 中，混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80，混合均匀；然后继续加入 450 <math>\mu</math>L 生理盐水定容至 1 mL。</p> <p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-<math>\beta</math>-CD in saline) Solubility: ≥ 2.5 mg/mL (8.16 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (8.16 mM, 饱和度未知) 的澄清溶液。</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 20% 的 SBE-<math>\beta</math>-CD 生理盐水水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (8.16 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (8.16 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]. Quintas-Cardama A, et al. Preclinical characterization of the selective JAK1/2 inhibitor INCB018424: therapeutic implications for the treatment of myeloproliferative neoplasms. <i>Blood</i>, 2010, 115(15), 3109-3117.</p> <p>[2]. Verstovsek S, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. <i>N Engl J Med</i>, 2012, 366(9), 799-807.</p> <p>[3]. Harrison C, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. <i>N Engl J Med</i>. 2012 Mar 1;366(9):787-98.</p>
实验参考：	
Cell Assay	<p>Cells are seeded at <math>2 \times 10^3</math>/well of white bottom 96-well plates, treated with Ruxolitinib (INCB018424) from DMSO stocks (0.2% final DMSO concentration), and incubated for 48 hours at 37°C with 5% CO<sub>2</sub>. Viability is measured by cellular ATP determination using the Cell-Titer Glo luciferase reagent or viable cell counting. Values are transformed to percent inhibition relative to vehicle control, and IC<sub>50</sub> curves are fitted according to nonlinear regression analysis of the data using PRISM GraphPad.</p> <p>[1]</p>
Animal Administration	<p>Mice are fed standard rodent chow and provided with water ad libitum. Ba/F3-JAK2V617F cells (<math>10^5</math> per mouse) are inoculated intravenously into 6- to 8-week-old female BALB/c mice. Survival is monitored daily, and moribund mice are humanely killed and considered deceased at time of death. Treatment with vehicle (5% dimethyl acetamide, 0.5% methocellulose) or Ruxolitinib (INCB018424) begin within 24 hours of cell inoculation, twice daily by oral gavage. Hematologic parameters are measured using a Bayer Advia120 analyzed, and statistical significance is determined using Dunnett testing. [1]</p>
Kinase Assay	<p>Recombinant proteins are expressed using Sf21 cells and baculovirus vectors and purified with affinity chromatography. JAK kinase assays use a homogeneous time-resolved fluorescence assay with the peptide substrate (-EQEDEPEGDYFEWLE). Each enzyme reaction is carried out with Ruxolitinib or control, JAK enzyme, 500 nM peptide, adenosine triphosphate (ATP; 1mM), and 2%</p>

	dimethyl sulfoxide (DMSO) for 1 hour. The 50% inhibitory concentration ( $IC_{50}$ ) is calculated as INCB018424 concentration required for inhibition of 50% of the fluorescent signal. [1]
<b>References</b>	<p>[1]. Quintas-Cardama A, et al. Preclinical characterization of the selective JAK1/2 inhibitor INCB018424: therapeutic implications for the treatment of myeloproliferative neoplasms. <u>Blood</u>. 2010, 115(15), 3109-3117.</p> <p>[2]. Verstovsek S, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. <u>N Engl J Med</u>, 2012, 366(9), 799-807.</p> <p>[3]. Harrison C, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. <u>N Engl J Med</u>. 2012 Mar 1;366(9):787-98.</p>



源叶生物