产品名称：TG101209
产品别名：TG101209

生物活性：

Description

TG101209 is a selective JAK2 inhibitor with IC_{50} of 6 nM, less potent to Flt3 and RET with IC_{50} of 25 nM and 17 nM, appr 30-fold selective for JAK2 than JAK3, and sensitive to JAK2V617F and MPLW515L/K mutations.

IC_{50} & Target

JAK2	JAK3	RET	FLT3
6 nM (IC_{50})	169 nM (IC_{50})	17 nM (IC_{50})	25 nM (IC_{50})

In Vitro

TG101209 is an orally bioavailable, small molecule, ATP-competitive inhibitor towards several tyrosine kinases. TG101209 inhibits growth of Ba/F3 cells expressing JAK2V617F or MPLW515L mutations with an IC50 of 200 nM. In a human JAK2V617F-expressing acute myeloid leukemia cell line, TG101209 induces cell cycle arrest and apoptosis, and inhibits phosphorylation of JAK2V617F, STAT5 and STAT3. TG101209 suppresses growth of hematopoietic colonies from primary progenitor cells harboring JAK2V617F or MPL515 mutations[1]. TG101209 significantly reduces STAT5 phosphorylation without affecting the total amount of STAT5 protein[2]. TG101209 inhibits survivin and reduces phosphorylation of STAT3 in HCC2429 and H460 lung cancer cells. TG101209 results in radio sensitization of HCC2429 and H460 lung cancer cells in vitro[3]. A recent study indicates TG101209 abrogates BCR-JAK2 and STAT5 phosphorylation, decreases Bcl-xL expression and triggers apoptosis of transformed Ba/F3 cells[4].

In Vivo

TG101209 (100 mg/kg) effectively prolongs the survival in JAK2V617F-induced disease (10 days). Compared with placebo-treated animals, TG101209-treated animals exhibit statistically significant, dose-dependent reduction in the circulating tumor cell burden at day +11 to 20%[1].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (98.10 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9621 mL	9.8103 mL	19.6205 mL
	5 mM	0.3924 mL	1.9621 mL	3.9241 mL
	10 mM	0.1962 mL	0.9810 mL	1.9621 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: ≥ 2.75 mg/mL (5.40 mM); Clear solution

此方案可获得 ≥ 2.75 mg/mL (5.40 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 27.5 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% corn oil Solubility: ≥ 2.75 mg/mL (5.40 mM); Clear solution 此方案可获得 ≥ 2.75 mg/mL (5.40 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 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Pardanani A, et al. TG101209, a small molecule JAK2-selective kinase inhibitor potently inhibits myeloproliferative disorder-associated JAK2V617F and MPLW515L/K mutations. Leukemia. 2007 Aug;21(8):1658-68. [2]. Ma AC, et al. A novel zebrafish jak2a(V581F) model shared features of human JAK2(V617F) polycythemia vera. Exp Hematol. 2009 Dec;37(12):1379-1386.e4. [3]. Sun Y, et al. Inhibition of JAK2 signaling by TG101209 enhances radiotherapy in lung cancer models. J Thorac Oncol. 2011 Apr;6(4):699-706 [4]. Cuesta-Dominguez A, et al. Transforming and tumorigenic activity of JAK2 by fusion to BCR: molecular mechanisms of action of a novel BCR-JAK2 tyrosine-kinase. PLoS One. 2012;7(2):e3245

实验参考：

Cell Assay	In brief, approximately 2×10^3 cells are plated into microtiterplate wells in 100 mL RPMI-1640 growth media with indicated concentrations of TG101209. The relative growth of cells is quantified at 24-hour intervals using Cell Proliferation Kit II (XTT) as per manufacturer's guidelines. After incubation, 20 mL of XTT is added to the wells and allowed to incubate for 4-6 hours. The colored formazan product is measured spectrophotometrically at 450 nm with correction at 650 nm, and IC_{50} values are determined using the GraphPad Prism 4.0 software. Data are subjected to a non-linear regression-fit analysis and IC_{50} values are determined as the concentration that inhibits proliferation by 50%. All experiments are done in triplicate and the results normalized to growth of untreated cells. [1]
Animal Administration	Severe combined immunodeficiency (SCID) mice are intravenously injected with 10 times 10^6 sorted GFP-positive BaF/3 cells expressing JAK2V617F (Ba/F3-V617F-GFP). TG101209 is administered by oral gavage at the indicated doses beginning day +3 after tumor cell infusion and ending on day +20. On day +11 following tumor cell injection, 1 mL blood is collected by terminal cardiac bleeding from the mouse that receives vehicle, and 0.1 mL of blood is collected by non-lethal retro-orbital collection from each of the three six-mouse groups dosed with 10, 30 or 100 mg/kg b.i.d. (twice daily) of TG101209, and samples pooled within the dose groups. Blood mononuclear cells are isolated by a Ficoll cushion centrifugation method (600 RCF and 30 min). The isolated cells are subjected to FACS analysis to determine the percentage of GFP-positive tumor cells (that is, Ba/F3-V617F-GFP cells). [1]
References	[1]. Pardanani A, et al. TG101209, a small molecule JAK2-selective kinase inhibitor potently inhibits myeloproliferative disorder-associated JAK2V617F and MPLW515L/K mutations. Leukemia. 2007 Aug;21(8):1658-68. [2]. Ma AC, et al. A novel zebrafish jak2a(V581F) model shared features of human JAK2(V617F) polycythemia vera. Exp Hematol. 2009 Dec;37(12):1379-1386.e4.

	[3]. Sun Y, et al. Inhibition of JAK2 signaling by TG101209 enhances radiotherapy in lung cancer models. J Thorac Oncol. 2011 Apr;6(4):699-706 [4]. Cuesta-Dominguez A, et al. Transforming and tumorigenic activity of JAK2 by fusion to BCR: molecular mechanisms of action of a novel BCR-JAK2 tyrosine-kinase. PLoS One. 2012;7(2):e3245