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产品名称:

4-(5-amino-2-(pyridin-3-yl)thiazolo[5,4-d]pyrimidin-7-yl)-N-p-tolylpiperazine-1-carboxamide

产品别名: **PI4KIII beta inhibitor 3**

生物活性:

Description	PI4KIII beta inhibitor 3 is a novel and high effective PI4KIIIβ inhibitor with IC50 of 5.7 nM.				
IC50 & Target	PI4KIIIβ				
	5.7 nM (IC50)				
In Vitro	PI4KIII beta inhibitor 3 is a PI4KIII inhibitor extracted from patent WO/2013034738 A1, the compound of formula 3, has an IC50 of 5.7 nM. PI4KIII beta inhibitor 3 exerts significant immunosuppressive activity, with IC50 value of 3 nM in the mixed lymphocyte reaction (MLR) assay. PI4KIII beta inhibitor 3 inhibits IL2 and IFNγ secretion with IC50 values of less than 1nM in each case. Thus, PI4KIII beta inhibitor 3 is shown to be as effective at inhibiting IL2 and IFNγ secretion as conventional immunosuppressants such as cyclosporine A. IC50 on IFNγ and IL-2 release of Cyclosporine A are 2nM and less than 1 nM respectively[1].				
In Vivo	PI4KIII beta inhibitor 3 (40 mg/kg per day, n=12) is able to delay the onset of arthritic symptoms and also to decrease symptom severity in a preventive model of arthritis compared to a vehicle control (MC 1%, n=12). PI4KIII beta inhibitor 3 reduces the anti-CII IgG titre and histological scores in the collagen-induced arthritis mouse model. Oral administration of PI4KIII beta inhibitor 3 results in prolonged graft survival in 3 out of 6 grafts in each group at day 30. Several grafts continued beating after withdrawal of the treatment (up to 60 days), indicating the induction of a certain type of graft tolerance. To evaluate the operational tolerance phenotype, animals with functional graft at day 60 are challenged with a second graft from the same donor strain or from a third party. No treatment is applied. The second grafts from the third party are rejected at day 8 (n=2) whereas second grafts from the same donor strain are functional for more than 90 days (n=2)[1].				
Solvent&Solubility	In Vitro: DMSO : 20 mg/mL (44.79 mM; Need ultrasonic)				
	Preparing Stock Solutions	Solvent	Mass		
		Concentration	1 mg	5 mg	10 mg
		1 mM	2.2395 mL	11.1975 mL	22.3949 mL
		5 mM	0.4479 mL	2.2395 mL	4.4790 mL
	10 mM	0.2239 mL	1.1197 mL	2.2395 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。					
References	[1]. Jean Herman, et al. Autoimmune and inflammatory disorder therapy. From PCT Int. Appl. (2013), WO 2013034738 A1				
实验参考:					



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Animal Administration	<p>Mice[1]</p> <p>DBA1 male mice, 8-10 weeks old, are distributed in 2 groups according to the treatment. Twelve animals received daily treatment with vehicle (1% methylcellulose), twelve others receive PI4KIII beta inhibitor 3 at 40 mg/kg/d in 1% methylcellulose. The treatment initiation started the day before the intradermal injection at the base of the tail of 100 µg of emulsified chicken collagen II in presence of complete Freund adjuvant and added heat-killed Mycobacterium butyricum. Daily inspection of the mice is performed to weight animals and quantify disease score according to the following scale (score 0: normal; score 1 : redness and/or swelling in one joint; score 2: redness and/or swelling in more than one joint; score 3: redness and/or swelling in the entire paw; score 4: deformity and/or ankylosis). On the day of sacrifice (day 42) serum are collected and anti-collagen II antibody titers are determined by ELISA. Joints are harvested, fixed in 6% paraformaldehyde, decalcified in formic acid 6% for 48 h, sliced and stained by hematoxylin and eosin staining. Hyperplasia of the synovium, infiltration of mono and polymorphonuclear cells and pannus formation parameters are scored blindly.</p>
References	<p>[1]. Jean Herman, et al. Autoimmune and inflammatory disorder therapy. From PCT Int. Appl. (2013), WO 2013034738 A1</p>

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