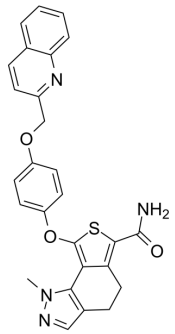
TD-198946

Cat. No.:	HY-15642
CAS No.:	364762-86-7
Molecular Formula:	$C_{27}H_{22}N_4O_3S$
Molecular Weight:	482.55
Target:	Others
Pathway:	Others
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 28 mg/mL (58.03 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0723 mL	10.3616 mL	20.7232 mL
5 mM	0.4145 mL	2.0723 mL	4.1446 mL
10 mM	0.2072 mL	1.0362 mL	2.0723 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

TD-198946, a thienoindazole derivative, is a potent chondrogenic agent.

In Vitro

TD-198946 is a potent chondrogenic agent. TD-198946 strongly induces chondrogenic differentiation without promoting hypertrophy in cell and metatarsal organ cultures. TD-198946 induces stronger Col2a1 promoter activity than insulin in ATDC5 cells. In C3H10T1/2 cells, ATDC5 cells and primary mouse chondrocytes, TD-198946 dose-dependently stimulates endogenous expression of the chondrocyte markers Col2a1 and Acan, with maximum effects around 1-10 μM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

When administered directly into the joint space, TD-198946 successfully prevents and repaires degeneration of the articular cartilage. TD-198946 exerts its effect through the regulation of Runx1 expression, which is downregulated in both mouse and human OA cartilage compared with normal tissue[1]. TD-198946 has disease-modifying effects on progressed osteoarthritis. TD-198946 may prevent the progression of osteoarthritis by acting on the remaining chondrocytes rather than repairing damaged cartilage, it may be most effective as a therapeutic during the early or middle stages of osteoarthritis, before the articular cartilage is fully eroded[2]. Cartilaginous cell-sheets are generated by culturing mouse and canine costal

chondrocytes and human mesenchymal stem cells with TD-198946 on temperature-responsive dishes. The transplanted cell-sheets are then successfully used to promote the reconstruction of permanent cartilage, with no evidence of chondrocyte hypertrophy in the knee articular cartilage defects created in mice and canines[3].

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PROTOCOL

Animal Administration [1]

Mice: Each of the prevention and repair models had two groups: (1) TD-198946-treated animals and (2) saline-treated animals. In all the mice tested the left knee joints underwent the operation and the right knee joints are sham-operated. Mice are re-anaesthetised and given a 10 μL intra-articular injection of TD-198946 or saline immediately after surgery (prevention model) or 4 weeks following surgery (repair model) every 5 days for 8 or 4 weeks, respectively[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Front Cell Dev Biol. 2023 May 10.

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REFERENCES

[1]. Yano F, et al. A novel disease-modifying osteoarthritis drug candidate targeting Runx1. Ann Rheum Dis. 2013 May;72(5):748-53.

[2]. Yano F, et al. Disease-modifying effects of TD-198946 on progressed osteoarthritis in a mouse model. Ann Rheum Dis. 2014 Nov;73(11):2062-4.

[3]. Yano F, et al. Cell-sheet technology combined with a thienoindazole derivative small compound TD-198946 for cartilage regeneration. Biomaterials. 2013 Jul;34(22):5581-7.

[4]. Kobayashi M, Chijimatsu R, Hart DA, et al. Evidence that TD-198946 enhances the chondrogenic potential of human synovium-derived stem cells through the NOTCH3 signaling pathway. J Tissue Eng Regen Med. 2021;15(2):103-115.

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