For Research Use Only

CHIR-99021

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Catalog Number: CM00839

产品信息

Catalog Number:
CM00839

CAS号:
252917-06-9

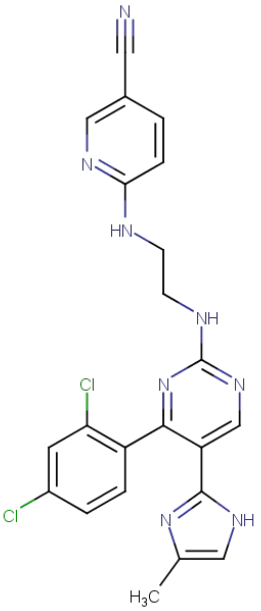
分子式:
$C_{22}H_{18}Cl_2N_8$

主要靶点:
Wnt/beta-catenin|GSK-3|Autophagy

主要通路:
PI3K/Akt/mTOR信号通路|自噬|细胞骨架|干细胞

分子量:
465.34

溶解度:
DMSO:9.3 mg/mL (20 mM)



靶点活性

GSK-3β:6.7 nM (cell free)|GSK-3α:10 nM (cell free)

体外活性

CHIR 99021 inhibited human GSK-3β (Ki: 9.8 nmol/L). It exhibited from 500-fold to >10,000-fold selectivity for GSK-3 versus 20 other protein kinases [1]. CHIR99021 can induce the reprogramming of mouse embryonic fibroblasts transduced by only two factors, Oct4 and Klf4. When combined with Parnate, an inhibitor of lysine-specific demethylase 1, CHIR99021 can cause the reprogramming of human primary keratinocyte transduced with the two factors, Oct4 and Klf4 [2]. In the presence of CHIR-99021 the viability of the ES-D3 cells was reduced by 24.7% at 2.5 μM, 56.3% at 5 μM, 61.9% at 7.5 μM and 69.2% at 10 μM CHIR-99021 with an IC50 of 4.9 μM. In ES-D3 cells cultivation with CHIR-99021 resulted in significant activation of the Wnt/beta-catenin pathway [3].

体内活性

In ZDF rats, a single oral dose of CHIR 99021 rapidly lowered plasma glucose, with a maximal reduction of nearly 150 mg/dl 3–4 h after administration. Importantly, reduced fasting hyperglycemia was achieved while plasma insulin remained at or below control levels throughout the time course of the experiment. The response was reproducible and dose-related (e.g., mild lowering at 8 mg/kg and maximal lowering at 30–48 mg/kg) [1].

动物实验

Blood was obtained by shallow tail snipping at lidocaine-anesthetized tips. Blood glucose was measured directly or heparinized plasma was collected for measurement of glucose or insulin. Animals were pre-bled and randomized to vehicle control or GSK-3 inhibitor treatment groups. For glucose tolerance tests (GTTs), animals fasted throughout the procedure with food removal early in the morning, 3 h before the first prebleed (db/db mice), or the previous night, 16 h before the bleed (ZDF rats). When the time course of plasma glucose and insulin changes in fasting ZDF rats was measured, food was removed ~16 h before test agent administration. The glucose challenges in the GTT were 1.35 g/kg i.p. (ipGTT) or 2 g/kg via oral gavage (oGTT). CHIR-99021 were formulated as solutions in 20 mmol/l citrate-buffered 15% Captisol or as fine suspensions in 0.5% carboxymethylcellulose [1].

细胞实验

The Wnt/beta-catenin reporter assay was performed with the M50 Super 8× TOPFlash and M51 Super 8× FOPFlash vector containing the firefly luciferase gene under the control of TCF/LEF binding sites or mutated bindings sites. 12,500 cells were seeded overnight on gelatine-coated 96-well plates in LIF-containing ES cell medium. On the next day, the cells were transfected using Lipofectamine with one of the aforementioned vectors plus pGL4.75 [hRluc/CMV] encoding the renilla luciferase reporter gene hRluc as a transfection control. Six hours after transfection the medium was changed to medium devoid of LIF, with reduced serum, and supplemented with 5 μM CHIR-99021. The Dual-Luciferase? reporter assay system was employed 48 and 72 h after the medium change to follow the luminescence reaction using a GloMax?-multi detection system [4].

描述

CHIR-99021 (CT99021) is a GSK-3α / β inhibitor (IC50: 10/6.7 nM).

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years

For technical support and original validation data for this product please contact
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