For Research Use Only

AT7519

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Catalog Number: CM03366

产品信息

Catalog Number:
CM03366

CAS号:
844442-38-2

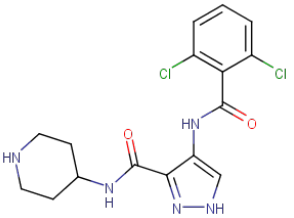
分子式:
$C_{16}H_{17}Cl_2N_5O_2$

主要靶点:
GSK-3|Apoptosis|CDK

主要通路:
PI3K/Akt/mTOR信号通路|凋亡|干细胞|细胞周期

分子量:
382.24

溶解度:
Ethanol:<1 mg/mL,H2O:<1 mg/mL,DMSO:10 mg/mL (26.16 mM)



靶点活性

CDK2:10-210 nM|CDK6:10-210 nM|CDK4:10-210 nM|CDK9:10-210 nM|CDK1:10-210 nM

体外活性

AT7519 is an ATP competitive CDK inhibitor with a Ki value of 38 nM for CDK1. AT7519 is inactive against all non-CDK kinases with the exception of GSK3β (IC50 = 89 nM). AT7519 shows potent antiproliferative activity in a variety of human tumor cell lines with IC50 values ranging from 40 nM for MCF-7 to 940 nM for SW620 consistent with the inhibition of CDK1 and CDK2. [1] AT7519 induces dose-dependent cytotoxicity in multiple myeloma (MM) cell lines with IC50 values ranging from 0.5 to 2 μM at 48 hours, with the most sensitive cell lines being MM.1S (0.5 μM) and U266 (0.5 μM) and the most resistant MM.1R (>2 μM). It does not induce cytotoxicity in peripheral blood mononuclear cells (PBMNC). AT7519 partially overcomes the proliferative advantage conferred by IL6 and IGF-1 as well as the protective effect of bone marrow stromal cells (BMSCs). AT7519 induces rapid dephosphorylation of RNA pol II CTD at serine 2 and serine 5 sites, and leads to the inhibition of transcription, partially contributing to AT7519 induced cytotoxicity of MM cells. AT7519 induces activation of GSK-3β by down-regulating GSK-3β phosphorylation, which also contributes to AT7519 induced apoptosis independent of the inhibition of transcription. [2]

体内活性

A twice daily dosing of AT7519 (9.1 mg/kg) causes tumor regression of both early-stage and advanced-stage s.c. tumors in the HCT116 and HT29 colon cancer xenograft models. [1] AT7519 treatment (15 mg/kg) inhibits tumor growth and prolongs the median overall survival of mice in the human MM xenograft mouse model in association with increased caspase 3 activation. [2]

细胞实验

Cells are incubated with different concentrations of AT7519 for 24 or 48 hours at 37 °C. Cell viability is assessed by measuring 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrasodium bromide (MTT) dye absorbance. DNA synthesis is measured by tritiated thymidine uptake (3H-TdR). Apoptosis is assessed by using Annexin V/PI staining. The percentage of cells undergoing apoptosis is defined as the sum of early apoptosis (Annexin V-positive cells) and late apoptosis (Annexin V-positive and PI-positive cells(Only for Reference)

描述

AT7519 is a CDK1/2/4/6/9 inhibitor (IC50: 10-210 nM). It is less effective to CDK3 and little active to CDK7.

储存

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