Datasheet

Inhibitors / Agonists / Screening Libraries

A DRUG SCREENING EXPERT

Product Name	:	FRAX486
Catalog Number	:	T6840
CAS Number	:	1232030-35-1
Molecular Formula	:	C25H23Cl2FN6O
Molecular Weight	:	513.39

Description: FRAX486 is a potent p21-activated kinase (PAK) inhibitor with IC50 values of 14, 33, 39 and 575 nM for PAK1, PAK2, PAK3 and PAK4 respectively.

Storage: 2 years -80°C in solvent; 3 years -20°C powder;

Solubility	DMSO	10.3 mg/mL (20 mM)
	(< 1 mg/ml refers to the product slightly soluble or insoluble)	

Receptor (IC50)	PAK1	14nM
	PAK2	33nM
	PAK3	39nM
	PAK4	575nM

In vitro Activity

In WPMY-1 cells, FRAX486 induces concentration-dependent (1-10 μM) degeneration of actin filaments. This was paralleled by attenuation of proliferation rate, being observed from 1 to 10 μM FRAX486. Cytotoxicity of FRAX486 in WPMY-1 cells is time- and concentration-dependent. In WPMY-1 cells, effects of FRAX486 on actin organization, survival, and proliferation occurred already at concentrations of 1-5 μM. In these concentrations, full inhibition of PAK1-3 may be expected, while PAK4 may be inhibited only partially[2].

In vivo Activity

FRAX486 crosses the blood-brain barrier and that therapeutically useful concentrations of FRAX486 are in the brain as early as 1 h and remain as long as 24 h after administration, with the maximum concentration in the target tissue at 8 h. Daily dosing results in steady-state levels of FRAX486 in the brain. FRAX486 specifically rescues the Fmr1 KO abnormality in which the spine phenotype is present in apical neurons and not simply decreasing spine density irrespective of genotype or existence of a phenotype. Also, FRAX486 reduces hyperactivity and stereotypical movements, both of which are phenotypes that characterize the mouse model of Fragile X syndrome[3].

Cell Assay

Cells are grown in 96-well plates (20,000 cells/well) for 24 h, before FRAX486, IPA3, or DMSO are added in indicated concentrations (1, 5, 10 μM). Subsequently, cells are grown for different periods (24, 48, 72 h). Separate controls are performed for each period. At the end of this period, 10 μl of [2-(2-methoxy-4-nitrophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfophenyl)-2H-tetrazolium monosodium salt (WST-8) from CCK-8 is added, and absorbance in each well is measured at 450 nm after incubation for 2 h at 37°C.(Only for Reference)

Cell line: WPMY-1 cells(an immortalized cell line obtained from nonmalignant human prostate stroma)

Animal Experiment

Animal Model: C57BL/6 mice

Reference

1. Hayashi-Takagi A, et al. Proc Natl Acad Sci U S A. 2014, 111(17):6461-6.
2. Wang Y, et al. PLoS One. 2016, 11(4):e20153312.
3. Dolan BM, et al. Proc Natl Acad Sci U S A. 2013, 110(14):5671-6.

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