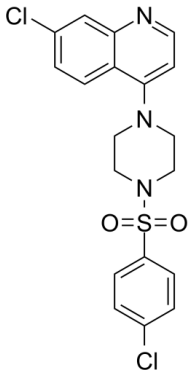
Data Sheet

Product Name:	KM11060
Cat. No.:	CS-5499
CAS No.:	774549-97-2
Molecular Formula:	C19H17Cl2N3O2S
Molecular Weight:	422.33
Target:	Autophagy; CFTR
Pathway:	Autophagy; Membrane Transporter/Ion Channel
Solubility:	10 mM in DMSO



BIOLOGICAL ACTIVITY:

KM11060 is a novel corrector of the F508del-CFTR trafficking defect. Target: CFTR in vitro: Small-molecule correctors such as KM11060 may serve as useful pharmacological tools in studies of the F508del-CFTR processing defect and in the development of cystic fibrosis therapeutics. KM11060 rescues F508del-CFTR trafficking in cultured cells and native epithelial tissues. KM11060 partially corrects F508del-CFTR processing and increases surface expression to 75% of that observed in cells incubated at low temperature. Up to 50% of the F508del-CFTR in cells treated with KM11060 was complex-glycosylated, indicating passage through the Golgi. KM11060 as a promising compound for further development of CF therapeutics. [1] in vivo: In LPS-induced acute lung inflammation, blockade of PSGL-1 (P-selectin glycoprotein ligand-1) or P-selectin, antagonism of PAF by WEB2086, or correction of mutated CFTR trafficking by KM11060 could significantly increase plasma lipoxin A4 levels in F508del relevant to wildtype mice. [2]

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay [1] The parental CFBE41o- cell line was originally developed from CF bronchial cells (F508del/F508del) and later transduced with wild-type or F508del-CFTR using the TranzVector lentivirus system. CFBE41o- cells were grown on 24 mm transwell filters and exposed to 0.1% DMSO (untreated control) or 10 μM KM11060 (in DMSO) for 48 h at 37°C. Low-temperature rescue of F508del-CFTR was carried out at 29°C for 48 h. RNA was extracted with TRIzol, except for an extra acid phenol/chloroform extraction to remove contaminating genomic DNA before adding alcohol and the addition of 10 μg of Glycoblue as a carrier. All RNA samples were treated with DNase. Animal administration [2] We found that blockade of PSGL-1 (by anti-PSGL MAB, 1 mg/kg, iv), P-selectin (by anti-P-selectin MAB, 1 mg/kg, iv), or PAF (by its receptor antagonist, WEB2086, 2 mg/kg, iv), and correction of mutated CFTR trafficking (by corrector KM11060, 2.5 mg/kg, ip) significantly increased plasma lipoxin A4 levels in the LPS-challenged F508del mice compared to the vehicle-treated LPS-challenged F508del mice.

References:

[1]. Robert R, et al. Structural analog of sildenafil identified as a novel corrector of the F508del-CFTR trafficking defect. Mol Pharmacol. 2008 Feb;73(2):478-89.

[2]. Wu H, et al. Lipoxin A4 and platelet activating factor are involved in E. coli or LPS-induced lung inflammation in CFTR-deficient mice. PLoS One. 2014 Mar 26;9(3):e93003.

CAIndexNames:

Quinoline, 7-chloro-4-[4-[(4-chlorophenyl)sulfonyl]-1-piperazinyl]-

SMILES:

O=S(N1CCN(C2=CC=NC3=CC(Cl)=CC=C23)CC1)(C4=CC=C(Cl)C=C4)=O

Caution: Product has not been fully validated for medical applications. For research use only.

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