Product Data Sheet

Product Name: ZD8321
Cat. No.: GC32005

Chemical Properties

Cas. No.	182073-77-4		
SMILES	COC(N[C@@H](C(C)C)C(N1[C@@H](CCC1)C(N[C@@H](C(C)C)C(C(F)(F)F)=O)=O)=O)=O		
Formula	$C_{18}H_{28}F_3N_3O_5$	M.Wt	423.43
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	ZD8321		

Protocol

Cell experiment:	HUVECs are cultured in RPMI 1640 containing 5% FBS for 6 h in collagen-coated, 24-well plates before the experiment. Some of the confluent HUVECs are further incubated with TNFα (1 ng/mL) and ZD8321 (0-50 mM), or with human NE (0-100ng/mL) for 4 h at 37°C. For adhesion assays, cancer cells resuspended in RPMI 1640 containing 5% FBS are added to each HUVEC-layered well. The plates are shaken at 700 rpm for 10 min at room temperature, washed twice with PBS, and examined by phase-contrast microscopy to determine the number of cells bound onto the HUVEC monolayer. The adhesive reactions of neutrophils to HUVEC are also analyzed in this manner[2].

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References:

[1]. Veale CA, et al. Orally active trifluoromethyl ketone inhibitors of human leukocyte elastase. J Med Chem. 1997 Sep 26;40(20):3173-81.
[2]. Nozawa F, et al. Elastase activity enhances the adhesion of neutrophil and cancer cells to vascular endothelial cells. J Surg Res. 2000 Dec;94(2):153-8.

Background

ZD8321 is a potent inhibitor of human Neutrophil elastase (NE) with a Ki of 13±1.7 nM.

TNFα-activated HUVEC is dose dependently inhibited by ZD8321.The adhesion between cancer cells with high elastase activity and TNFα-activated HUVEC is also inhibited by ZD8321. Expression of cell surface E-selectin by NE stimulation is suppressed in the

presence of ZD8321. The concentration of soluble E-selectin in the medium increases after adhesive reaction between neutrophils and HUVEC. This increase is also dose dependently inhibited by ZD8321[2].

[1]. Veale CA, et al. Orally active trifluoromethyl ketone inhibitors of human leukocyte elastase. J Med Chem. 1997 Sep 26;40(20):3173-81. [2]. Nozawa F, et al. Elastase activity enhances the adhesion of neutrophil and cancer cells to vascular endothelial cells. J Surg Res. 2000 Dec;94(2):153-8.

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