Product Data Sheet

Product Name: E6446
Cat. No.: GC33900

Chemical Properties

Cas. No.	1219925-73-1		
SMILES	C1(C2=CC=C(OCCCN3CCCC3)C=C2)=NC4=CC=C(OCCCN5CCCC5)C=C4O1		
Formula	$C_{27}H_{35}N_3O_3$	M.Wt	449.59
Solubility	DMSO : 8.33 mg/mL (18.53 mM; ultrasonic and warming and heat to 60°C)	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	E6446		

Protocol

Cell experiment:

E6446 is assayed for the suppression of BALB/c mouse spleen interleukin-6 (IL-6) production in response to stimulation by oligonucleotide CpG1668. E6446 is added to dissociated splenocytes (5 × 105 per well in complete RPMI/10% fetal bovine serum in a 96-well plate) before addition of TLR agonists. Cells are stimulated for 72 hours, and supernatants are removed for ELISA analysis of IL-6. Mouse bone marrow-derived dendritic cells (BMDCs) are generated by culturing BALB/c marrow cells in RPMI containing 100 ng/mL Flt3 ligand for 7 days. Cells (1 × 105) in 50 µL are assayed for IL-6 production after overnight or 24-hour stimulation with various TLR ligands. For studies using human peripheral blood mononuclear cells, Ficoll-separated mononuclear cells are isolated from healthy volunteer donors, washed, and plated with stimulatory oligonucleotide CpG2216 in complete RPMI for 72 hours. Interferon in supernatant is quantified by ELISA[1].

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Animal experiment:

Mice[1]MRL/lpr mice are dosed orally five times a week with 20 or 60 mg/kg E6446 or 60 mg/kg hydroxychloroquine beginning at 5 weeks of age. Cytoxan is administered at 50 mg/kg i.p. every 10 days. A serum sample is taken immediately before the beginning of treatment to monitor changes in autoreactive antibodies. Subsequently, serum samples are collected approximately monthly and analyzed for anti-dsDNA by ELISA after 1:500 dilution. Body weights and urine samples are taken at the same interval, and proteinuria is assessed by ChemStrips. Anti-nuclear antibodies (ANA) are assessed using commercially available HEp2 slide kits, with serum diluted to 1:100 in kit buffer. ANA scores are read blinded[1].

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References:

[1]. Lamphier M, et al. Novel small molecule inhibitors of TLR7 and TLR9: mechanism of action and efficacy in vivo. Mol Pharmacol. 2014 Mar;85(3):429-40.
[2]. Franklin BS, et al. Therapeutical targeting of nucleic acid-sensing Toll-like receptors prevents experimental cerebral malaria. Proc Natl Acad Sci U S A. 2011 Mar 1;108(9):3689-94.

Background

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E6446 is an inhibitor of Toll-like receptor (TLR) 7 and 9 signaling in a variety of human and mouse cell types and inhibits DNA-TLR9 interaction in vitro.

[1] Marc Lamphier, et al. Mol Pharmacol. 2014 Mar;85(3):429-40.

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