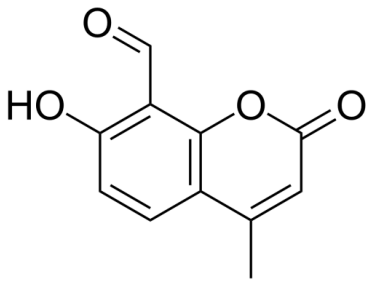
Data Sheet

Product Name:	4μ8C
Cat. No.:	CS-6409
CAS No.:	14003-96-4
Molecular Formula:	C11H8O4
Molecular Weight:	204.18
Target:	IRE1
Pathway:	Cell Cycle/DNA Damage
Solubility:	DMSO : ≥ 27 mg/mL (132.24 mM)



BIOLOGICAL ACTIVITY:

4μ8C (IRE1 Inhibitor III) is a small-molecule inhibitor of **IRE1α**. **In Vitro:** When applies to the media of ER stressed cultured cells, 4μ8C (IRE1 Inhibitor III) inhibits Xbp1 splicing in a concentration-dependent manner. 4μ8C dissociates slowly from IRE1, but ishout of inhibitor leads to rapid recovery of Xbp1 splicing in cells[1].The IRE1 endoribonuclease inhibitor 4μ8c prevents the splicing of the XBP1 mRNA in response to ER stress caused by mutant proinsulin production[2]. The inositol-requiring enzyme 1α (IRE1α) is a serine-threonine kinase that plays crucial roles in activating the unfolded protein response. 4μ8C treatment dramatically inhibits IL-4 production by $CD4^+$ T cells under Th0 conditions because both the IL-4 levels in the culture supernatant and the percentage of IL-4 positive cells are reduced by 4μ8C treatment. In addition, both IL-5 and IL-13 production are significantly reduced upon treatment with 4μ8C[3]. **In Vivo:** 4μ8c (IRE1 Inhibitor III) (i.p. injection; 10 mg/kg/day for 4 more weeks) leads to a significant reduction (45.2%) in atherosclerotic lesion area in en face aorta preparations. 4μ8c can effectively mitigate plaque development in mice[4].
4μ8C (orally; 10, 50, or 100 mg/kg) suppresses passive cutaneous anaphylaxis (PCA) in mice (ED50 = 25.1 mg/kg)[5].
4μ8C reverses the ER stress-dependent loss of several known RIDD targets, with an EC_{50} of approximately 4 μM, approximating that of inhibition of XBP1 target gene activation[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [2]INS-1 (Insulin 2 C96Y-GFP) cells (clone #4S2) cells are either left untreated or treated with 2 μg/mL doxycycline, 2 μg/mL doxycycline and 5 μM 4μ8C or 5 μM 4μ8C alone. After 48 h 50,000 cells/100 μL of media from each treatment well are seeded into a 96-well plate in duplicates. The CellTiter 96 AQueous Non-Radioactive Cell Proliferation Assay MTS is performed. The absorbance at 490 nm is then measured with a plate reader.[2].

References:

[1]. Cross BC, et al. The molecular basis for selective inhibition of unconventional mRNA splicing by an IRE1-binding small molecule. Proc Natl Acad Sci U S A. 2012 Apr 10;109(15):E869-78.

[2]. Zhang L, et al. IRE1 inhibition perturbs the unfolded protein response in a pancreatic β-cell line expressing mutant proinsulin, but does not sensitize the cells to apoptosis. BMC Cell Biol. 2014 Jul 10;15:29.

[3]. Kemp K, et al. The serine-threonine kinase inositol-requiring enzyme 1α (IRE1α) promotes IL-4 production in T helper cells. J Biol Chem. 2013 Nov 15;288(46):33272-82.

[4]. Tufanli O, et al. Targeting IRE1 with small molecules counteracts progression of atherosclerosis. Proc Natl Acad Sci U S A. 2017 Feb 21;114(8):E1395-

E1404.

[5]. Nam ST, et al. Suppression of IgE-mediated mast cell activation and mouse anaphylaxis via inhibition of Sykactivation by 8-formyl-7-hydroxy-4-methylcoumarin, 4μ8C. Toxicol Appl Pharmacol. 2017 Oct 1;332:25-31.

CAIndexNames:

2H-1-Benzopyran-8-carboxaldehyde, 7-hydroxy-4-methyl-2-oxo-

SMILES:

O=CC1=C(O)C=CC2=C1OC(C=C2C)=O

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA