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PAS Kinase Inhibitor, BioE-1115 - Calbiochem BioE-1115, PASKi

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Unit	EA

Description

A cell-permeable quinoxaline-carboxylic acid compound that acts as a selective PAS kinase/PASK inhibitor (IC50 ~ 4 nM) with little or no potency against a panel of 49 other kinases (IC50 >= 10 &#181,M) and effectively inhibits cellular PASK-T307 autophosphorylation (IC50 ~ 1 &#181,M, 16 h drug treatment in PASK-transfected HEK293T cultures with 1% FBS). Similar to siRNA-mediated PASK knockdown, BioE-1115 treatment is shown to effectively prevent sterol regulatory element binding protein SREBP-1c maturation without affecting Akt/mTOR pathway signaling, resulting in impaired cellular SREBP transcription activity in HepG2 cultures (% inhibition/[drug] = 40%/30 &#181,M & & 65%/50 &#181,M by SRE-Luc reporter assay, overnight drug treatment prior to 100 nM insulin stimulation for 6 h). Oral administration is reported to effectively reduce high-frucose diet/HFrD-induced dyslipidemia (% reduction of liver triglyceride/serum triacylglyerol/dose = 48/26/30 mg kg-1 & 63/55/100 mg kg-1, Daily oral dosage administered in the last wk of a 3 wk HFrD period, followed by a 24 h fasting and a 12 refed period prior to tissue collection) and insulin resistance (% reduction of serum glucose/insulin/dose = 23/14/30 mg kg-1 & 28/31/100 mg kg-1) in rats by selectively suppressing SREBP-1 maturation and thereby inhibiting SREBP-1c, but not SRREBP-2, target genes transcription in liver, but not in abdominal fat or gastrocnemius muscle in vivo (% Gpat1/Fasn/Scd1/Acc1/Fae mRNA reduction/plasma [BioE-1115] in &#181,g/mL/dose = 40/34/36/27/34/2.07/10 mg kg-1, 59/56/51/48/54/7.65/30 mg kg-1, 76/5967/62/74/42.2/100 mg kg-1) without affecting liver or body weight., BioE-1115, PASKi, A cell-permeable, orally available, non-toxic quinoxaline-carboxylic acid based compound that acts as a highly potent, selective, and reversible inhibitor of Per-Arnt-Sim Kinase (PASK, IC50 ~ 4 nM). Exhibits excellent selectivity over 49 other kinases (IC50 >10 &#181,M) and displays about 2,500-fold greater potency for PASK over casein kinase 2alpha. Blocks PASK autophosphorylation at Thr307 in a dose-dependent manner (IC50 ~ 1 &#181,M) without affecting the insulin-induced phosphorylation of either Akt or S6K. Effectively blocks the maturation of SREBP-1 in hepatic tissue of high fructose fed wild-type Sprague-Dawley rats. Shown to normalize hepatic and serum triglyceride levels, reduce blood glucose levels, and partially reverse insulin resistance in animal models (30 mg/kg. p.o.).Please note that the molecular weight for this compound is batch-specific due to variable water content.