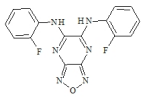

BAM15, ST056388, mitochondrial protonophore uncoupler that does not depolarize the plasma membrane

IDNUMBER ST056388

Other identifiers: SBB001916, ST4027337, T4021910, TBB011486, T3149443, ST236891

Formula: C16H10F2N6O

MW: 340.29

NAME: (2-fluorophenyl){6-[(2-fluorophenyl)amino](1,2,5-oxadiazolo[3,4-e]pyrazin-5-yl)}amine

SMILES: c12c(nc(c(n1)Nc1c(F)cccc1)Nc1c(F)cccc1)non2

InChI=1S/C16H10F2N6O/c17-9-5-1-3-7-11(9)19-13-14(20-12-8-4-2-6-10(12)18)22-16-15(21-13)23-25-24-16/h1-8H,(H,19,21,23)(H,20,22,24)

InChIKey=OEGJBRZAJRPPHL-UHFFFAOYSA-N

MDL: MFCD00373912

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Reference:

Brandon M. Kenwood1, Janelle L. Weaver, et.al. Identification of a novel mitochondrial uncoupler that does not depolarize the plasma membrane. Mol Metabolism. Online Nov 27, 2013. http://dx.doi.org/10.1016/j.molmet.2013.11.005

Abstract

Chemical mitochondrial uncouplers are lipophilic weak acids that increase proton transport into the mitochondrial matrix via a pathway independent of ATP synthase, thereby uncoupling nutrient oxidation from ATP production. These molecules enable determination of maximal cellular respiration and have antioxidant effects that protect from ischemia-reperfusion injury. However, the most widely used proton transporter uncouplers have off-target activity that lead to a range of undesired effects including plasma membrane depolarization, mitochondrial inhibition, and cytotoxicity. To identify new mitochondrial uncouplers that lack off-target activity at the plasma membrane, we screened a small molecule chemical library. Herein we report the identification and validation of a novel mitochondrial protonophore uncoupler (2-fluorophenyl){6-[(2-fluorophenyl)amino](1,2,5-oxadiazolo[3,4-e]pyrazin-5-yl)}amine, named BAM15, that does not depolarize the plasma membrane and protects mice from acute renal ischemic-reperfusion injury. Thus, BAM15 represents a reliable new tool for the analysis of cellular bioenergetic function that has therapeutic potential by altering mitochondrial function in vivo.