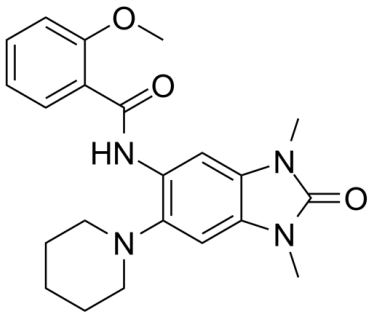
Data Sheet

Product Name:	GSK-5959
Cat. No.:	CS-4867
CAS No.:	901245-65-6
Molecular Formula:	C22H26N4O3
Molecular Weight:	394.47
Target:	Epigenetic Reader Domain
Pathway:	Epigenetics
Solubility:	DMSO : 13 mg/mL (32.96 mM; Need ultrasonic and warming)



BIOLOGICAL ACTIVITY:

GSK-5959 is a potent, selective and cell permeable BRPF1 bromodomain inhibitor with IC50 ~ 80 nM. Exhibits >100-fold selectivity for BRPF1 over a panel of 35 other bromodomains, including BRPF2/3 and BET family bromodomains. IC50 value: 80 nM Target: BRPF1 in vitro: GSK-5959 inhibits BRPF1 interaction with histone H3. A cellular protein interaction assay measuring the displacement of NanoLuc-tagged BRPF1 bromodomain from Halotagged histone H3 is employed to demonstrate GSK-5959 is cell permeability and disruption of chromatin binding with IC50 of 0.98 μM. GSK-5959 is used at 10 μM final concentration in various in vitro assays.

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay [1] HEK293 cells (8 x 105) were plated in each well of a 6-well plate and co-transfected with Histone H3.3-HaloTag (NM_002107) and NanoLuc-BRPF1 isoform 1 (P55201-1) bromodomain amino acids 625-735 or isoform 2 (P55201-2) bromodomain amino acids 625-741. Isoform 2 has an insertion S660 -> SEVTELD in the bromodomain. Twenty hours post-transfection cells were collected, washed with PBS, and exchanged into media containing phenol red-free DMEM and 4% FBS in the absence (control sample) or the presence (experimental sample) of 100 nM NanoBRET 618 fluorescent ligand (Promega). Cell density was adjusted to 2 x 105 cells/ml and then re-plated in a 96-well assay white plate (Corning Costar #3917). Inhibitors were then added directly to media at final concentrations between 0-33 μM and the plates were incubated for 18hrs at 37oC in the presence of 5% CO2. NanoBRET furimazine substrate (Promega) was added to both control and experimental samples at a final concentration of 10 μM. Readings were performed within 5 minutes using the CLARIOstar (BMG) equipped with 450/80 nm bandpass and 610 nm longpass filters with a 0.5sec reading setting. A corrected BRET ratio was calculated and is defined as the ratio of the emission at 610 nm/450 nm for experimental samples (i.e. those treated with NanoBRET fluorescent ligand) subtracted by the emission at 610 nm/450 nm for control samples (not treated with NanoBRET fluorescent ligand). BRET ratios are expressed as milliBRET units (mBU), where 1 mBU corresponds to the corrected BRET ratio multiplied by 1000.

References:

[1]. Demont EH, et al. 1,3-Dimethyl Benzimidazolones Are Potent, Selective Inhibitors of the BRPF1 Bromodomain. (2014) ACS Med Chem Lett. 5(11):1190-1195.

CAIndexNames:

Benzamide, N-[2,3-dihydro-1,3-dimethyl-2-oxo-6-(1-piperidinyl)-1H-benzimidazol-5-yl]-2-methoxy-

SMILES:

O=C(NC1=C(N2CCCCC2)C=C(N3C)C(N(C)C3=O)=C1)C4=CC=CC=C4OC

Caution: Product has not been fully validated for medical applications. For research use only.

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