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Centre for AIDS Reagent

Data Sheet

PRODUCT NAME	(+)-JQ-1
REPOSITORY REFERENCE	#100 226
CAS No.	1268524-70-4
MedChemExpress Cat. No.	HY-13030
MWt	456.99
Formula	C23H25CIN4O2S
Purity	>97%
Solubility	DMSO: ≥ 45 mg/mL
Mechanisms	Pathways: Epigenetics; Target: Epigenetic Reader Domain
Biological Activity	(+)-JQ1 is a BET bromodomain inhibitor, with IC50 of 77 nM/33 nM for BRD4(1/2). IC50 Value: 77 nM(for BRD4(1)); 33 nM(for BRD4(2)) Target: BRD4 in vitro: (+)-JQ1 enantiomer binds directly into the Kac binding site of BET bromodomains. (+)-JQ1 (500 nM) binds BRD4 competitively with chromatin resulting in differentiation and growth arrest of NMC cells. (+)-JQ1 (500 nM) attenuates rapid proliferation of NMC 797 and Per403 cell lines as demonstrated by reduced Ki67 staining. (+)-JQ1 (500 nM) potently decreases expression of both BRD4 target genes in NMC 797 cells. (+)-JQ1 inhibits cellular viability with IC50 of 4 nM in NMC 11060 cells. (+)-JQ1 results in robust inhibition of MYC expression in MM cell lines. (+)-JQ1 inhibits proliferating of KMS-34 and LR5 with IC50 of 68 nM and 98 nM, respectively. (+)-JQ1 (500 nM)-treated MM.1S cells results in a pronounced decrease in the proportion of cells in S-phase, with a concomitant increase in cells arrested in G0/G1. (+)-JQ1 (500 nM) results in pronounced cellular senescence by beta-galactosidase staining. (+)-JQ1 (800 nM) exposure leads to a significant reduction in cell viability among the majority of CD138+ patient-derived MM samples tested. (+)-JQ1 inhibits growth of LP-1 cells with GI50 of 98 nM. (+)-JQ1 (625 nM) results in an increase in the percentage of LP-1 cells in G0/G1. (+)-JQ1 (500 nM) suppresses the expression of MYC,

BRD4 and CDK9 in LP-1 cells. in vivo: (+)-JQ1 (50 mg/kg) inhibits tumors growth in mice with NMC 797 xenografts. (+)-JQ1 (50 mg/kg) results in effacement of NUT nuclear speckles in mice with NMC 797 xenografts, consistent with competitive binding to nuclear chromatin. (+)-JQ1 (50 mg/kg) induces strong (grade 31) keratin expression in NMC 797 xenografts. (+)-JQ1 (50 mg/kg) promotes differentiation, tumor regression and prolonged survival in mice models of NMC xenografts. (+)-JQ1 (50 mg/kg) results in a significant prolongation in overall survival of SCID-beige mice orthotopically xenografted after intravenous injection with MM.1S-luc+ cells compared to vehicle-treated animals. (+)-JQ1 (50 mg/kg i.p.) leads to a highly significant increase in survival of mice bearing Raji xenografts.

Reference

[1]. Selective inhibition of BET bromodomains By Filippakopoulos, Panagis; Qi, Jun; Picaud, Sarah; Shen, Yao; S
Fedorov, Oleg; Morse, Elizabeth M.; Keates, Tracey; Hickman, Tyler T.; Felletar, Ildiko; et al From Nature. 2010
23;468(7327):1067-73. Epub 2010 Sep 24.
Abstract
Epigenetic proteins are intently pursued targets in ligand discovery. So far, successful efforts have been limite
modifying enzymes, or so-called epigenetic 'writers' and 'erasers'. Potent inhibitors of histone binding module
been described. Here we report a cell-permeable small molecule (JQ1) that binds competitively to acetyl-lysin
motifs, or bromodomains. High potency and specificity towards a subset of human bromodomains is explaine
structures with bromodomain and extra-terminal (BET) family member BRD4, revealing excellent shape comp
the acetyl-lysine binding cavity. Recurrent translocation of BRD4 is observed in a genetically-defined, incurabl
human squamous carcinoma. Competitive binding by JQ1 displaces the BRD4 fusion oncoprotein from chroma
squamous differentiation and specific antiproliferative effects in BRD4-dependent cell lines and patient-derive
models.

CONTRIBUTOR MedChem Express

ACKNOWLEDGEMENTS

Publications should acknowledge the contributor and the Centre for AIDS Reagents. Acknowledgments should read: "The *Name of Reagent* (*Repository Number*) was obtained from the Centre for AIDS Reagents, NIBSC, UK, supported by EURIPRED (EC FP7 INFRASTRUCTURES-2012 - INFRA-2012-1.1.5.: Grant Number 31266). www.euripred.eu/