Product Data Sheet

Product Name: YM-155 hydrochloride
Cat. No.: GC15632

Chemical Properties

Cas. No.	355406-09-6		
Chemical Name	1-(2-methoxyethyl)-2-methyl-3-(pyrazin-2-ylmethyl)benzo[f]benzimidazol-3-ium-4,9-dione;chloride		
SMILES	CC1=[N+](C2=C(N1CCOC)C(=O)C3=CC=CC=C3C2=O)CC4=NC=CN=C4.[Cl-]		
Formula	$C_{20}H_{19}ClN_4O_3$	M.Wt	398.84
Solubility	≥ 19.45 mg/mL in DMSO, ≥ 4.34 mg/mL in EtOH with ultrasonic and warming, ≥ 48.1 mg/mL in Water with ultrasonic	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	YM-155 hydrochloride		

Protocol

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Kinase experiment:

A 2,767-bp sequence of human survivin gene promoter is isolated from human genomic DNA by PCR using Pyrobest polymerase and the following primers: 5'-GCGCGCTCGAGTCTAGACATGCGGATATATTC-3' and 5'-GCGCGAA-GCTTTGGCGGTTAATGGCGCGC-3'. The resulting PCR fragment is digested with XhoI/HindIII and ligated into the XhoI/HindIII cleavage site of the pGL3-Basic vector. The resulting plasmid is named pSUR-luc. DNA sequencing is done on all amplified sequences by a DNA sequencer. The activity of pSUR-luc is confirmed by luciferase assay with transiently transfected HeLa-S3 cells. Luciferase assay is done. The pGL3 control vector, which contains the SV40 promoter and enhancer sequences, is used. HeLa cells are stably transfected with pSUR-luc and pSV2bsr by Lipofect-AMINE 2000. After blasticidin selection at 10 μg/mL, a single colony is chosen based on appropriate luciferase signals and genetic stability over time and named HeLa-SURP-luc. CHO cells are stably transfected with pGL3-control and pSV2bsr. After blasticidin selection at 10 μg/mL, a single colony is chosen based on appropriate luciferase signals and genetic stability over time and named CHO-SV40-luc. Stocked cells from the HeLa-SURP-luc and CHO-SV40-luc clones are used for chemical screening and characterization of YM155. YM155 in DMSO are added to the cells, which had been seeded the previous day on 96-well plastic plates at 5×103 per well. Luciferase activity is measured 24 hours later. IC50 is calculated by logistic analysis.

Cell experiment:

The antiproliferative activity of YM-155 is measured. After treatment with YM-155 for 48 h, the cell count is determined by sulforhodamine B assay. The GI50 value is calculated by logistic analysis, which is the drug concentration resulting in a 50% reduction in the net protein increase (as measured by sulforhodamine B staining) in control cells during the drug incubation. The assay is done in triplicate, and the mean GI50 value is obtained from the results of four independent assays.

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Animal experiment:	Five-week-old male nude mice (BALB/c nu/nu) are used for the assay. PC-3 cells (2×106-3×106) are injected into the flanks of the mice and allowed to reach a tumor volume of > 100 mm3 in tumor volume (length×width2×0.5). YM-155 is s.c. administered as a 3-day continuous infusion per week for 2 weeks using an implanted micro-osmotic pump or i.v. administered five times a week for 2 weeks. The percentage of tumor growth inhibition 14 days after initial YM-155 administration is calculated for each group using the following formula: MTV=100×{1-[(MTV of the treated group on day 14)-(MTV of the treated group on day 0)]/[(MTV of the control group on day 14)-(MTV of the control group on day 0)]}, where MTV is mean tumor volume. For both the frozen tumors and plasma samples, survivin expression levels are analyzed by Western blotting and YM-155 drug concentration by high-performance liquid chromatography/triple quadrupole mass spectrometry (LC/MS/MS) using validated methods.

References:

[1]. Nakahara T, et al. YM155, a novel small-molecule survivin suppressant,

induces regression of established human hormone-refractory prostate tumor xenografts. Cancer Res. 2007 Sep 1;67(17):8014-21.
[2]. Iisa T, et al. Radiosensitizing effect of YM155, a novel small-molecule survivin suppressant, in non-small cell lung cancer cell lines. Clin Cancer Res. 2008 Oct 15;14(20):6496-504.
[3]. Guo K, et al. A combination of YM-155, a small molecule survivin inhibitor, and IL-2 potently suppresses

renal cell carcinoma in murine model. Oncotarget. 2015 Aug 28;6(25):21137-47.

Background

YM-155 hydrochloride is a novel small-molecule suppressant of surviving, the smallest member of inhibitor of apoptosis (IAP) gene family. It exhibits a potent suppressive activity against survivin but has little effect on expression levels of other IAP family members or B-cell lymphoma 2 (BCL-2) related proteins. YM155 also suppresses proliferation in a broad range of human cancer cell lines, induces tumor regression in non-small cell lung cancer (NSCLC), melanoma, bladder, aggressive non-Hodgkin lymphoma, and breast cancer xenograft models, reduces spontaneous metastases, and significantly prolongs the survival of animal harboring established metastatic tumors derived from a human triple-negative breast cancer (TNBC) cell lines.

References:

1.Naoki Kaneko, Kentaro Yamanaka, Aya Kita, Kenji Tabata, Takafumi Akabane, and Masamichi Mori. Synergistic antitumor activities of sepantronium bromide (YM155), a surviving suppressant, in combination with microtubule-targeting agents in triple-negative breast cancer cells. Biol Pharm Bull 2013.

2.Yan-Fang Tao, Jun Lu, Xiao-Juan Du, Li-Chao Sun, Xuan Zhao, Liang Peng, Lan Cao, Pei-Fang Xiao, Li Pang, Dong Wu, Na Wang, Xing Feng, Yan-Hong Li, Jian Ni, Jian Wang and Jian Pan. Survivin selective inhibitor YM155 induce apoptosis in SK-NEP-1 Wilms tumor cells. BMC Cancer 2012, 12:619

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