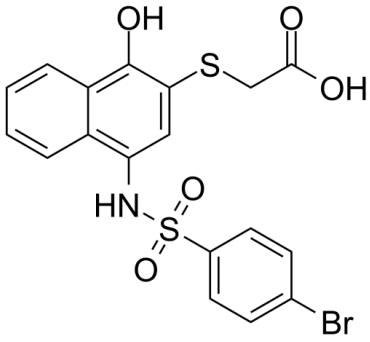
Data Sheet

Product Name:	UMI-77
Cat. No.:	CS-5046
CAS No.:	518303-20-3
Molecular Formula:	C18H14BrNO5S2
Molecular Weight:	468.34
Target:	Bcl-2 Family
Pathway:	Apoptosis
Solubility:	DMSO : ≥ 28 mg/mL (59.79 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

UMI-77 is a selective **Mcl-1** inhibitor, which shows high binding affinity to **Mcl-1** (IC_{50}=0.31 μM). UMI-77 binds to the BH3 binding groove of **Mcl-1** with K_i of 490 nM, showing selectivity over other members of anti-apoptotic Bcl-2 members. IC50 & Target: IC50: 0.31±0.11 μM (Mcl-1), 10.2±2.24 μM (Bcl-2), 36.09±13.80 μM (Bcl-xL)[1]

Ki: 0.49±0.06 μM (Mcl-1), 5.33±1.0 μM (A1/Bfl-1), 8.19±1.91 μM (Bcl-w), 23.83±1.81 μM (Bcl-2), 32.99±4.33 μM (Bcl-xL)[1] **In Vitro:** Competitive binding curve of UMI-77 against Mcl-1 is obtained by FP based binding assay using fluorescent labeled Bid BH3 peptide with an IC_{50} of 1.87±0.22 μM. UMI-77 potently inhibits the cell growth of BxPC-3 and Panc-1 cell lines with IC_{50} values of 3.4 μM and 4.4 μM respectively, and shows 3 to 5 times less potency in inhibition of the cell growth of two other tested cell lines MiaPaCa-2 (12.5 μM) and AsPC-1 (16.1 μM). The cell growth inhibition potency of UMI-77 correlates with the highest expression of Mcl-1 and Bak, and lowest expression of Bcl-xL in the sensitive cell lines, BxPC-3 and Panc-1. Capan-2 cells are showing similar sensitivity to UMI-77 (IC_{50} of 5.5 μM) as BxPC-3 and Panc-1, although has low Mcl-1 levels[1]. **In Vivo:** UMI-77 exhibits moderate metabolic stability with a half-life of 45 minutes.The maximum tolerated dose (MTD) of UMI-77 in SCID mice is determined. Administered 60 mg/kg i.v. for 5 consecutive days per week for two weeks does not cause any loss in the animal weight and there is no obvious sign of toxicity during the course of the treatment. Increasing the dose to 80 mg/kg show severe animal weight loss (>20%), therefore 60 mg/kg is used as a therapeutic dose for the in vivo efficacy studies. Daily treatment with UMI-77 for 5 consecutive days a week for two weeks results in statistically significant tumor growth inhibition by 65% and 56% in comparison with the controls in day 19 ($p<0.0001$) and day 22 ($p<0.003$) respectively[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]**Human PC cell lines AsPC-1, BxPC-3 and Capan-2** are cultured in RPMI 1640 medium, while Panc-1 and MiaPaCa are cultured in DMEM medium, all supplemented with 10% fetal bovine serum. The cell growth inhibition after treatment with increasing concentrations of the compounds (e.g., **UMI-77; 1,10, and 100 μM**) is determined by WST-8 assay[1].

Animal Administration: [1]Mice[1]

For BxPC-3 subcutaneous model, 10×10^6 cells are subcutaneously injected into the flanks of **4-5 week old female severe combined immune deficient mice (ICR-SCID)**. Palpable tumors start to appear in 3-5 weeks. Tumors are measured twice weekly. To prevent any pain or discomfort, mice are euthanized and their tumors remove once they reach ~1800 mg burden. Tumors are then dissected into 50 mg pieces and re-transplanted into naïve ICR-SCID for serial propagation. Animals are treated with either vehicle or **UMI-77 given i.v. (60 mg/kg) on day three post BxPC-3 transplantation for two weeks (5 days a week)**. Tumor weight is recorded throughout the treatment period. At the end of the treatment period, animals are euthanized and their tumors harvested for protein isolation and western blot analysis for apoptotic markers.

References:

[1]. Abulwerdi F, et al. A novel small-molecule inhibitor of mcl-1 blocks pancreatic cancer growth in vitro and in vivo. Mol Cancer Ther. 2014 Mar;13(3):565-575.

CAIndexNames:

Acetic acid, 2-[[4-[[(4-bromophenyl)sulfonyl]amino]-1-hydroxy-2-naphthalenyl]thio]-

SMILES:

O=C(O)CSC1=CC(NS(=O)(C2=CC=C(Br)C=C2)=O)=C3C=CC=CC3=C1O

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