

Product Data Sheet

Product Name: Capzimin

Cat. No.: GC32815

Chemical Properties

Cas. No. 2084868-04-0

SMILES O=C(C1=CC2=CC=CC(SSC3=C4N=CC(C(NCCC5=NC=CS5)=O)=CC4=CC=C3)=C2N=C1)NCCC6=NC=CS6

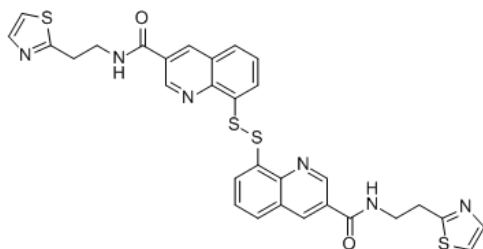
Formula $C_{30}H_{24}N_6O_2S_4$ M.Wt 628.81

Solubility DMSO : ≥ 55.67 mg/mL (88.53 mM) Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

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

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Kinase experiment: Fluorescence polarization assays are performed in low-volume 384 well solid black plates in quadruplicate. The assays are performed in buffer containing 50 mM Tris-HCl pH7.5, 1mM MgCl₂, 50 μ M ATP, 1 mM DTT and 0.01% NP-40. The components for the assay are added in the follow sequence: 1) 5 μ L compound (Capzimin, et al.) (in 3% DMSO) at different concentrations, 2) 5 μ L of diluted human 26S proteasome, and 3) 5 μ L of substrate (3 nM Ub4- peptideOG). 100 μ M Zn(cyclen)₂⁺ is present in the titration reaction for the experiments performed with Zn(cyclen)₂⁺. Fluorescence polarization is measured at 30°C with excitation at 480 nm and emission at 520 nm. Collected data is normalized to DMSO control and fitted to a dose-response curve to determine the IC₅₀ value[1].

Cell experiment: HCT116 cells are treated with different concentrations of 3021 or Capzimin for 72 hours in normal or low serum medium and then mixed with CellTiter-Glo reagent to estimate cell proliferation. Measured luminescence values are normalized to DMSO control and data are fitted to a dose-response equation to determine the GI₅₀[1].

References:

[1]. Li J, et al. Capzimin is a potent and specific inhibitor of proteasome isopeptidase Rpn11. Nat Chem Biol. 2017 May;13(5):486-493.

Background

Capzimin is a potent and moderately specific proteasome isopeptidase Rpn11 inhibitor.

Capzimin (3027) shows 80-fold selectivity for Rpn11 over Csn5, 10-fold over AMSH and 6-fold over BRCC36 (IC₅₀=30 μ M, 4.5 μ M and 2.3 μ M respectively). Capzimin is screened against the NCI panel of 60 cancer cell lines. The median GI₅₀ is 3.3 μ M. Capzimin exhibits promising activity in leukemia cells including the SR and K562 cell lines (GI₅₀ values of 0.67 μ M and 1 μ M respectively), as well as several solid tumor cell lines including NCI-H460 (non-small cell lung cancer; GI₅₀= 0.7 μ M) and MCF7 (breast cancer; GI₅₀=1.0 μ M). Immunoblotting for the processed form of caspase 3 and

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caspase-cleaved poly ADP-ribose polymerase in HCT116 cells confirm that Capzimin not only blocks cell growth, but also induces apoptosis[1].

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