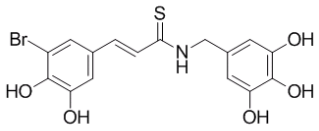
Data Sheet

Product Name:	NT157
Cat. No.:	HY-100037
CAS No.:	1384426-12-3
Molecular Formula:	$C_{16}H_{14}BrNO_5S$
Molecular Weight:	412.26
Target:	Insulin Receptor
Pathway:	Protein Tyrosine Kinase/RTK
Solubility:	DMSO: ≥ 30 mg/mL



BIOLOGICAL ACTIVITY:

NT157is a selective inhibitor of IRS–1/2, IC50 values at sub–micromolar doses (ranging from 0.3 to 0.8 μM) .
IC50 value: 0.3 to 0.8 μM [1]
Target: Insulin receptor
in vitro: NT157 significantly affects the cells' migratory ability, as confirmed by a wound–healing assay. NT157 induces cytostatic effects, as evidenced by G2/M cell cycle arrest, and does not affect apoptosis. NT157, a novel small–molecule that specifically targets IRS protein, in OS cells. NT157 is a small–molecule inhibitor that induces Ser–phosphorylation and consequently the degradation of IRS–1 and IRS–2. NT157 efficiently affects migration ability of MG–63 and U–2OS OS cells. NT157 treatment induces cell cycle arrest and inhibits IGF system signaling. [1] The density of LNCaP cells grown in FBS was decreased approximately 20% at 1 μM, approximately 70% at 2 μM, and >90% at 5 μM (IC50, 1.4 μM). Growth of LNCaP cells is suppressed >60% when cultured in CSS but still exhibited significant density at 2 μM and maximal decreased density at 5 μM. The density of FBS–cultured PC3 cells was similarly decreased by NT157 treatment (40% at 2 μM and > 70% at 5 μM; IC50, 2.5 μM). [2]
in vivo: NT157 suppresses growth of LNCaP xenografts following castration. NT157 treatment affects IGF1R and IRS targets in xenografts and significantly delays castration–resistant progression of LNCaP androgen–responsive xenografts when combined with castration. NT157 potentiates docetaxel activity in PC3 xenografts.[2]

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay (Western blotting) [1] NT157 was dissolved in dimethyl sulfoxide (DMSO) to generate a 10-mM stock solution, which was stored at -80°C.?? Cells were treated with NT157 (0.3-1.3 μM) for 48 h or left untreated, and cell lysates were prepared and processed. The membranes were incubated overnight with the following primary antibodies: anti-Shc clone PG-797, anti GAPDH, anti-β-actin, anti-phospho-Akt (Ser473) clone 736E11, anti-Akt, anti-ERK, anti-phospho-ERK (Tyr202/Tyr204), anti-IRS-1, anti-IRS-2, and phospho-IRS-1 (Tyr612); anti-rabbit or anti-mouse antibodies conjugated to horseradish peroxidase were used as secondary antibodies. Animal administration [2] For xenograft studies, 2 × 106 LNCaP (suspended in 0.1 mL Matrigel) or PC3 cells (suspended in 0.1 mL serum-free DMEM) were inoculated s.c. in the flank of 6- to 8-week-old male athymic nude mice via a 27-gauge needle under isoflurane anesthesia. For LNCaP xenografts, when tumor volume exceeded 200 mm3, mice were castrated and randomly selected for treatment with 50 mg/kg NT157 or vehicle (10% 2-HP-beta-CD + 0.67% NaCl/H2O) injected i.p. three times per week. Each experimental group consisted of 12 mice. Tumor volume was measured twice weekly (length × width × depth × 0.5432). Data points were expressed as average tumor volume ± SEM. When PC3 tumors reached 100 mm3, mice were randomly selected for treatment with 50 mg/kg NT157 or vehicle (10% 2-HP-beta-CD + 0.67% NaCl/H2O) injected i.p. three times per week or treated with 10 mg/kg docetaxel injected i.p. three times a week for 1 week or combination of 50 mg/kg NT157 and 10 mg/kg docetaxel as indicated. Experimental groups consisted of 7 mice (vehicle), 9 mice (NT157), 10 mice (docetaxel), and 16 mice (combination). Tumor volume and body weight (BW) were measured once weekly. Data points were expressed as average tumor volume ± SEM.

References:

[1]. Garofalo C, et al. Preclinical Effectiveness of Selective Inhibitor of IRS–1/2 NT157 in Osteosarcoma Cell Lines. Front Endocrinol (Lausanne). 2015 May 13; 6:74.

[2]. Ibuki N, et al. The tyrphostin NT157 suppresses insulin receptor substrates and augments therapeutic response of prostate cancer. Mol Cancer Ther. 2014 Dec;13(12):2827–39.

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