Product Data Sheet

Product Name: ATN-161
Cat. No.: GC34133

Chemical Properties

Cas. No.	262438-43-7		
SMILES	O=C(N)C[C@@H](C(N)=O)NC([C@H](CS)NC([C@H](CO)NC([C@H](CC1=CNC=N1)NC([C@H]2N(C(C)=O)CCC2)=O)=O)=O)=O		
Formula	$C_{23}H_{35}N_9O_8S$	M.Wt	597.64
Solubility	Soluble in DMSO	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	ATN-161		

Protocol

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Cell experiment:

Ninety-six well microtiter plates are coated with fibronectin(20 μg/mL) overnight at 4°C. HUVECs are then trypsinized as described above and resuspended in 1% FBS-MEM for cell counting. Cell suspensions with 10,000 cells/mL are prepared in serum-reduced conditions by using 1% FBS-MEM, or 1% FBS-MEM containing either ATN-161 (1 μM) or ATN-163 (scrambled peptide as control; 1μM) to allow interference by the peptide during the ligand binding process (i.e., binding of α5β1 to fibronectin). Cells are thereafter plated into each well (2,000 cells/well in 200 μL) of the fibronectin-coated 96-well plates. Cells are incubated at 37°C for 48 hr under these serum-reduced conditions in order to evaluate effects of ATN-161 on EC survival and proliferation. Estimation of cell number is performed by adding 40 μL MTT to each well and incubating for 2 hr at 37°C. Media is then removed, cells are solubilized in 100 μL DMSO and optical density is measured at 560 nm. Experiments are performed in triplicate[1].

Animal experiment:

Mice[1] Eight-week-old male BALB/c mice are acclimated for 1 week while caged in groups of 5. Mice are fed a diet of animal chow and water ad libitum throughout the experiment. CT-26 cells (10,000 cells in 50 μL HBSS) are injected into the spleens of 40 BALB/c mice to produce liver metastases. Mice are randomly assigned to 1 of 4 treatment groups (10 mice per group): (A) control (saline/saline), (B) 5-FU alone, (C) ATN-161 alone and (D) ATN-161 plus 5-FU. Body weight at randomization is similar among groups. Treatment with ATN-161 (100 mg/kg) or saline is started on day 4 after CT-26-cell injection and is administered every third day thereafter by intraperitoneal injection. In previous studies, administration of the peptide every third day has been shown to be adequate for sustained inhibition of integrin α5β1 activity. Mice are allowed to recover for 1 week from the surgical procedure and effects of anesthesia with pentobarbital (Nembutal, 50 mg/kg). On day 7, mice are anaesthetized again and osmotic pumps.

References:

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[1]. Stoeltzing O, et al. Inhibition of integrin alpha5beta1 function with a small peptide (ATN-161) plus continuous 5-FU infusion reduces colorectal liver metastases and improves survival in mice. Int J Cancer. 2003 Apr 20;104(4):496-503.
[2]. Wang W, et al. The antiangiogenic effects of integrin alpha5beta1 inhibitor (ATN-161) in vitro and in vivo. Invest Ophthalmol Vis Sci. 2011 Sep 14;52(10):7213-20.

Background

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Background

ATN-161 is a peptide derived from fibronectin and an integrin αVβ3 and αVβ5 antagonist.[1] It binds to αVβ3 and αVβ5 receptors (K_ds = 0.69 and 1 ?M, respectively) in MDA-MB-231 breast cancer cells, as well as inhibits the interaction between αVβ5 and human angiotensin-converting enzyme 2 (ACE2) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein in a concentration-dependent manner in cell-free assays.[1,2] ATN-161 reduces viral titers in Vero E6 cells infected with SARS-CoV-2 (EC_{50} = 3.16 ?M).[2] It inhibits VEGF-induced migration and capillary tube formation of primary human choroidal endothelial cells when used at a concentration of 0.1 ?M.[3] ATN-161 (1 mg/kg) reduces tumor growth and metastasis in an MDA-MB-231 mouse xenograft model and infarct volume and edema in a mouse model of ischemic stroke induced by middle cerebral artery occlusion (MCAO).[1,4]

1.Khalili, P., Arakelian, A., Chen, G., et al.A non-RGD-based integrin binding peptide (ATN-161) blocks breast cancer growth and metastasis in vivoMol. Cancer Ther.5(9)2271-2280(2006) 2.Beddingfield, B.J., Iwanaga, N., Chapagain, P.P., et al.The integrin binding peptide, ATN-161, as a novel therapy for SARS-CoV-2 infectionJACC Basic Transl. Sci.6(1)1-8(2021) 3.Wang, W., Wang, F., Lu, F., et al.The antiangiogenic effects of integrin α5β1 inhibitor (ATN-161) in vitro and in vivoInvest. Ophthalmol. Vis. Sci.52(10)7213-7220(2011) 4.Edwards, D.N., Salmeron, K., Lukins, D.E., et al.Integrin α5β1 inhibition by ATN-161 reduces neuroinflammation and is neuroprotective in ischemic strokeJ. Cereb. Blood Flow Metab.40(8)1695-1708(2020)

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