Data Sheet (Cat.No.T217148)

TargetMol

Arg-PEG1-Tαsyn

Chemical Properties

CAS No. :

Formula:

Molecular Weight:

Storage: Keep away from direct sunlight
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Arg-PEG1-Tαsyn is a PROTAC degrader targeting α-synuclein (α-syn), with a DC50 of 0.28μM in U251 cells. This compound utilizes arginine (Arg) as the E3 ligase ligand and a benzothiazole-aniline variant as the warhead for α-syn targeting. It effectively degrades both wild-type α-syn and its A53T mutant in mammalian cells. In vitro, Arg-PEG1-Tαsyn significantly reduces α-syn aggregation via the E3 ubiquitin ligase UBR1. In vivo, it demonstrates good safety and significantly improves dopaminergic neuron damage and motor dysfunction. Arg-PEG1-Tαsyn is useful in Parkinson's disease research.
Targets(IC50)	PROTACs
In vitro	Arg-PEG1-Tα-syn significantly reduces α-syn A53T in U251 cells at concentrations of 0-10 μM over 48 hours with a DC_{50} of 0.28 μM, achieving a D max of 90.5% at 5 μM. At 1 μM, Arg-PEG1-Tα-syn degrades α-syn A53T progressively over 0-72 hours in U251/α-syn A53T cells. The compound consistently degrades α-syn in various cell lines, including U251/α-syn WT, U251/α-syn A53T, 293/α-syn WT, 293/α-syn A53T, SH-SY5Y/α-syn WT, and SH-SY5Y/α-syn A53T over 48 hours at 1 μM. The α-syn A53T reduction by Arg-PEG1-Tα-syn is reversible by MG132 but not by Chloroquine. In U251 cells, it regulates α-syn WT and α-syn A53T via E3 ubiquitin ligase UBR1, as demonstrated by shRNA knockdown of UBR1, UBR2, UBR4, and UBR5, at 1 μM over 48 hours. Additionally, Arg-PEG1-Tα-syn, at 0-5 μM over 48 hours, reduces α-syn A53T aggregation in SH-SY5Y cells overexpressing α-syn WT or α-syn A53T, protecting them from related toxicity.
In vivo	Arg-PEG1-Tα-syn, administered orally in various concentrations mixed with OP50 bacteria from the L1 larval stage to the fifth day of adulthood, effectively reduces α-synuclein aggregates in the Caenorhabditis elegans strain NL5901. This compound significantly improves the morphology of neuronal cell bodies and synapses and partially restores the functional deficits of dopaminergic neurons caused by α-synuclein pathology. Additionally, when administered within the 0-10 μM concentration range under the same conditions, Arg-PEG1-Tα-syn effectively ameliorates motor dysfunction in a dose-dependent manner attributed to α-synuclein pathology, as evidenced in transgenic worms overexpressing human α-syn A53T. The compound demonstrates good safety profiles in both the UM0020 strain and wild-type worms.

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