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Amide Linked Coumarin Scaffolds Inhibit α Synuclein and Tau Aggregation for Neurodegenerative Drug Leads

Coumarin-amide analogs inhibit toxic alpha-synuclein and tau aggregation for Alzheimer's and Parkinson's therapies.

Alzheimer's Disease (AD) and Parkinson's Disease (PD) are the most prevalent neurodegenerative disorders characterized by continuous loss of functional neurons. Progressive augmentation of each of the former diseases is predicted to double in 2060 and 2040, reaching 13.9 and 1.2 million, respectively, in the US alone. Currently commercialized monoclonal antibodies for treatment of AD and PD are designed to disaggregate amyloid beta plaque, but they are not designed to prevent the formation of toxic oligomers – which is a promising and unique solution. Researchers at Purdue University have discovered a method by using coumarin scaffold coupled via amide linker to inhibit the aggregation of proteins, alpha-synuclein (α-syn) and tau, responsible for PD and AD, respectively. Biophysical methods such as thioflavin T fluorescence assays (ThT), photo-induced cross-linking of unmodified proteins (PICUP), cell-based assays, and electron microscopic observations were used to evaluate the effect of analogs on inhibition of α-syn and tau aggregation. The results showed that the dihydroxy and aminoindoles have promising effects on the inhibition of α-syn and tau protein aggregation. We believe that this technology provides a great drug discovery pathway towards treatments for AD, PD, and other neurodegenerative disorders.

Technology Validation:

In fibril formation assays using ThT and TEM, two compounds have met the cut-off criterion of 5% fibril reduction or less and reduced the formation of α-syn oligomers.

Advantages:

-Successfully inhibit α-syn and tau aggregation, which are responsible for AD and PD

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Category
Pharmaceuticals/Drug Discovery & Development

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View online

Applications:

-Alzheimer's Disease

-Parkinson's Disease

-Neurodegenerative disorders

TRL: Pharmaceuticals

Intellectual Property:

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