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Small Molecule Stimulators of the Core Particle of the Proteasome

Small molecule stimulators of the 20S core particle of the proteasome enhance the degradation of disordered proteins, offering a new therapeutic pathway for neurodegenerative conditions like Alzheimer's and Parkinson's.

Researchers at Purdue University have developed small molecule stimulators of the enzyme responsible for routine protein degradation, the 20S core particle of the proteasome (20S CP). The researchers were motivated to develop 20S CP stimulators as a pharmaceutical intervention to degrade the damaged and disordered proteins associated with a variety of disease states including Alzheimer's and Parkinson's. The hit compound discovered by Purdue's researchers stimulates catalytic activity of the 20S CP. This stimulator molecule increased the degradation of a peptide probe as well as several full-length proteins by the 20S CP versus a control without the stimulator. In a cell line expressing alpha-synuclein, a protein found aggregated in neurodegenerative diseases, the stimulator enhanced degradation of this protein 200-300 percent. The researchers are now developing derivatives of the hit compound towards a new therapeutic lead. These new molecules pave the way for a drug to prevent debilitating and life-threatening diseases like Alzheimer's and Parkinson's Diseases.

Advantages:

-Stimulates 20S core of the proteasome

-Selective for 20S CP versus 26S proteasome

Potential Applications

-Treatment of Alzheimer's and Parkinson's diseases

-Treatment for aging and disease processes associated with protein aggregation

TRL: 3

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Intellectual Property:

Provisional-Patent, 2019-08-16, United States | NATL-Patent, 2020-08-14, China | NATL-Patent, 2020-08-14, Japan | NATL-Patent, 2020-08-14, Europe | PCT-Patent, 2020-08-14, WO | NATL-Patent, 2022-01-14, United States

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