Novel Small Molecules to Prevent Neurodegenerative Diseases

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INVENTION NOVELTY

UCSF scientists have developed a novel biophysical-biochemical screening platform to identify small molecules that prevent the oligomerization of alpha-synuclein: the rate-limiting step in the formation of toxic fibrils in the pathologies of Parkinson's disease, Lewy Body Dementia, and other neurodegenerative diseases. With this technology, novel families of small molecules have been found with the capacity to reverse multiple pathogenic markers of disease progression in cells.

VALUE PROPOSITION

- The novel two stage screening platform combines a biophysical screen for direct binders of the monomeric alpha-synuclein (pre-oligomerized) with high-throughput biochemical screens for alpha-synuclein oligomerization in which the oligomerization process is directly and sensitively measured or by cellular screens for reversal of alpha-synuclein impaired phagocytosis, a measure of perturbed vesicular dynamics.
- The novel family of compounds reverses multiple pathogenic markers of disease in cells, including alpha-synuclein oligomerization and dysfunctional vesicular dynamics.
- Only symptomatic treatments are currently available to treat these diseases, and therapies that treat the underlying pathology are urgently needed.

TECHNOLOGY DESCRIPTION

Parkinson's disease and other synucleinopathies are characterized by oligomerization and aggregation into larger fibrils of the protein alpha-synuclein. Multiple lines of evidence have pointed to the formation of pre-fibril oligomers as directly contributing to the pathologies of these disorders in addition to forming the building blocks of fibrils themselves. Therapies that could stabilize the monomeric, pre-oligomer state of alpha-synuclein would have the capacity to halt and potentially reverse this pathogenic state.

Using Surface Plasmon Resonance (SPR) technology to measure drug-target binding, and novel biochemical assays for direct measurements of oligomerization (including bioluminescent fragment complementation and FRET), UCSF scientists have identified families of small molecules that directly prevent oligomerization of alpha-synuclein. In cell-

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OTHER INFORMATION

KEYWORDS

Alpha-synuclein, Synucleinopathy, Parkinson's Disease, Dementia with Lewy Bodies, Alzheimer's Disease

CATEGORIZED AS

- **Medical**
  - Disease: Central Nervous System

RELATED CASES

2019-033-0

based assays of pathogenesis, these small molecules demonstrate the capacity to reverse oligomerization.

LOOKING FOR PARTNERS

To develop & commercialize the technology as:

- A high-throughput screening platform for alpha-synuclein oligomerization disrupting compounds
- Therapies for synucleinopathies including Parkinson's disease, Lewy Body Dementia, Multiple Systems Atrophy, Alzheimer's disease, and others.

STAGE OF DEVELOPMENT

Pre-Clinical

RELATED MATERIALS

- Not available at this time (in preparation)

DATA AVAILABILITY

Under CDA / NDA

PATENT STATUS

Country	Type	Number	Dated	Case
European Patent Office	Published Application	3941452	01/26/2022	2019-033

Additional Patent Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Graphene Oxide Based Affinity Grids As Sample Supports For High- Resolution Cryo Electron Microscopy.

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