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A Label-Free alpha-Synuclein Aggregate Detection Assay

Stanford researchers have developed a label-free assay to detect protein aggregation and established a proof of concept in α-synuclein aggregates. This strategy significantly improves the ability to detect and measure protein aggregation without the use of additives which can impair readouts of aggregates.

α-Synuclein is strongly associated with neurodegenerative diseases such as Parkinson's disease (PD), dementia with Lewy bodies (DLB), and multiple system atrophy (MSA). Aggregated α-synuclein, is a hallmark of these diseases. Mutations in the α-synuclein gene have also been linked to familial PD, highlighting its direct involvement in the disease process. Current methods to detect α-synuclein aggregates heavily rely on fluorescent additives which can affect the degree of aggregation. This hinders both the detection as well as the ability to develop therapeutics targeting these aggregates.

To address these limitations, Stanford researchers developed an optical sensing assay to improve α-synuclein aggregate detection without using fluorescent additives. The key innovation is a microprobe-based method, which captures α-synuclein aggregates from cerebrospinal fluid (CSF) and monitors their growth in real time. This approach offers several advantages, including eliminating additives that may interfere with aggregation studies, allowing for the isolation and further analysis of α-synuclein aggregates, and providing direct observation of aggregation kinetics. The method has been successfully tested on PD patient samples, and analyzers with multi-channel capabilities enable high-throughput testing for clinical and research applications.

The optical sensing α-synuclein aggregate detection assay is carried out in **two** steps. A time trace of label-free optical sensing responses is recorded during the experiment process.
(1) A pre-coated microprobe is dipped into a CSF sample to capture small α-

synuclein aggregates (seeds).
(2) The microprobe is dipped into a pure ?-synuclein solution to form large α-synuclein aggregates.

Stage of Development
Proof of Concept – verified from PD patient samples

Applications

- Diagnostic for PD, DLB, MSA, and Alzheimer's
- Therapeutics development
- Expansion to other protein aggregation diseases

Advantages

- Label/additive free assay
- Applicable with patient samples
- High throughput
- Isolation of protein aggregate direct from patient samples

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