

A Cell-Based Seeding Assay for Huntingtin Aggregation

Tech ID: 29135 / UC Case 2018-193-0

SUMMARY

UCLA researchers from the Department of Psychiatry has created a novel cell-based seeding assay for sensitive, specific and high throughput detection of mutant Huntingtin proteins in biological samples.

BACKGROUND

Huntington's disease (HD) is a lethal genetic disorder that is caused by mutations in the huntingtin protein (mHTT). Genetic errors cause an elongated repeat motif to result in a polyglutamine (polyQ) stretch in the expressed protein, causing it to form aggregates. These aggregates accumulate in the nerve cells eventually lead to their breakdown, incurring debilitating effects. Current molecular methods of diagnosing HD include direct detection, in vitro aggregation detection and cell based detection. Direct detection of HTT uses antibodies, which can only detect a subset of HTT in soluble, monomer forms. In vitro aggregation detection lacks sensitivity. Other existing cell based detection approaches are prone to false positives and are labor intensive.

INNOVATION

A novel high throughput cell-based seeding assay was developed to detect mutant HTT proteins. This approach utilizes a transgenic cell line that expresses a form of mHTT, which is linked to a green fluorescent protein (GFP), making any aggregates easily quantifiable. The cell line has a very low baseline level of aggregates. However, it can be highly specifically induced to form aggregates with even very small aggregate seeds are introduced from HD patients or mouse samples. The readout correlates well with the amount of seeds added and with the disease stage of the HD patients.

APPLICATIONS

Huntington's Disease diagnosis

- ▶ Drug discovery
- ▶ Clinical trial biomarker

ADVANTAGES

- ▶ Specific
- ▶ Sensitive
- ▶ High throughput
- ▶ Correlates with disease progression
- ▶ Compatible with biological samples

PATENT STATUS

Country	Type	Number	Dated	Case
European Patent Office	Published Application	3694536	08/19/2020	2018-193
United States Of America	Published Application	20200255487	08/13/2020	2018-193

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OTHER INFORMATION

KEYWORDS

Huntington's Disease, Huntingtin, mHTT, protein aggregation, in vitro aggregation, cell-based assay

CATEGORIZED AS

- ▶ **Biotechnology**
 - ▶ Health
- ▶ **Medical**
 - ▶ Diagnostics
 - ▶ Disease: Central Nervous System
 - ▶ Research Tools
 - ▶ Screening
- ▶ **Research Tools**
 - ▶ Cell Lines
 - ▶ Expression System
 - ▶ Screening Assays

RELATED CASES

2018-193-0

- ▶ [Novel Mouse Model for Huntingtons Disease](#)
- ▶ [Transgenic Mouse Model of Parkinson's Disease with Age-Dependent Hypokinetic Motor Deficits, Dopaminergic Neuron Loss, and Alpha Synuclein Accumulation](#)
- ▶ [Rosa HD](#)

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