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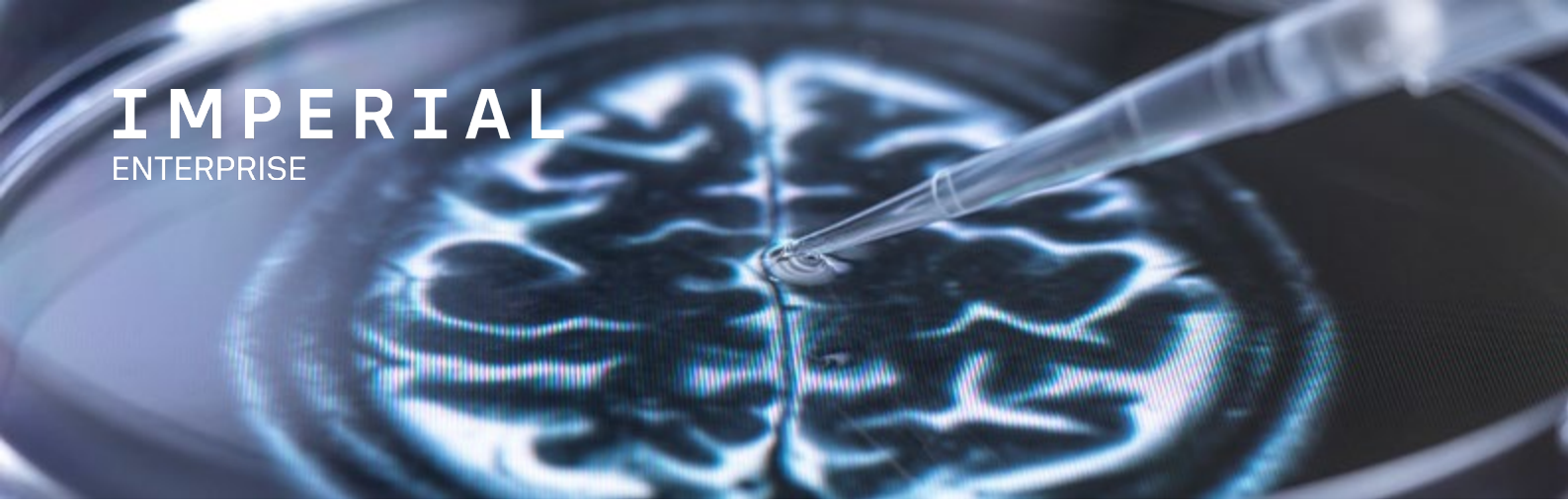

In situ RTQuIC seeding amplification assay for neurodegeneration

A seeding amplification assay with spatial resolution that visualises protein misfolding and aggregation in intact biological samples to study the mechanisms of neurodegeneration and cross-seeding between diseases.

Proposed Use

- Neurodegenerative Disease Research: greater depth of investigation into misfolded proteins in diseases like Parkinson's and Alzheimer's, advancing understanding of disease mechanisms.
- Biomarker Development: revealing early diagnostic markers for neurodegenerative diseases for tailored treatments in personalized medicine.
- Clinical Diagnostics: improving the depth and complexity for early detection of neurodegenerative diseases through protein misfolding analysis in healthcare.

Problem Addressed

Neurodegenerative diseases, such as Alzheimer's, Parkinson's, and prion diseases, are caused by the misfolding and accumulation of protein aggregates, leading to brain cell dysfunction and death. With global aging populations, these diseases are increasingly prevalent, with Alzheimer's affecting over 50 million people globally and Parkinson's impacting more than 10 million. As the burden of these diseases grows, early diagnosis and effective treatments remain critical.

Current diagnostic methods, like MRI, PET scans, and CSF protein biomarker analysis, are more effective in later stages and often fail to detect early misfolding or disease progression. Parkinson's disease is diagnosed based on motor symptoms, which emerge only after significant neurodegeneration. Seed amplification assays hold promise but lack spatial resolution, making it difficult to understand where misfolding begins and how it spreads within tissues. These limitations highlight the need for more precise, complex, and early diagnostic tools for better patient care and therapeutic development.

Benefits

- **Spatial Resolution:** Visualises protein misfolding at cellular and subcellular levels.
- **In Situ Analysis:** Provides real-time observation of protein seeding in intact tissue.
- **Real-time Tracking:** Enables dynamic tracking of misfolding activity over time.
- **Cross-Seeding Exploration:** Studies protein interactions across diseases, advancing understanding of neurodegenerative mechanisms.
- **Early Diagnosis:** Enhances early detection of protein misfolding.

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Technology Overview

This technology is a seed amplification assay with spatial resolution that enables the visualisation of protein misfolding and aggregation within tissue samples. By applying recombinant proteins to intact biological samples, the system tracks the seeding activity of misfolded proteins, such as alpha-synuclein and tau, in situ, providing spatially precise data on how these proteins propagate across cells and anatomical regions. This method can use standard histological techniques to prepare tissue samples, followed by incubation in a controlled environment to detect misfolding, which is then visualised using immunohistochemistry, fluorescence microscopy, or microplate-based screening. Preliminary testing with human post-mortem tissue has yielded promising results, demonstrating the ability to observe protein seeding in situ, providing insights into disease mechanisms that were previously inaccessible. The technology could also be applied to any intact biological sample, such as animal tissue, engineered cell lines and tissues, and even patient-derived cells.

Intellectual property information

UK Priority Application - GB2410222.0 - In situ seeding amplification assay

Inventor information

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