

Diagnostic prototype for dementia detection

Proteinopathies are diseases associated with the abnormal production, folding, and aggregation of proteins. Presence of protein aggregates are regarded as hallmarks of neurodegenerative disorders (e.g. plaques in Alzheimer's disease and Lewy bodies in Parkinson's disease).

Diagnostic and therapeutic research have typically focused on detecting and targeting large insoluble aggregates, which present the following challenges:

- **Expensive medical imaging techniques:** low accessibility and specificity, incl PET and SPECT. Time-consuming, require expertise examination.
- **Healthy vs disease:** protein aggregates such as plaques are also naturally present in healthy individuals.
- **Limited clinical use:** pathological assessment rely on histological examination of post-mortem brain tissue.
- **Disease specificity:** same type of protein aggregates can be common to several diseases, e.g. tau in tauopathies and a-synuclein in a-synucleinopathies.

The Method

A new technique to characterise toxic aggregates in biofluids based on their features, to allow for early detection of specific proteinopathies and assessment of disease progression. Two aspects:

Super-resolution Imaging

- Quantitative and qualitative imaging
- Identification of protein aggregates sub-populations
- High resolution allowing for low concentrations
- Patients biofluids

Computational analysis

- Deep learning-based prediction
- Protein aggregates analysis (up to 1µm):
 - Morphology
 - Toxicity
 - Abundance
- Proteinopathies risk and detection

Priority application GB2214417.4(Filed on 30th Sept 2022)

Validation

Current data

- Toxicity assay shows disease-specific aggregates.
- Immunostaining in donor patient brain sections.
- Aggregates derived from post-mortem samples and CSF of Alzheimer's disease (AD), Parkinson's disease (PD) and dementia with Lewy bodies (DLB) and healthy control donors with high prediction score of test samples.

Upcoming samples

- CSF samples from longitudinal studies for AD and PD for early laboratory prognosis.
- Blood samples: AD, PD, DLB and controls.

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Quantitative super-resolution imaging of pathological aggregates reveals distinct toxicity profiles in different synucleinopathies

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