# OligoFIT

**Oligomer-Focused Screening and Individualized Therapeutics to target Neurodegenerative Disorders**

Clinicians typically diagnose Parkinson's disease by recognition of the cardinal symptoms of tremors or rigidity in movement along with other more subtle indications. However, these signs usually suggest an advanced stage of the disease and can vary significantly in severity between individuals. Earlier diagnosis is desirable as it offers more chances to intervene and research looking at protein levels in patients as markers for disease is actively being pursued. To further complicate matters, Parkinson's disease belongs to a group of related conditions called synucleinopathies (that include multiple system atrophy and dementia with Lewy bodies). These share a link to the alpha-synuclein protein, that can form abnormal protein deposits called Lewy bodies that disrupt the brain's normal functioning.

How is it possible for a single protein to lead to different diseases with varied progression in different people? This hotly debated question forms the focus for our research project. Clues may lie in the ability of alpha-synuclein to adopt discrete shapes (conformations). The proteins clump together in small mobile aggregates that can travel out of the cells; we call these "oligomers". A range of confounding factors unique to individuals (i.e. genetics, underlying health conditions, environmental exposure) may influence the particular shape or abundance of oligomer populations. It is as yet unclear if the behaviours of individual oligomer conformations lead to different disease outcomes as it has been suggested for prion diseases. Can such differences explain the diversity of disease manifestations and help to stratify patients?

To test this hypothesis, we will characterise oligomers, study their aggregation behaviour and investigate their relevance in processes linked to disease. We will develop highly sensitive biosensors that can recognise discrete forms of alpha-synuclein (and other proteins of interest). By rapid screening of patient samples, we can try to link clinical notes with any prevalent single oligomer or a specific mixture of species. If distinct "oligomer signatures" point towards specific disease type or status, it could be possible to tailor therapies. This information can inform vaccine designs that target discrete oligomers and could lead to personalised treatments opportunities for people. Nuanced and balanced appreciation of oligomer subtypes and diversity within patient samples is missing from the diagnostic landscape. Novel biosensors can be rapidly used at point-of-care to support medical diagnosis and enrich clinical notes.

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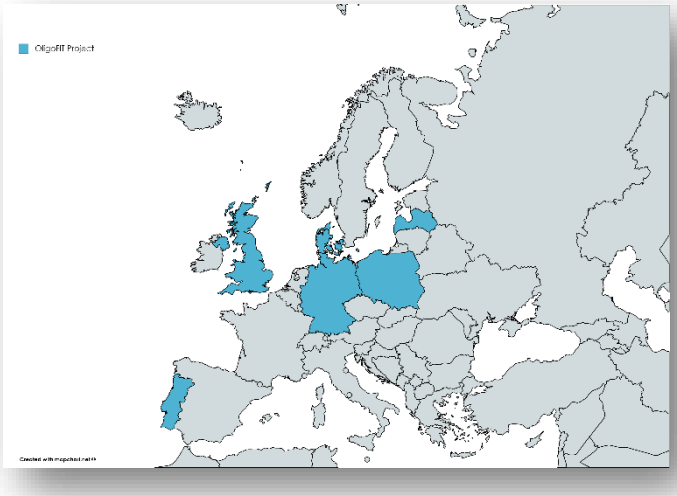


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