

## **APGeM**

Pre-clinical genotype-phenotype predictors of Alzheimer's disease and other dementias

Alzheimer's disease, Lewy-body dementias (including Parkinson's disease) and other neurodegenerative dementias are major causes of disease, reduced patient- and caregiver quality of life, and increasing societal health costs. All have lengthy (decades) pre-dementia- and pre-clinical stages, but patients will have suffered irreversible brain damage and destruction of centres essential for memory, planning and independent daily activities before reaching dementia.

Close to dementia, disease progression accelerates and multiple disease mechanisms typical for each disease drive disease progression. To intervene prior to irreversible brain damage, we must identify disease activity much earlier, and differentiate the initial disease mechanisms eliciting the disease.

To accomplish this, APGeM will exploit new techniques for gene analysis that identify genetic (pre-morbid) risk factors, taking into account effects of multiple genes and small risk contributions from many genes. This information will be coupled to early pre-clinical and pre-dementia disease phenotypes, acquired from new advanced imaging techniques (PET and MRI), and neurochemistry. The significance of risk prediction from this early geno- and phenotype-matching will be evaluated in longitudinal clinical studies in participating countries.

In addition to the funded partners (below), essential contributions to genetics and imaging come from Icelandic and Czech partners (Hreinn Stefánsson and Irena Rektorová). Expected final results are early detection both of disease activity, and of disease mechanisms for individual patients. Hopefully, this will pave the way for future focused and individualized intervention.

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<sup>\*</sup> Contributions from participating JPND Member Countries are currently being finalised for this project