EMIF Deliverable 3.13: 10 Assays of biomarkers for clinical use

Executive summary

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EMIF-MBD sought to identify protein biomarkers, building on pre-existing data and samples and utilising pre-established data nominating markers for replication. In total 34 previously nominated protein targets were assayed in EMIF-MBD using a combination of immunocapture platforms. Following analysis, seven proteins were predictive of amyloid positivity with an AUC of >0.7 in both APOE +ve and –ve individuals. This indicates that these biomarkers are of utility for recruitment to clinical trials to reduce screen failure rate when seeking participants for disease modification studies. These data are being submitted for publication, the abstract of which is copied below:

A minimally invasive and cost-effective blood biomarker of Alzheimer's disease pathology could facilitate clinical trials by contributing to rapid and effective selection of research participants. We have previously investigated, discovered and replicated plasma protein biomarkers that could be used to triage potential participants for PET or CSF measures of AD pathology. The EMIF-AD multimodal biomarker discovery study sought to undertake further replication of these candidate plasma biomarkers in a large, pragmatic multi-centre, multi-cohort sample collection. Targeted plasma analyses of thirty-four proteins with prior evidence for prediction of pathology were conducted in up to 1000 samples from cognitively healthy elderly individuals, people with mild cognitive impairment and in patients with mild AD dementia, selected from the EMIF catalogue seeking to balance amyloid positive and negative individuals. Proteins were measured using Luminex xMAP, ELISA and Meso Scale Discovery assays. Seven proteins replicated in their biomarker ability to predict amyloid pathology, remaining significant after multiple testing corrections ($q<0.05$). These seven proteins form a biomarker panel that, along with age, could significantly discriminate between individuals with high and low amyloid pathology with an area under the curve (AUC) of 0.74. The performance of this biomarker panel remained consistent when tested in APOE □4 non-carrier individuals only (AUC = 0.74). These seven proteins form a biomarker panel that is the product of over a decade of research, is biologically relevant and measurable using practical immunocapture arrays and could significantly reduce the cost incurred to clinical trials through screen failure due to absence of amyloid pathology.

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