DETECTION OF B-AMYLOID AGGREGATES IN CSF FROM TRANSGENIC ANIMAL MODELS OF ALZHEIMER’S DISEASE USING THE AMORFIX AGGREGATED ABETA ASSAY (A4)

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Introduction: The accumulation of β-amyloid (Aβ) aggregates is a hallmark of Alzheimer’s Disease (AD) in humans, and a number of animal models have been developed to mimic AD pathology. Changes in CSF levels of Aβ are considered useful biomarkers for evaluating therapeutic efficacy in pre-clinical animal trials. The A4 was developed to provide a quantitative method for detection of aggregated species of Aβ in brain, plasma, and CSF from animal models of AD.

Methods: Tests were performed on pooled CSF, as well as CSF obtained from individual animals. Aggregated Aβ was isolated using an affinity-based enrichment method. Aβ was released with disaggregants and detected using an ultra-sensitive immunoassay using the N-terminal antibody 4G10 and C-terminal antibodies 1F8 and/or 2H12.

Results: Aggregated Aβ was detected in CSF from transgenic mouse and rat models of AD as early as 4 months of age whereas there was no detectable signal in CSF from non-transgenic animals. We also observed an age-dependent increase in aggregates.

Conclusions: The A4 provides an immunochemical method for early detection and quantification of aggregated Aβ in CSF from transgenic mouse and rat models of AD. The A4 quantitatively measures changes in aggregated Aβ and provides a means to screen lead compounds early in disease progression. This should reduce the overall time and cost for pre-clinical trials and provide a novel measurement of therapeutic efficacy. The identification of aggregated Aβ in CSF supports development of the aggregated peptide as a biomarker for diagnosis and clinical monitoring of human Alzheimer’s disease.