NOVEL BIOMARKER ASSAY FOR AMYLOID-B PROTOFIBRILS THAT AVOIDS INTERFERENCE BY TREATMENT ANTIBODY

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Introduction: Soluble amyloid-β (Aβ) oligomers/protofibrils have been suggested to play a central role in the pathogenesis of Alzheimer’s disease. mAb158 is a conformation-selective monoclonal antibody with high affinity for Aβ protofibrils. The previously developed mAb158-based sandwich ELISA specifically detects Aβ protofibrils in biological samples without interference from Aβ monomers or the amyloid precursor protein (APP). The mAb158-based sandwich ELISA is suitable for measuring clearance of soluble Aβ protofibrils in brain TBS extracts from mAb158 treated mice, since the levels of treatment antibody in these samples are very low. However, in CSF, where mAb158 concentrations are relatively high, changes in Aβ protofibril levels cannot be reliably determined by the mAb158-based protofibril ELISA due to potential assay-interference by the treatment antibody.

Aim: To develop an alternative mAb158-based method for detecting Aβ protofibril clearance in biological samples, while avoiding interference by treatment antibody.

Method: This pull-down method is based on a two-step immunoprecipitation, in which mAb158 is added to mAb158-treated and placebo-treated samples in excess. Hence, mAb158-treated and placebo-treated samples can be regarded as equal, and interference by the treatment antibody is avoided.

Results: Brain TBS extracts were analyzed by the mAb158-based protofibril ELISA and the novel mAb158 pull-down biomarker assay in parallel. Importantly, both assays were able to detect significant and comparable reductions of soluble Aβ protofibrils in mAb158-treated tg-APP\textsubscript{ArcSwe} mice compared to placebo-treated mice.

Conclusion: The novel mAb158-based biomarker assay presented here is able to detect true Aβ protofibril clearance in biological samples, while avoiding interference by the treatment antibody.