IN VIVO AND EX VIVO IMAGING OF AMYLOID BETA CASCADE AGGREGATES WITH A PRONUCLEON™ PEPTIDE IN EXPERIMENTAL ALZHEIMER'S DISEASE (AD) MOUSE MODEL

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Introduction: Accumulation of amyloid beta (Ab) cascade elements are considered hallmarks in AD. Aggregation and deposition of Ab in vivo may precede clinical symptoms by many years. Imaging of Amyloid aggregates (AG) could therefore provide earlier diagnostic utility for early AD. We demonstrate that a novel Pronucleon™ peptide that preferentially binds to AG could serve for neuroimaging of plaque in AD mouse models.

Aims: The primary objective was to develop and deploy an imaging agent that will provide an early measure of AG and plaque burden in a relevant AD model.

Methods: Pronucleon™ peptide that identifies AG was first examined as an ex vivo stain for amyloid plaques. Transgenic mouse brains (APP Swedish/London mutation) and human AD post-mortem sections were co-stained with ThioS and anti-amyloid antibody (6E10) to verify and quantify plaque burden. Pronucleon™ was administered (intranasal or intravenous) in the hAPP transgenic mice that developed extensive plaque pathology. Sections were subjected to ex vivo analyses of ThioS and 6E10 staining. Fluorescence microscopy was used to demonstrate that Pronucleon™ peptides adhere to Ab aggregates and plaques.

Results and conclusions: Ex vivo (mice AD model and human) and in vivo (mice AD model) exposure to Pronucleon™ peptide labeled plaques ex vivo in the hippocampus and cortex. A significant positive correlation was observed between Pronucleon™ peptide labeling and ThioS staining. These data suggest that the Pronucleon™ peptide can efficiently cross the blood brain barrier, label plaque Ab elements and that Pronucleon™ may serve for in vivo AD plaque imaging in humans.