Beta-Amyloid 1–42

Alzheimer's disease (AD) is a complex progressive neurodegenerative disease that affects approximately 14 million people in Europe and the United States, including almost one-half of the population aged 85 years and over (43%).

Alzheimer's disease is the most common cause of dementia and it is characterized by a neuroaxonal and synaptic degeneration that is accompanied by intraneuronal neurofibrillary tangles and the accumulation of extracellular plaques in specific brain regions. These features are reflected in the AD cerebrospinal fluid (CSF) by decreased concentrations of β(beta)-amyloid 1-42. β-amyloid is produced by the proteolytic cleavage of amyloid precursor protein, which is a large transmembrane protein that appears to be involved in synaptic plasticity and learning. The cleavage of this protein generates varying lengths of β-amyloid peptides (38–43 amino acids) that accumulate in the extracellular space to form extracellular plaques. Of these peptides, β-amyloid 1–42 (Aβ42) is the major form that is associated with AD.

β-amyloid 1-42 as a biomarker in diagnostics

CSF levels of Aβ42 have been shown to have diagnostic utility for discriminating AD dementia cases from cognitively normal controls at the earliest stages of the disease progression. Aβ42 drops significantly 5-10 years prior to the establishment of cognitive impairment symptoms. Aβ42 can be used for diagnostics of AD in both the prodromal and dementia stage of the disease, and it is now included in the diagnostic research criteria for AD.

Monoclonal antibodies specific to β-amyloid 1-42

We provide well-characterized human beta-amyloid-specific mouse monoclonal antibodies (MAbs) for the detection of Aβ42 in human CSF. These antibodies were developed against synthetic peptides that correspond to fragments of the Aβ42 sequence.

Quantitative and highly specific sandwich immunoassays for β-amyloid 1-42

We recommend two MAb combinations for the development of a sandwich immunoassay to measure Aβ42 in human CSF samples: BAM7cc–BAM113cc and BAM7cc–BAM120cc. Both of the Hytest assay prototypes are capable of detecting native β-amyloid in human CSF. Limit of detection values are provided in Table 1.

The specificity of assays BAM7cc-BAM113cc and BAM7cc-BAM120cc was confirmed using different synthetic human β-amyloid peptides. Cross-reactivity to Aβ40, Aβ41 and Aβ43 was measured at concentration of 50 ng/ml of each tested peptide and was found to be very low as denoted in Table 2.

Table 1.
Recommended capture-detection pairs. Data is based on the results that were obtained using a sandwich chemiluminescence immunoassay (CLIA).

Capture MAb	Detection MAb	LoD (pg/ml)
BAM7cc	BAM113cc	5.3
BAM7cc	BAM120cc	13.4

CLINICAL UTILITY
- **Alzheimer's disease**

The calibration curves for the prototype assays are provided in Figure 1.

Table 2.
Cross-reactivity of the prototype assays to different synthetic human β-amyloid peptides.

Synthetic peptide	BAM7cc-BAM113cc	BAM7cc-BAM120cc
β-amyloid 1-40 (Aβ40)	0.01%	0.004%
β-amyloid 1-41 (Aβ41)	0.6%	0.4%
β-amyloid 1-43 (Aβ43)	0.11%	0.07%

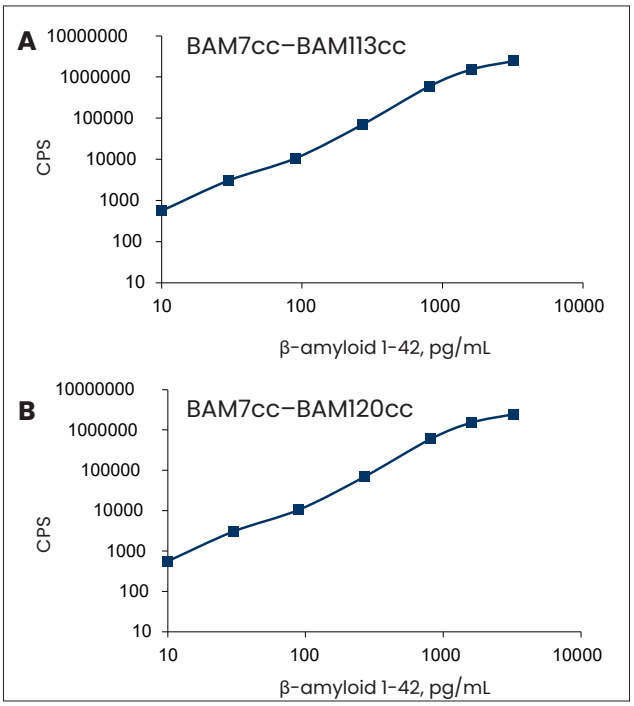

Figure 1.
Calibration curves for the MAb pairs BAM7cc– BAM113cc (A) and BAM7cc-BAM120cc (B). The capture antibody BAM7cc was coated onto a Costar EIA/RIA black plate in PBS and incubated at RT for 40 minutes. Synthetic human β-amyloid 1-42 (AnaSpec Cat.# AS-24224) and the biotinylated detection MAb BAM120cc (or BAM 113cc) were diluted in a PBS buffer containing 7.5% BSA and 0.1% Tween20, and incubated for 1 hour at RT. After washing, the plates were incubated with Streptavidin poly-HRP for 5 minutes and washed again. SuperSignal ELISA Femto Maximum Sensitivity Substrate was added, and the luminescence was measured using a Victor Multi Label Counter.

Measuring patient CSF samples

In order to conduct correlation studies between Hytest's assay prototypes and the commercially available INNOTEST® β-AMYLOID(1-42) assay, we obtained CSF samples from 30 patients of different ages (ranging from 45 to 90 years).

Figure 2 shows the correlation studies between the prototype immunoassays and INNOTEST β-AMYLOID(1-42).

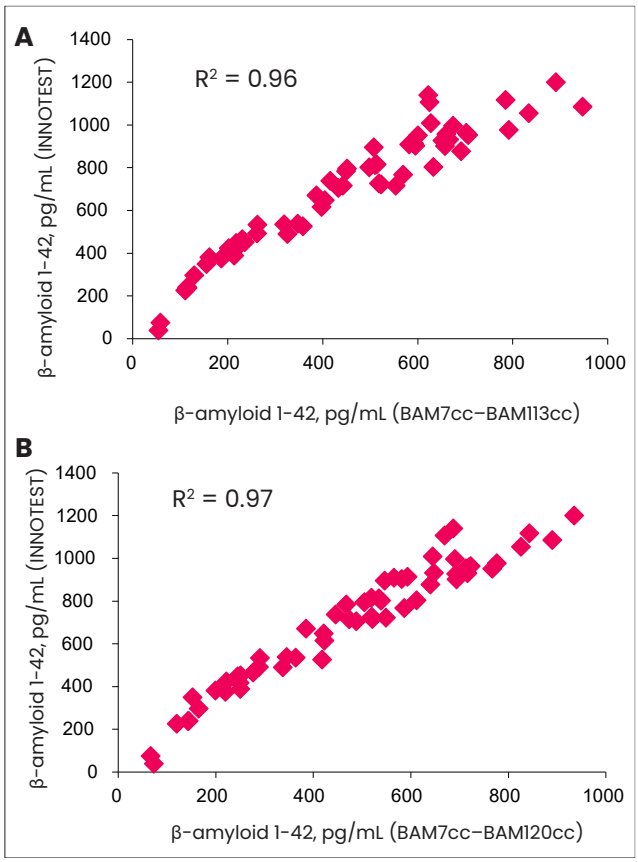

Figure 2.
Correlation studies between the immunoassays BAM7cc–BAM113cc (A) and BAM7cc–BAM120cc (B) and INNOTEST β-AMYLOID(1-42) assay. The correlation coefficients (Pearson) between the assays and the INNOTEST assay are provided in the picture.

ORDERING INFORMATION

MONOCLONAL ANTIBODIES

Product name	Cat. #	MAb	Subclass	Remarks
Beta-amyloid, human	4BA3	BAM7cc	IgG1	*In vitro*, EIA
		BAM113cc	IgG1	*In vitro*, EIA
		BAM120cc	IgG1	*In vitro*, EIA

HYTEST LTD
Intelligate 1, 6th floor, Joukahaisenkatu 6 • FI-20520 Turku, FINLAND
Tel. +358 2 512 0900 • E-mail: hytest@hytest.fi • HYTEST.FI