



A β -40 (AMYLOID BETA PROTEINS 40)

The Singulex A β -40 and A β -42 assays allow the quantification of amyloid beta proteins from human plasma with exceptional sensitivity, enabling use of A β -40/A β -42 as a velocity biomarker in Alzheimer's disease studies and to evaluate therapeutic interventions.

BIOLOGY AND DISEASES

Amyloid beta proteins (40 and 42 amino acids) are the main constituent of amyloid plaques in the brains of Alzheimer's disease (AD) patients. In healthy and disease states A β -40 is the more common form (10–20X higher than A β -42) of the two in both cerebrospinal fluid (CSF) and plasma. In patients with AD, A β -42 primarily aggregates and deposits in the brain forming plaques. Thus the concentration of A β -42 is decreased in the CSF of many AD patients. Recent studies suggest that a decrease in A β -42 concentrations (with a paralleled change in the ratio of A β -40/A β -42) in CSF and plasma are predictive of the onset of AD.

THERAPIES

There is no cure for Alzheimer's disease and currently available therapeutics minimize some symptoms but do not slow disease progression. Numerous experimental approaches focus on minimizing A β -42 levels by preventing production or lowering A β -42 concentrations, and stimulating the immune system to attack A β proteins as well as preventing A β proteins from aggregating and forming plaques. An important component in designing therapeutic trials is to identify patients who are at risk for developing AD, such that studies can be performed in a cost effective and timely manner. Hence these biomarkers would be invaluable for understanding A β levels as surrogate endpoints, allowing efficient study design.

UNMET NEED

Preventive therapy is a major focus as the best way to manage AD. Guidelines describe the need for noninvasive biomarkers that can be used to predict and diagnose AD. Such information will be invaluable for clinical study design, as well as the evaluation of therapeutic effectiveness. Measuring A β -40 and A β -42 concentrations in plasma may provide such information. In healthy normal humans, plasma concentrations range from 200–400 pg/mL (A β -40) and 15–30 pg/mL (A β -42). However with AD, A β -42 levels decrease, often undetectable by currently available EIA technology. Furthermore, interventional strategies based on depleting A β -42 formation require methods that measure decreases in A β -42. Thus there is a need to accurately and precisely quantify low concentrations of amyloid proteins in plasma.

SINGULEX ANSWER

The Singulex A β -40 and A β -42 assays allow for the quantification of very low levels and changes of amyloid beta proteins in plasma. These measurements provide promise for more efficient clinical study design and assessment of therapeutic efficacy. The assays quantify as little as 0.1 pg/mL A β -42 and 10 pg/mL A β -40 (<20% CV). This enables accurate quantification of A β proteins in healthy states and the accurate assessment of A β -42 velocity with respect to disease progression and therapeutic intervention. The Singulex A β -40 and A β -42 assays have been validated for use in cerebrospinal fluid.

This assay will allow investigators to:

1. Identify subjects with potential high risk for developing AD and identify subjects in early phases of disease development.
2. Design more robust clinical and preclinical studies when A β protein concentrations are used as a therapeutic endpoint.
3. Understand how A β protein levels change in humans as they transition from healthy to diseased states.

ERENNA TECHNOLOGY ACCESS PROGRAM.

Through the Erenna Technology Access Program (ETAP), Singulex offers an interactive, results-driven solution to biomarker challenges faced by the pharmaceutical industry during product development. Singulex assists the development programs of our ETAP collaborators by developing customer-driven assays and access to a menu of fully-validated assays. Participants in ETAP gain access to the Singulex Erenna Immunoassay System, our proven expertise developing high-value immunoassays and our world-class customer support. Together with Singulex, our ETAP collaborators are expanding the utility of protein biomarkers and using them as tools to measure disease progression, drug efficacy and toxicity.

TABLE 1: Specifications of Singulex Aβ-40 and Aβ-42 assays.

Attribute	Aβ-40 Assay	Aβ-42 Assay
LoD	6 pg/mL	0.1 pg/mL
LLoQ	12.5 pg/mL	0.5 pg/mL
Range	6–3000 pg/mL	0.1–250 pg/mL
Healthy human plasma levels: avg (range)	400 pg/mL (175–858 pg/mL)	15.8 pg/mL (18.5–35.1 pg/mL)

Erenna® System

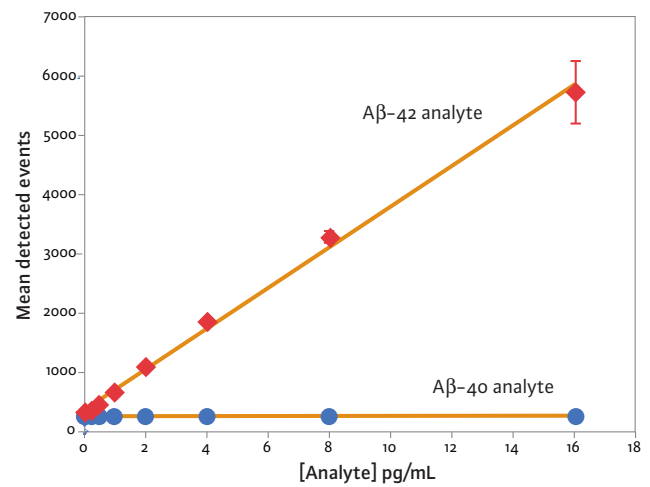
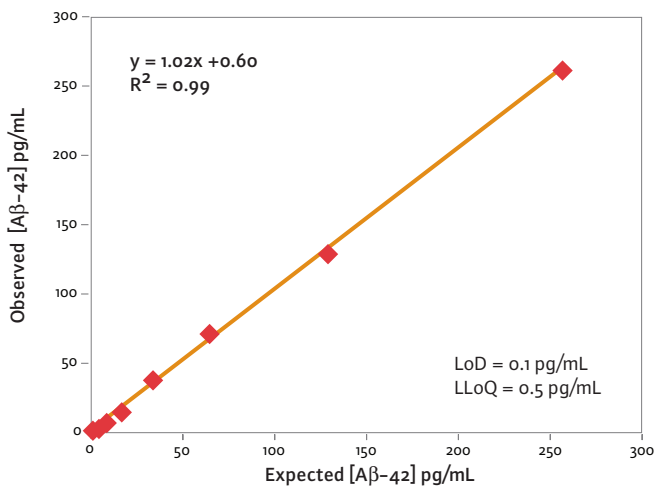
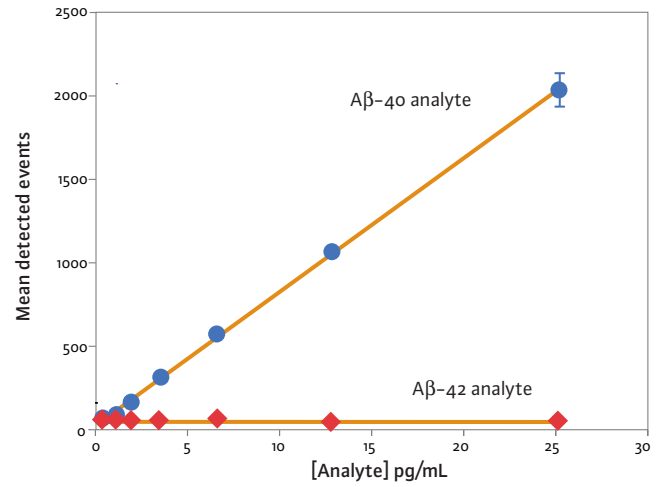
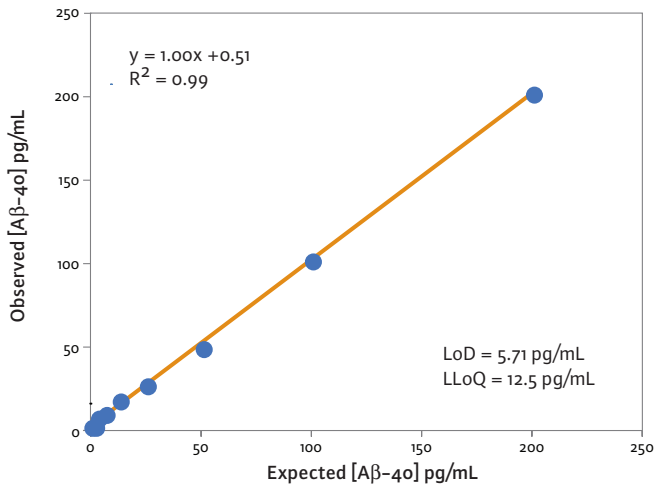


FIGURE 1: Aβ-40 and Aβ-42 assays standard curve data.

FIGURE 2: Specificity and linearity of Aβ-40 and Aβ-42 assays.

These standard curves are for representational purposes only. A standard curve must be run with each assay.

Copyright © 2009, Singulex Inc. Singulex and Erenna are trademarks of Singulex, Inc.