Araclon Biotech
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ABtest® Service

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Araclon Biotech

Company Information

Araclon Biotech

Mission is to research and develop immunotherapies and diagnostic methods used in the treatment of degenerative diseases.

Key Facts

- Araclon has been an affiliate of Grifols Group since March 2012

- Araclon is based in Spain and in the US.

- A company dedicated to the research and development of therapies and diagnostic methods to be applied to degenerative diseases, currently focusing on Alzheimer's disease

- Current lines of investigation are:

  1. Early diagnosis of Alzheimer's disease
  2. Therapy for Alzheimer's disease (preventive immunotherapy).
  3. Development of a therapy against Parkinson's disease.
  4. Searching of biomarkers for Fibromyalgia.

ABtest® Service

Comprehensive and direct quantification of **beta-amyloid** 1-40, and 1-42

Araclon Biotech

Our product:

A service for the quantification of Aβ in blood

Aβ**FP**
Beta-amyloid peptide free in plasma

Aβ**PB**
Beta-amyloid peptide bound to plasma components

Aβ total in Plasma

ABtest Service: For the quantification of Aβ40 and Aβ42 for both free and total fractions in plasma.

- An ELISA colorimetric assay, coupled with an automated testing system
- All components developed in-house
- As a Service we can control the conditions of each and every test.

# ABtest40 and ABtest42. Validation parameters

Accuracy

Precision was assessed with the same five samples repeated in the same and additional runs with 3 different ABtest batches. The coefficient of variation was always below 10%, for all intra-assay, inter-assay and inter-batch, in the entire range of concentration levels of the assay.

Abtest kits are specific for the target Aβ40 or Aβ42, with no cross-reactivity with similar molecules . Other Aβ peptides do not produce a signal including Aβ40 in ABtest42 and viceversa. LLOQ for ABtest40 is 7.6pg/ml and 3.6pg/ml for ABtest42. This has been empirically validated following Clinical and Laboratory Institute guidelines.

ABtest40. accuracy

ABtest42. accuracy
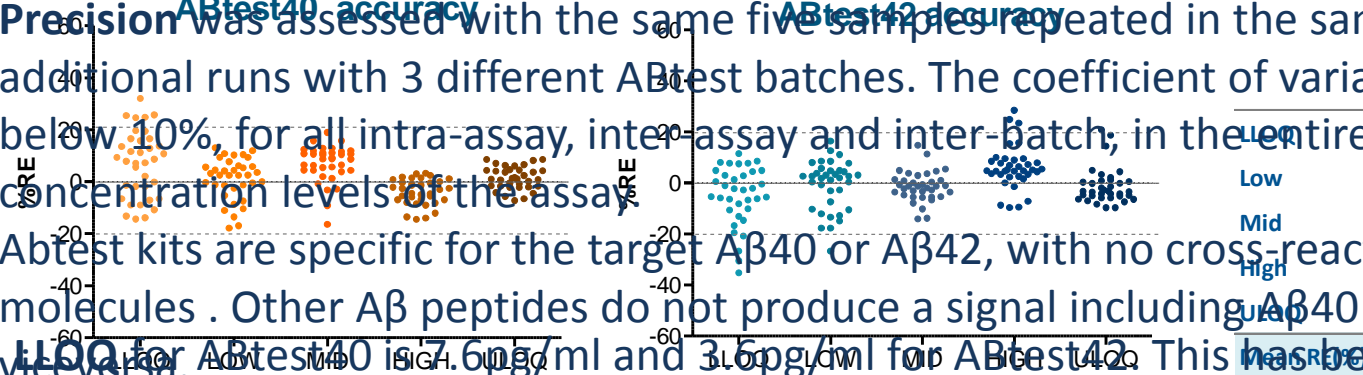
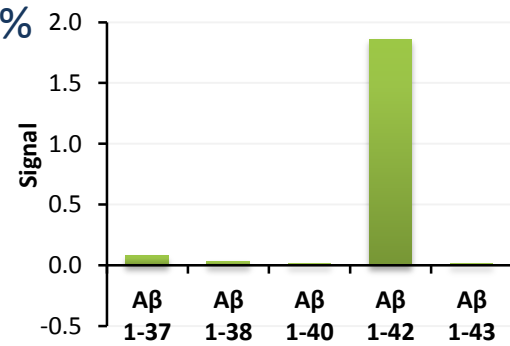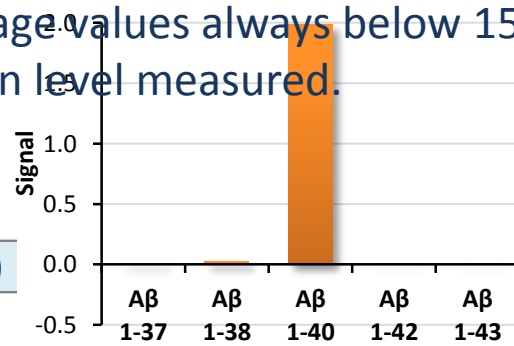|	Accuracy (RE, %)	
	ABtest40	ABtest42
Low	11.2	10.4
Low	6.5	7.5
Mid	8.8	4.5
High	4.8	8.0
High	3.2	5.3
Mean RE%	6.9	7.1

Precision

Accuracy was evaluated with five samples covering the entire quantification range of the assay. The relative error was within the acceptance criteria, with average values always below 15% independent the concentration level measured.

Precision Summary	ABtest40	ABtest42
Intra-assay CV (%)	5.8	5.4
Inter-assay CV (%)	7.7	7.5
Inter-batch CV (%)	4.4	9.8

Specificity

ABtest40: C-terminal Aβ

ABtest42: C-terminal Aβ

Sensitivity

	LLOQ	Precision (CV)	Accuracy (RE)
ABtest40	7.60pg/ml	21.6%	3.4%
ABtest42	3.60pg/ml	18.1%	16.8%

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Ratios v PET from AIBL Collaboration
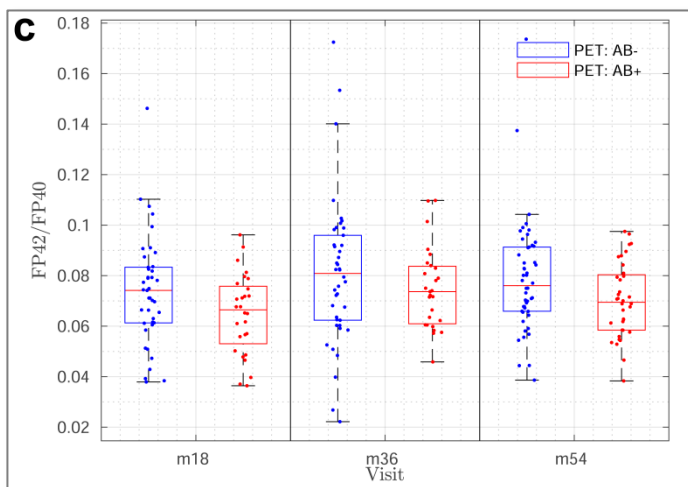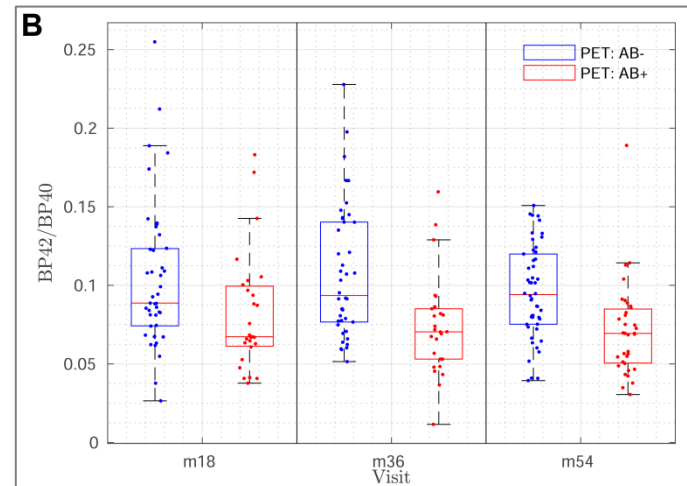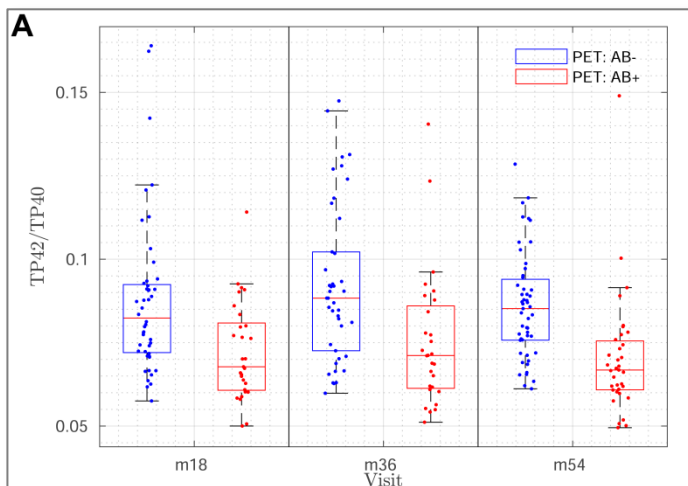
- We analyzed plasma samples from 104 healthy control individuals at the 18, 36 and 54 month time points (55 with 3 a-PET scans, 13 with 2 a-PET scans and 36 with 1 a-PET; from visit 2 to visit 4).
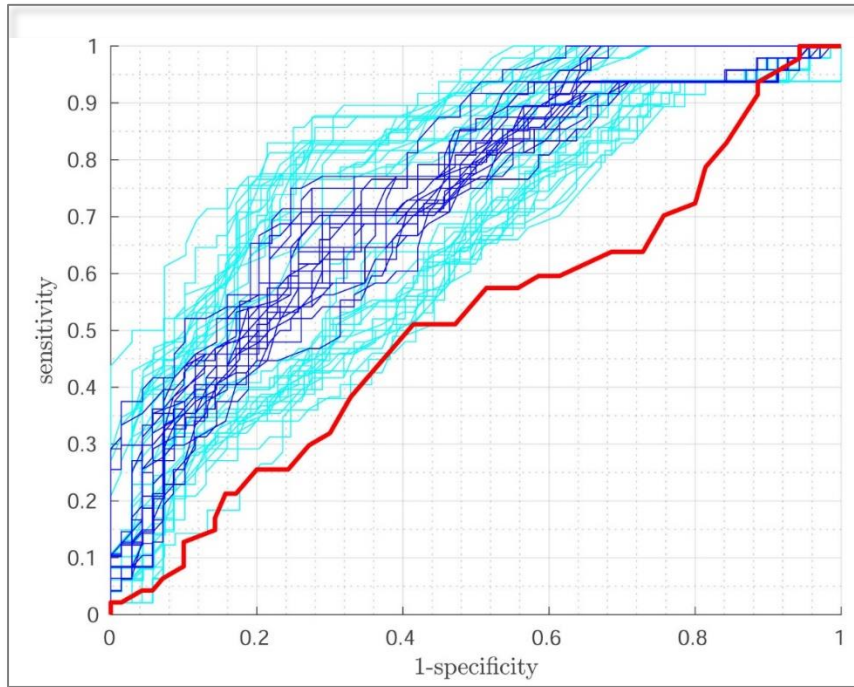
- The plasma assays were performed blinded to the characteristics of the individuals
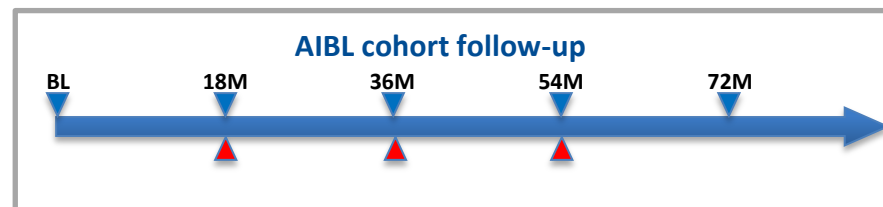
ROC comparison: AIBL

Model: Age + APOE4
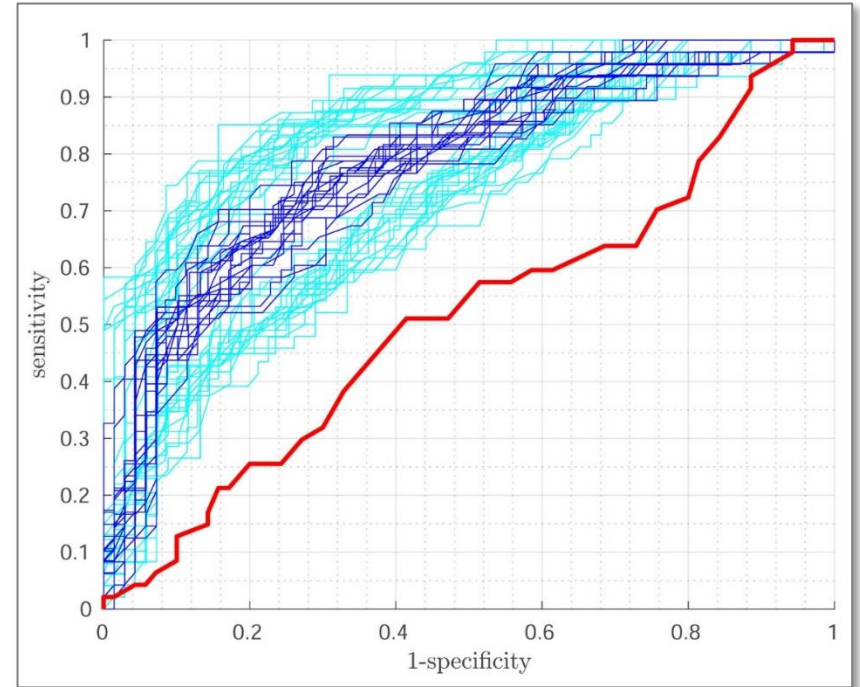
Model: log(TP42/40) + Age + APOE4

Optimization of PPV: AIBL

ABtest PPV model:
Optimized ABtest PPV with relation to prevalence and a model using APOE4 status and age.

AB255 – A multi center ABtest trial

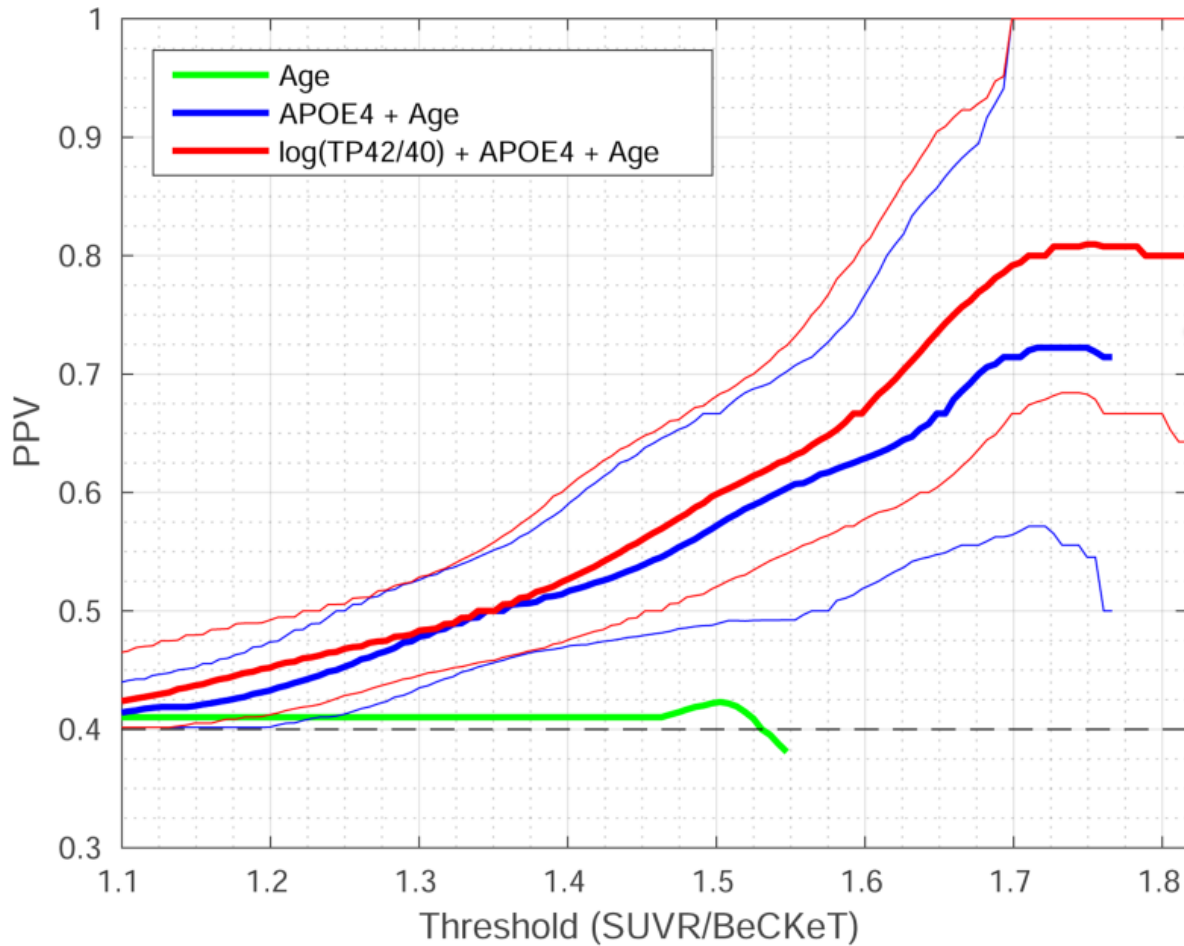| N	Baseline	12 months	24 months
HC	83	80	76
MCI-FDGneg	104	96	91
MCI-FDGpos	39	31	30

Correlation FDG / ABtest: An inverse relationship between TP42/40 and risk of AD as measured by FDG PET, supporting amyloid PET findings.
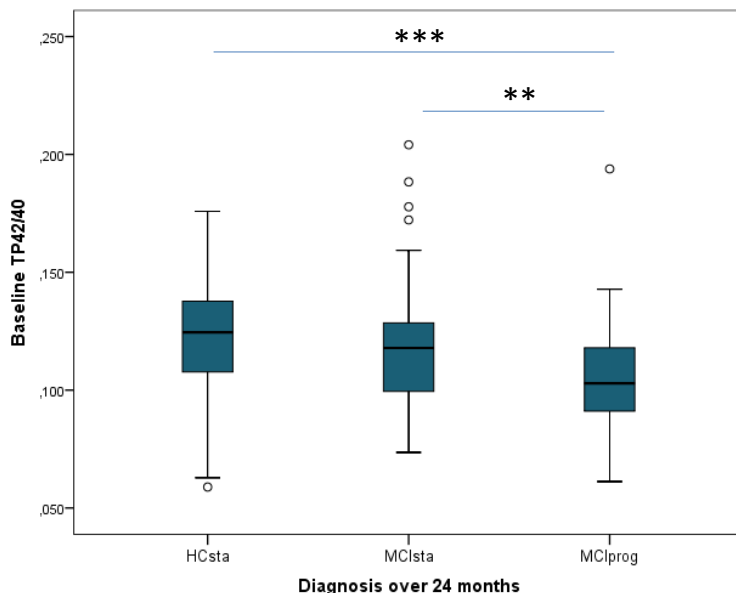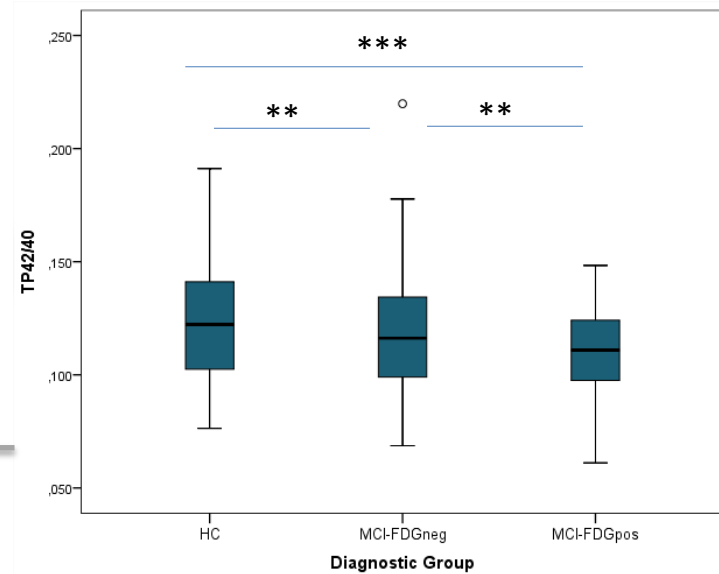
Progressors vs Stable: Baseline levels of TP42/40 are predictive of MCI who later progress to AD in the 24 months follow up, progressors have significantly lower levels of TP42/40 at baseline.

* = p<0.05; ** = p<0.01; *** = p<0.001 In U Mann-Whitney test

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Plasma biomarkers in middle-aged individuals at risk for Alzheimer Disease (ACS-Araclon study).

P value for the interaction term between the plasma variable and the central biomarker (slope or intercept).

ACS	TP42 / TP40 P value	FP42 / TP42 P value
MCSUVR intercept	0.022	nsa
MCSUVR slope	nsa	0.00081
CSF Aβ42 intercept	0.0251	0.0238
CSF Aβ42 slope	nsa	nsa
Tau intercept	0.0292	nsa
Tau slope	0.00307	0.000876
pTau intercept	0.0324	nsa
pTau slope	0.000572	0.0066

MCSUVR; mean cortical standardized uptake value ratio.
(positivity defined as > 1.42). **nsa**: no significant association.

ACS linear mixed-effects models adjusted for: time, ApoE genotype, age, gender and family history (+/-).
AIBL linear mixed-effects models adjusted for: time, ApoE genotype.
ACS age ± SD at base line: 62 ± 8: AIBL age ± SD at base line: 72 ± 7.
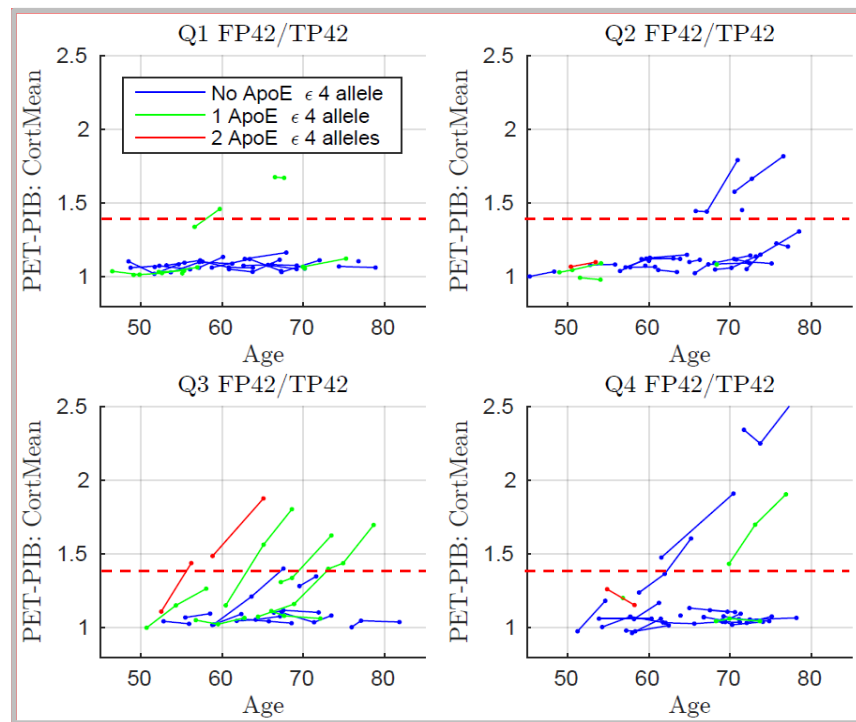
Fundació ACE Healthy Brain Initiative (FACEHBI): a longitudinal study of biomarkers and cognition in individuals with subjective cognitive decline

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O. Rodríguez-Gómez[1], A. Sanabria[1], A. Pérez-Cordón[1], S. Ruiz[1], M. Tarragona,[1] D. Sánchez-Ruíz[1], J. Pavía[2], F. Campos[2], A. Vivas[3], M. Gómez[3], M. Tejero[3], M. Alegret[1], A. Espinosa[1], G. Ortega[1] C. Abdelnour[1], I. Hernández[1], A. Ruiz[1], J. Giménez[3], F. Lomeña[2], L. Tárraga[1], O. Sotolongo-Grau[1], M. Boada[1][1]
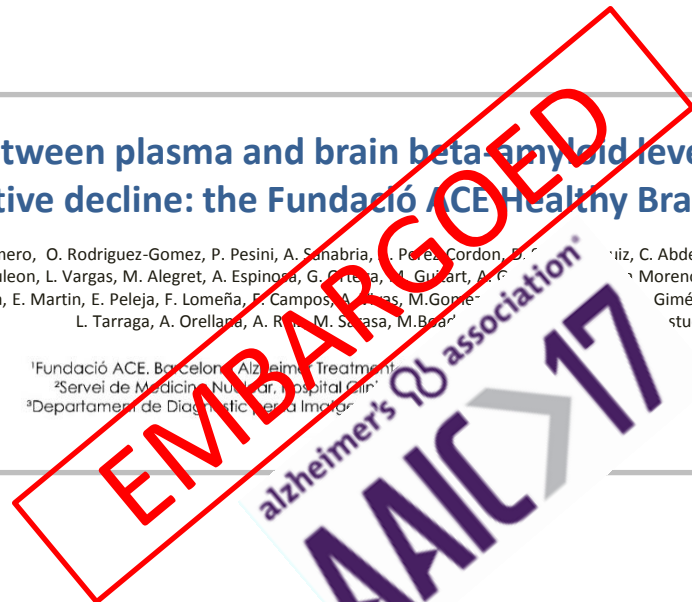
[1]Fundació ACE. Barcelona Alzheimer Treatment & Research Center, Barcelona,
[2]Servei de Medicina Nuclear, Hospital Clínic i Provincial. Barcelona, Spain
[3]Departament de Diagnòstic per la Imatge. Clínica Corachan, Barcelona, Spain

Correlations between plasma and brain beta-amyloid levels in individuals with subjective cognitive decline: the Fundació ACE Healthy Brain Initiative (FACEHBI).

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Itziar de Rojas, J. Romero, O. Rodriguez-Gomez, P. Pesini, A. Sanabria, A. Pérez Cordon, D. Sánchez Ruiz, C. Abdelnour, S. Valero, I. Hernandez, M. Rosende-Roca, A. Mauleon, L. Vargas, M. Alegret, A. Espinosa, G. Ortega, M. Guitart, A. Gailhajanet, Moreno Grau, O. Sotolongo-Grau, S. Ruiz, M. Tarragona, J. Serra, E. Martin, E. Peleja, F. Lomeña, F. Campos, A. Vivas, M.Gomez, M. Tejero, J. Giménez, V. Pérez-Grijalba, G.Martinez, L. Tarraga, A. Orellana, A. Ruiz, M. Sarasa, M.Boada, and the FACEHBI study.

[1]Fundació ACE. Barcelona Alzheimer Treatment
[2]Servei de Medicina Nuclear, Hospital Clínic
[3]Departament de Diagnòstic per la Imatge.

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Regulatory
Pathway

Regulatory Pathway:

Europe: CE Marked IVD for the quantification of beta amyloid proteins in blood.

USA: 1. CLIA Lab (San Marcos, Texas)
        2. LDT
        3. IUO
        4. Mid to long term goal is to have ABtest positioned as an IVD as an effective intervention becomes available.

Supporting Material: AIBL, ACS, ADNI, A4, LEARN, DPUK, EPAD, FACEHBI, AB255 and others.

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AIBL-Araclon-ACS-AB255-FACEHBI plasma Aβ biomarkers studies

CONCLUSIONS

- ✓ The TP42/40 ratio shows promise as a useful first-step screening tool for cohort enrichment in clinical trials to recruit individuals at increased risk of developing Alzheimer's disease.

- ✓ The TP42/40 shows promise as a tool to enrich cohorts for amyloid PET positivity

- ✓ Evaluation of plasma FP42/TP42 may be informative as a first-step screening tool to identify preclinical AD in cognitively normal middle-aged individuals.

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Availability

Availability:

We do not sell kits, we provide a service.

The ABtest Service is commercially accessible from anywhere in the world. We have two approved laboratories, Zaragoza, Spain and San Marcos, Texas.

Samples can be shipped in from anywhere in the world at -80ºC