DOI: 10.1002/alz70856_105032

BIOMARKERS

POSTER PRESENTATION

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

BIOMARKERS (NON-NEUROIMAGING)

Biomarkers and proteomics in amyloid PET negative persons with clinical signs of MCI or mild dementia

Richard Mohs[1] | Douglas W. Beauregard[1] | Allan I. Levey[2] | Erik C.B. Johnson[3] | Jessie Nicodemus-Johnson[4] | Robin Wolz[5] | John Dwyer[1]

[1]Global Alzheimer's Platform Foundation, Washington, DC, USA

[2]Emory University School of Medicine, Atlanta, GA, USA

[3]Goizueta Alzheimer's Disease Research Center, Atlanta, GA, USA

[4]Pentara Corporation, Salt Lake City, UT, USA

[5]IXICO, London, London, United Kingdom

Correspondence
Richard Mohs, Global Alzheimer's Platform Foundation, Washington, DC, USA.
Email: mohsrichard@yahoo.com

Abstract

Background: Screening for clinical trials identifies persons with clinical symptoms of Mild Cognitive Impairment (MCI) or Alzheimer's disease (AD) but no amyloid on PET. We compared blood biomarkers and proteomics in these screen failures with cognitively normal, amyloid PET negative persons and with amyloid PET positive MCI or mild AD patients.

Method: We analyzed data from 296 persons with clinical symptoms of MCI or mild AD from the Bio-Hermes study who were amyloid PET negative (MCI + AD AB-); we compared them with 313 Bio-Hermes participants who were cognitively normal and amyloid PET negative (CN AB-) and with 258 amyloid PET positive persons with clinical MCI or mild AD (MCI + AD AB+). Measures included regional amyloid PET, plasma A-beta40 and 42, total tau, *p*-tau 181, *p*-tau 217, NfL, GFAP, a panel of 69 cytokines (Fireplex) and 7596 proteins from the Somalogic panel.

Result: Relative to the CN AB- group, the MCI + AD AB- group were older, more cognitvely and functionally impaired, had slightly less education and were more likely to be non-white; the groups did not differ in gender or APOE4 rates. The groups did not differ on amyloid SUVR, *p*-tau 217, t-tau or GFAP. NfL was higher in MCI + AD AB- persons compared with CN AB- persons (Table 1 and 2). After using a False Discovery Rate adjustment there were no Somalogic proteins significantly different in MCI + AD AB- participants vs CN AB- participants. Several proteins were different in amyloid PET positive persons compared with amyloid PET negative parsons (Figure 1).

Conclusion: NfL data indicate very significant neurodegeneration in symptomatic but amyloid PET negative clinical trial screen failures. Biomarkers reflecting amyloid and tau were not different and the proteomics profile did not find specific abnormalities in amyloid negative, symptomatic persons.

Table 1. Blood-based Biomarkers

		Cognitively Normal		Cognitively Impaired	
		CN Aβ- (N=313)	CN Aβ+ (N=84)	MCI + Mild AD Aβ- (N=296)	MCI + Mild AD Aβ+ (N=258)
Biomarker	**Lab**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
P-tau217 (U/mL)	Lilly	0.17 (0.06)	0.28 (0.10)	0.21 (0.14)	0.44 (0.26)
P-tau217 (ng/mL)	Gothenburg	2.11 (1.44)	3.50 (1.52)	2.49 (2.24)	4.81 (2.50)
T-tau (ng/L)	Quanterix	2.19 (2.19)	2.17 (0.98)	2.71 (6.77)	2.04 (1.00)
sNfL (pg/mL)	Merck	23.59 (13.03)	28.97 (14.71)	33.77 (30.89)	40.45 (28.38)
	Quanterix	21.22 (12.17)	25.80 (13.04)	30.44 (31.57)	36.23 (27.03)
	Roche	2.76 (1.48)	3.24 (1.85)	3.57 (3.00)	4.59 (3.55)
GFAP (pg/mL)	Merck	136.92 (68.83)	203.53 (102.95)	161.58 (157.38)	252.70 (118.24)
	Quanterix	122.23 (63.21)	181.38 (97.49)	146.53 (151.54)	230.16 (111.30)
	Roche	87.27 (44.26)	130.24 (72.99)	100.93 (95.06)	157.70 (66.83)

Abbreviations: CN, cognitively normal; MCI, mild cognitive impairment; AD, Alzheimer's disease; SD, standard deviation; P-tau217, phosphorylated tau 217, T-tau, total tau, GFAP, glial fibrillary acetic protein; NfL, neurofilament light

((Data source: file t_2_item_35_biomarker.rtf Jan 21))

Table 2. Blood-based Biomarkers Comparisons – Adjusted P Values for Multiple Comparisons

Populations Compared		CN Aβ+	MCI + Mild AD Aβ-	MCI + Mild AD Aβ-	MCI + Mild AD Aβ-	MCI + Mild AD Aβ+	MCI + Mild AD Aβ+
	Versus	**CN Aβ-**	**CN Aβ-**	**MCI + Mild AD Aβ+**	**CN Aβ+**	**CN Aβ-**	**CN Aβ+**
Biomarker	**Lab**						
P-tau217 (F=100.105; P<.0001)	Lilly	<.0001	0.1702	<.0001	0.0192	<.0001	<.0001
P-tau217 (F=79.512; P<.0001)	Gothenburg	<.0001	0.3421	<.0001	0.0004	<.0001	<.0001
T-tau F=1.473 (NS)	Quanterix	-	-	-	-	-	-
NfL (F=13.051; P<.0001)	Merck	0.8066	0.0003	0.1354	0.2619	<.0001	0.0059
NfL (F=10.638; P<.0001)	Quanterix	0.9113	0.0011	0.2579	0.2539	<.0001	0.0118
NfL (F=12.873; P<.0001)	Roche	0.9197	0.0259	0.0029	0.5996	<.0001	0.0018
GFAP (F=34.157; P<.0001)	Merck	0.0010	0.3410	<.0001	0.0415	0.0059	<.0001
GFAP (F=31.872; P<.0001)	Quanterix	0.0036	0.2866	<.0001	0.1141	<.0001	0.0106
GFAP (F=36.774; P<.0001)	Roche	0.0002	0.4109	<.0001	0.0093	<.0001	0.0361

Abbreviations: P-tau217, phosphorylated tau 217, T-tau, total tau; Nfl, neurofilament light; GFAP, GFAP, glial fibrillary acetic protein
Note: All other cytokines compared for populations listed were nonsignificant.

((Data source: file t_2_item_36_biomarkerstat.rtf Jan 21))

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

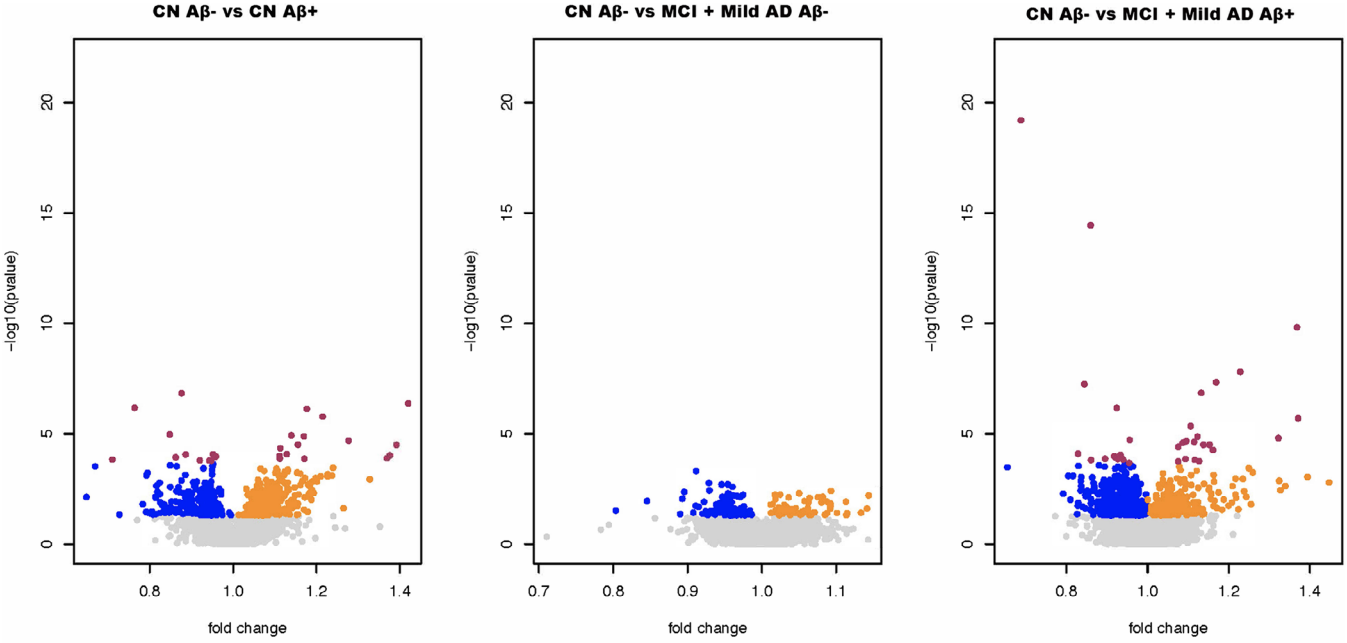

Figure 1: Proteomics Group Comparisons; Beyond FDR in Purple