

Supplementary data:

Table S1: result of group comparisons of proteins levels		
	<i>Plasma Protein</i>	<i>p value</i>
Cross-sectional	Apolipoprotein A-II (Apo A-II) (ng/ml)	0.0002
	Brain Natriuretic Peptide (BNP) (pg/ml)	0.0008
	Placenta Growth Factor (PLGF) (pg/ml)	0.0008
	Apolipoprotein E (Apo E) (ug/ml)	0.0013
	Alpha-1-Microglobulin (A1Micro) (ug/ml)	0.0034
	Interleukin-16 (IL-16) (pg/mL)	0.0034
	Serum Glutamic Oxaloacetic Transaminase (ug/mL)	0.0034
	Immunoglobulin M (IGM) (mg/mL)	0.0038
	Peptide YY (PYY) (pg/mL)	0.0040
	Eotaxin-3 (pg/mL)	0.0067
	Tenascin-C (TN-C) (ng/mL)	0.0067
	Alpha-2-Macroglobulin (A2Macro) (mg/mL)	0.0196
	Receptor for advanced glycosylation end (ng/mL)	0.0224
	Transthyretin (TTR) (mg/dl)	0.0224
	Pancreatic Polypeptide (PPP) (pg/ml)	0.0239
	Vitronectin (ug/ml)	0.0404
	Pregnancy-Associated Plasma Protein A (P (mIU/mL)	0.0412
	Thyroxine-Binding Globulin (TBG) (ug/mL)	0.0430
	Longitudinal	Matrix Metalloproteinase-10 (MMP-10) (ng/ml)
Angiotensin-Converting Enzyme (ACE) (ng/ml)		<0.0001
Alpha-1-Microglobulin (A1Micro) (ug/ml)		<0.0001

Apolipoprotein A-II (Apo A-II) (ng/ml)	<0.0001
TNF-Related Apoptosis-Inducing Ligand Re (ng/mL)	<0.0001
Factor VII (ng/mL)	<0.0001
AXL Receptor Tyrosine Kinase (AXL) (ng/mL)	<0.0001
Kidney Injury Molecule-1 (KIM-1) (ng/ml)	<0.0001
Transthyretin (TTR) (mg/dl)	<0.0001
Intercellular Adhesion Molecule 1 (ICAM- (ng/mL)	<0.0001
Interleukin-3 (IL-3) (ng/mL)	<0.0001
Placenta Growth Factor (PLGF) (pg/ml)	<0.0001
Sortilin (ng/mL)	<0.0001
Fibroblast Growth Factor 4 (FGF-4) (pg/mL)	<0.0001
Bone Morphogenetic Protein 6 (BMP-6) (ng/mL)	<0.0001
Trefoil Factor 3 (TFF3) (ug/ml)	<0.0001
Apolipoprotein D (Apo D) (ug/ml)	<0.0001
Thymus-Expressed Chemokine (TECK) (ng/mL)	0.0001
Tumor Necrosis Factor Receptor-Like 2 (T (ng/mL)	0.0001
Matrix Metalloproteinase-9 (MMP-9) (ng/mL)	0.0002
Macrophage Inflammatory Protein-3 alpha (pg/ml)	0.0003
Interleukin-16 (IL-16) (pg/mL)	0.0004
Monokine Induced by Gamma Interferon (MI (pg/ml)	0.0005
C-peptide (ng/ml)	0.0006
T Lymphocyte-Secreted Protein I-309 (I-3 (pg/mL)	0.0007
Testosterone- Total (ng/ml)	0.0007
Ciliary Neurotrophic Factor (CNTF) (pg/mL)	0.0007
Vascular Cell Adhesion Molecule-1 (VCAM- (ng/mL)	0.0011

L eptin (ng/mL)	0.0018
Neuronal Cell Adhesion Molecule (Nr-CAM) (ng/mL)	0.0022
Creatine Kinase-MB (CK-MB) (ng/mL)	0.0025
Cancer Antigen 19-9 (CA-19-9) (U/mL)	0.0026
CD40 Ligand (CD40-L) (ng/mL)	0.0029
Epidermal Growth Factor Receptor (EGFR) (ng/mL)	0.0031
Apolipoprotein C-III (Apo C-III) (ug/mL)	0.0043
Fatty Acid-Binding Protein- heart (FABP) (ng/mL)	0.0045
Immunoglobulin E (IgE) (ng/mL)	0.0053
Follicle-Stimulating Hormone (FSH) (mIU/mL)	0.0061
Peptide YY (PYY) (pg/mL)	0.0063
Chemokine CC-4 (HCC-4) (ng/mL)	0.0064
Epidermal Growth Factor (EGF) (pg/mL)	0.0073
Resistin (ng/ml)	0.0076
Insulin-like Growth Factor-Binding Prote (ng/mL)	0.0086
Interleukin-13 (IL-13) (pg/mL)	0.0087
E-Selectin (ng/mL)	0.0096
Myoglobin (ng/mL)	0.0105
Eotaxin-3 (pg/mL)	0.0195
von Willebrand Factor (vWF) (ug/mL)	0.0195
Heparin-Binding EGF-Like Growth Factor ((pg/mL)	0.0203
Superoxide Dismutase 1- Soluble (SOD-1) (ng/mL)	0.0245
Eotaxin-1 (pg/mL)	0.0300
Agouti-Related Protein (AGRP) (pg/mL)	0.0314
Prolactin (PRL) (ng/ml)	0.0314

Apolipoprotein(a) (Lp(a)) (ug/mL)	0.0377
Monocyte Chemotactic Protein 3 (MCP-3) (pg/mL)	0.0391
B Lymphocyte Chemoattractant (BLC) (pg/ml)	0.0392
Serum Glutamic Oxaloacetic Transaminase (ug/mL)	0.0421
Ferritin (FRTN) (ng/mL)	0.0464
Pulmonary and Activation-Regulated Chemo (ng/mL)	0.0464
Stem Cell Factor (SCF) (pg/mL)	0.0464
Tissue Inhibitor of Metalloproteinases 1 (ng/mL)	0.0464
Apolipoprotein A-I (Apo A-I) (mg/mL)	0.0466

Table S2: Cross sectional mean protein concentration					
Group		N	Mean	SD	SEM
Alpha-2-Macroglobulin (A2Macro) (mg/mL)	HC	49	0.02	0.11	0.02
	AD↑	85	0.08	0.09	0.01
Brain Natriuretic Peptide (BNP) (pg/ml)	HC	49	2.76	0.37	0.05
	AD↑	85	3.06	0.33	0.04
Eotaxin-3 (pg/mL)	HC	49	2.37	0.42	0.06
	AD↑	85	2.62	0.24	0.03
Immunoglobulin M (IgM) (mg/mL)	HC	49	0.38	0.25	0.04
	AD↓	85	0.21	0.24	0.03
Interleukin-16 (IL-16) (pg/mL)	HC	49	2.62	0.12	0.02
	AD↓	85	2.53	0.14	0.02
Pancreatic Polypeptide (PPP) (pg/ml)	HC	49	1.98	0.32	0.05
	AD↑	85	2.17	0.37	0.04
Peptide YY (PYY) (pg/mL)	HC	49	1.86	0.30	0.04
	AD↑	85	2.08	0.34	0.04
Thyroxine-Binding Globulin (TBG) (ug/mL)	HC	49	1.76	0.10	0.01
	AD↑	85	1.81	0.09	0.01
Apolipoprotein A-II (Apo A-II) (ng/ml)	HC	49	2.78	0.10	0.01
	AD↓	85	2.69	0.09	0.01
Placenta Growth Factor (PLGF) (pg/ml)	HC	49	36.96	10.57	1.51
	AD↓	85	26.89	15.40	1.67
Apolipoprotein E (Apo E) (ug/ml)	HC	49	1.85	0.15	0.02
	AD↓	85	1.72	0.20	0.02
Alpha-1-Microglobulin (A1Micro) (ug/ml)	HC	49	1.05	0.11	0.02
	AD↑	85	1.12	0.10	0.01
Serum Glutamic Oxaloacetic Transaminase (ug/mL)	HC	49	3.64	1.08	0.15
	AD↓	85	2.93	0.80	0.09

Table S3: Longitudinal mean protein concentration change over 1 year					
Group		N	Mean	SD	SEM
Alpha-1-Microglobulin (A1Micro) (ug/ml)	AD	85	-0.08	0.09	0.01
	HC	49	0.04	0.09	0.01
Angiotensin-Converting Enzyme (ACE) (ng/ml)	AD	85	0.02	0.09	0.01
	HC	49	-0.08	0.06	0.01
Agouti-Related Protein (AGRP) (pg/mL)	AD	85	-0.03	0.27	0.03
	HC	49	0.08	0.21	0.03
Apolipoprotein A-I (Apo A-I) (mg/mL)	AD	85	0.00	0.10	0.01
	HC	49	-0.05	0.11	0.02
Apolipoprotein A-II (Apo A-II) (ng/ml)	AD	85	0.01	0.13	0.01
	HC	49	-0.14	0.10	0.01
Apolipoprotein C-III (Apo C-III) (ug/mL)	AD	85	0.01	0.13	0.01
	HC	49	-0.08	0.16	0.02
Apolipoprotein D (Apo D) (ug/ml)	AD	85	-0.09	0.09	0.01
	HC	49	0.00	0.11	0.02
AXL Receptor Tyrosine Kinase (AXL) (ng/mL)	AD	85	-0.02	0.08	0.01
	HC	49	-0.09	0.07	0.01
B Lymphocyte Chemoattractant (BLC) (pg/ml)	AD	85	-0.04	0.13	0.01
	HC	49	-0.11	0.17	0.02
Bone Morphogenetic Protein 6 (BMP-6) (ng/mL)	AD	85	-0.16	0.34	0.04
	HC	49	0.06	0.14	0.02
Cancer Antigen 19-9 (CA-19-9) (U/mL)	AD	85	0.05	0.16	0.02
	HC	49	-0.04	0.13	0.02
CD40 Ligand (CD40-L) (ng/mL)	AD	85	0.13	0.45	0.05
	HC	49	-0.15	0.44	0.06
Creatine Kinase-MB (CK-MB) (ng/mL)	AD	85	-0.10	0.20	0.02
	HC	49	0.03	0.20	0.03
Ciliary Neurotrophic Factor (CNTF) (pg/mL)	AD	85	-0.11	0.35	0.04
	HC	49	0.09	0.24	0.03
C-peptide (ng/ml)	AD	85	0.04	0.19	0.02
	HC	49	-0.07	0.14	0.02
Epidermal Growth Factor (EGF) (pg/mL)	AD	85	0.09	0.55	0.06
	HC	49	-0.19	0.47	0.07
Epidermal Growth Factor Receptor (EGFR) (ng/mL)	AD	85	-0.37	0.88	0.09
	HC	49	0.10	0.66	0.09
Eotaxin-1 (pg/mL)	AD	85	0.08	0.22	0.02
	HC	49	-0.01	0.17	0.02
Eotaxin-3 (pg/mL)	AD	85	-0.16	0.29	0.03
	HC	49	-0.03	0.27	0.04
E-Selectin (ng/mL)	AD	85	-0.10	1.31	0.14
	HC	49	0.61	1.31	0.19
Fatty Acid-Binding Protein- heart (FABP) (ng/mL)	AD	85	0.00	0.29	0.03
	HC	49	-0.15	0.24	0.03
Factor VII (ng/mL)	AD	85	0.00	0.14	0.02
	HC	49	-0.11	0.07	0.01

Fibroblast Growth Factor 4 (FGF-4) (pg/mL)	AD	85	-0.07	0.36	0.04
	HC	49	0.19	0.23	0.03
Ferritin (FRTN) (ng/mL)	AD	85	-0.07	0.23	0.03
	HC	49	0.04	0.28	0.04
Follicle-Stimulating Hormone (FSH) (mIU/mL)	AD	85	0.04	0.08	0.01
	HC	49	-0.02	0.11	0.02
Heparin-Binding EGF-Like Growth Factor (pg/mL)	AD	85	-0.03	0.41	0.04
	HC	49	0.15	0.34	0.05
Chemokine CC-4 (HCC-4) (ng/mL)	AD	85	-0.01	0.12	0.01
	HC	49	-0.07	0.09	0.01
T Lymphocyte-Secreted Protein I-309 (I-3) (pg/mL)	AD	85	-0.04	0.23	0.02
	HC	49	0.09	0.14	0.02
Intercellular Adhesion Molecule 1 (ICAM-1) (ng/mL)	AD	85	-0.01	0.12	0.01
	HC	49	-0.12	0.11	0.02
Immunoglobulin E (IgE) (ng/mL)	AD	85	-0.01	0.26	0.03
	HC	49	-0.16	0.24	0.03
Insulin-like Growth Factor-Binding Protein (ng/mL)	AD	85	0.16	0.15	0.02
	HC	49	0.24	0.14	0.02
Interleukin-13 (IL-13) (pg/mL)	AD	85	0.01	0.19	0.02
	HC	49	-0.07	0.14	0.02
Interleukin-16 (IL-16) (pg/mL)	AD	85	0.06	0.20	0.02
	HC	49	-0.04	0.09	0.01
Interleukin-3 (IL-3) (ng/mL)	AD	85	0.07	0.31	0.03
	HC	49	-0.27	0.36	0.05
Kidney Injury Molecule-1 (KIM-1) (ng/ml)	AD	85	-0.28	0.27	0.03
	HC	49	-0.07	0.14	0.02
Leptin (ng/mL)	AD	85	0.04	0.23	0.02
	HC	49	-0.10	0.19	0.03
Apolipoprotein(a) (Lp(a)) (ug/mL)	AD	85	-0.03	0.15	0.02
	HC	49	0.08	0.30	0.04
Monocyte Chemoattractant Protein 3 (MCP-3) (pg/mL)	AD	85	-0.11	0.41	0.04
	HC	49	0.04	0.26	0.04
Monokine Induced by Gamma Interferon (MI) (pg/ml)	AD	85	0.07	0.15	0.02
	HC	49	-0.05	0.17	0.02
Macrophage Inflammatory Protein-3 alpha (pg/ml)	AD	85	-0.08	0.14	0.01
	HC	49	0.03	0.16	0.02
Matrix Metalloproteinase-10 (MMP-10) (ng/ml)	AD	85	-0.09	0.28	0.03
	HC	49	-0.44	0.20	0.03
Matrix Metalloproteinase-9 (MMP-9) (ng/mL)	AD	85	0.07	0.33	0.04
	HC	49	-0.13	0.20	0.03
Myoglobin (ng/mL)	AD	85	-0.04	0.19	0.02
	HC	49	0.06	0.19	0.03
Neuronal Cell Adhesion Molecule (N-CAM) (ng/mL)	AD	85	-0.01	0.31	0.03
	HC	49	-0.14	0.09	0.01
Pulmonary and Activation-Regulated Chemo (ng/mL)	AD	85	-0.05	0.09	0.01
	HC	49	-0.08	0.08	0.01
Placenta Growth Factor (PLGF) (pg/ml)	AD	85	11.47	19.64	2.13

	HC	49	-6.77	18.18	2.60
Prolactin (PRL) (ng/ml)	AD	85	0.00	0.16	0.02
	HC	49	-0.07	0.12	0.02
Peptide YY (PYY) (pg/mL)	AD	85	-0.09	0.28	0.03
	HC	49	0.08	0.30	0.04
Resistin (ng/ml)	AD	85	0.03	0.15	0.02
	HC	49	-0.03	0.08	0.01
Stem Cell Factor (SCF) (pg/mL)	AD	85	0.04	0.19	0.02
	HC	49	-0.03	0.15	0.02
Serum Glutamic Oxaloacetic Transaminase (ug/mL)	AD	85	1.57	3.85	0.42
	HC	49	0.47	1.25	0.18
Superoxide Dismutase 1- Soluble (SOD-1) (ng/mL)	AD	85	0.02	0.28	0.03
	HC	49	-0.09	0.21	0.03
Sortilin (ng/mL)	AD	85	0.03	0.10	0.01
	HC	49	-0.07	0.11	0.02
Thymus-Expressed Chemokine (TECK) (ng/mL)	AD	85	-0.03	0.11	0.01
	HC	49	-0.13	0.13	0.02
Testosterone- Total (ng/ml)	AD	85	0.04	0.48	0.05
	HC	49	-0.26	0.39	0.06
Trefoil Factor 3 (TFF3) (ug/ml)	AD	85	0.05	0.08	0.01
	HC	49	-0.03	0.10	0.01
Tissue Inhibitor of Metalloproteinases 1 (ng/mL)	AD	85	-0.01	0.10	0.01
	HC	49	0.03	0.10	0.01
Tumor Necrosis Factor Receptor-Like 2 (T (ng/mL)	AD	85	0.00	0.10	0.01
	HC	49	0.08	0.09	0.01
TNF-Related Apoptosis-Inducing Ligand Re (ng/mL)	AD	85	-0.04	0.08	0.01
	HC	49	-0.13	0.07	0.01
Transthyretin (TTR) (mg/dl)	AD	85	-0.03	0.13	0.01
	HC	49	-0.14	0.10	0.01
Vascular Cell Adhesion Molecule-1 (VCAM- (ng/mL)	AD	85	-0.02	0.08	0.01
	HC	49	0.04	0.08	0.01
von Willebrand Factor (vWF) (ug/mL)	AD	85	-0.37	0.58	0.06
	HC	49	-0.11	0.50	0.07

IC	Cluster Size	MNI Coordinates			Regions
		X	Y	Z	
A	1332	28	-18	-20	Left and Right Hippocampus, Left Thalamus, Left and Right Parahippocampal Gyri, Temporal Fusiform Gyri, Posterior Cingulate Cortices
	1313	-26	-18	-20	
	157	48	-56	18	
	111	54	-42	6	
	103	50	-44	-22	
	102	0	-32	36	
	100	30	42	26	
B	671	-22	-6	-22	Left and Right Hippocampus, Amygdala, Parahippocampal Gyri, Temporal Fusiform Cortices, Temporal Poles
	515	24	-4	-22	
	109	28	-6	-38	
C	600	24	2	-42	Left and Right Temporal Fusiform Cortices, Parahippocampal gyri, Temporal poles, and Right Inferior Temporal Gyrus
	352	-24	0	-40	
	137	60	-38	-16	
D	2217	62	-44	-12	Right Inferior, Middle and Superior Temporal Gyri, Supramarginal Gyrus, Angular Gyrus
E	585	-6	-22	6	Left and Right Thalamic Nuclei
F	367	-60	-54	-4	Left Middle and Inferior Temporal Gyri, Parahippocampal Gyrus, Temporal Fusiform Cortex
	258	-30	-2	-44	
	352	-24	0	-40	
	137	60	-38	-16	
G	565	-54	0	-22	Right Frontal Pole, Left Temporal Pole, Middle/Superior Temporal Gyri
	107	30	50	14	
H	1570	44	-4	-44	Right Temporal Pole, Middle/Inferior Temporal Gyri, Parahippocampal Gyrus, Temporal Fusiform cortex

IC	Cluster Size	MNI Coordinates			Regions
		X	Y	Z	
A	67	30	-44	-12	Right Temporal Occipital Fusiform Cortex and Lingual Gyrus
B	123	0	-8	36	Left and Right Anterior/Posterior Cingulate Gyri
C	70	-28	-46	-10	Left Temporal Occipital Cortices, Lingual Cortices, Temporal Fusiform Cortices and Parahippocampal Gyri
D	65	20	-4	-20	Left and Right Amygdala
	13	-18	-6	-20	
E	63	16	12	6	Right Caudate and Putamen
F	35	4	-18	38	Left and Right Posterior/Anterior Cingulate Gyri, Left Temporal Fusiform Cortices, Left Parahippocampal Gyrus, Right Amygdala and Middle Temporal Gyrus
	17	-34	-34	-22	
	17	30	2	-22	
	12	62	-6	-18	
G	51	-12	12	0	Left Caudate and Nucleus Accumbens
H	127	0	-30	32	Left and Right Posterior Cingulate Cortices
I	83	-26	-40	-16	Left and Right Temporal Fusiform Cortices, Temporal Occipital Fusiform Cortices, Left Parahippocampal Gyrus and Lingual Gyrus
	12	30	-38	-18	
J	46	-16	16	6	Left Caudate Nucleus
K	127	-16	8	12	Left Caudate, Anterior/Posterior Cingulate Gyrus, Right Amygdala
	14	-2	-2	36	
	14	28	2	-22	
	12	-2	-24	34	
L	99	-30	-50	-14	Left and Right Cingulate Gyri, Left Temporal Occipital and Posterior Fusiform Cortex
	68	0	-20	34	