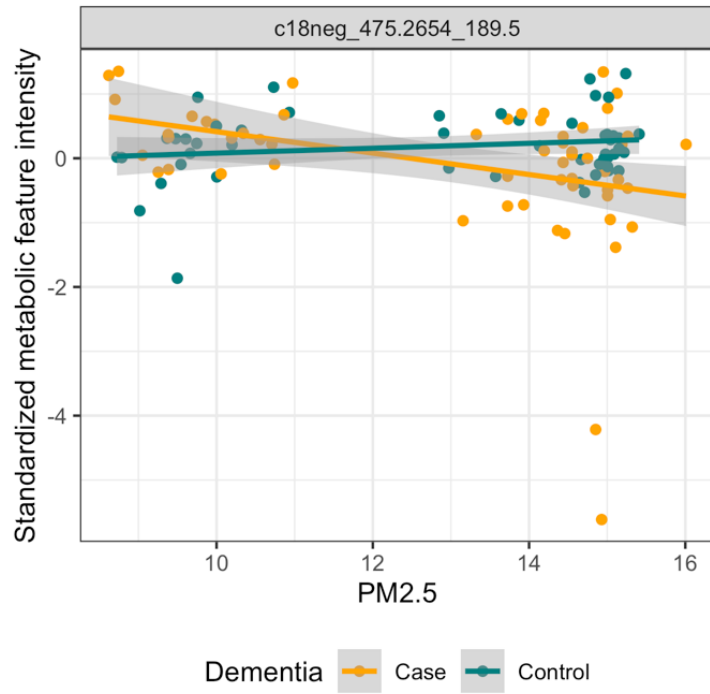


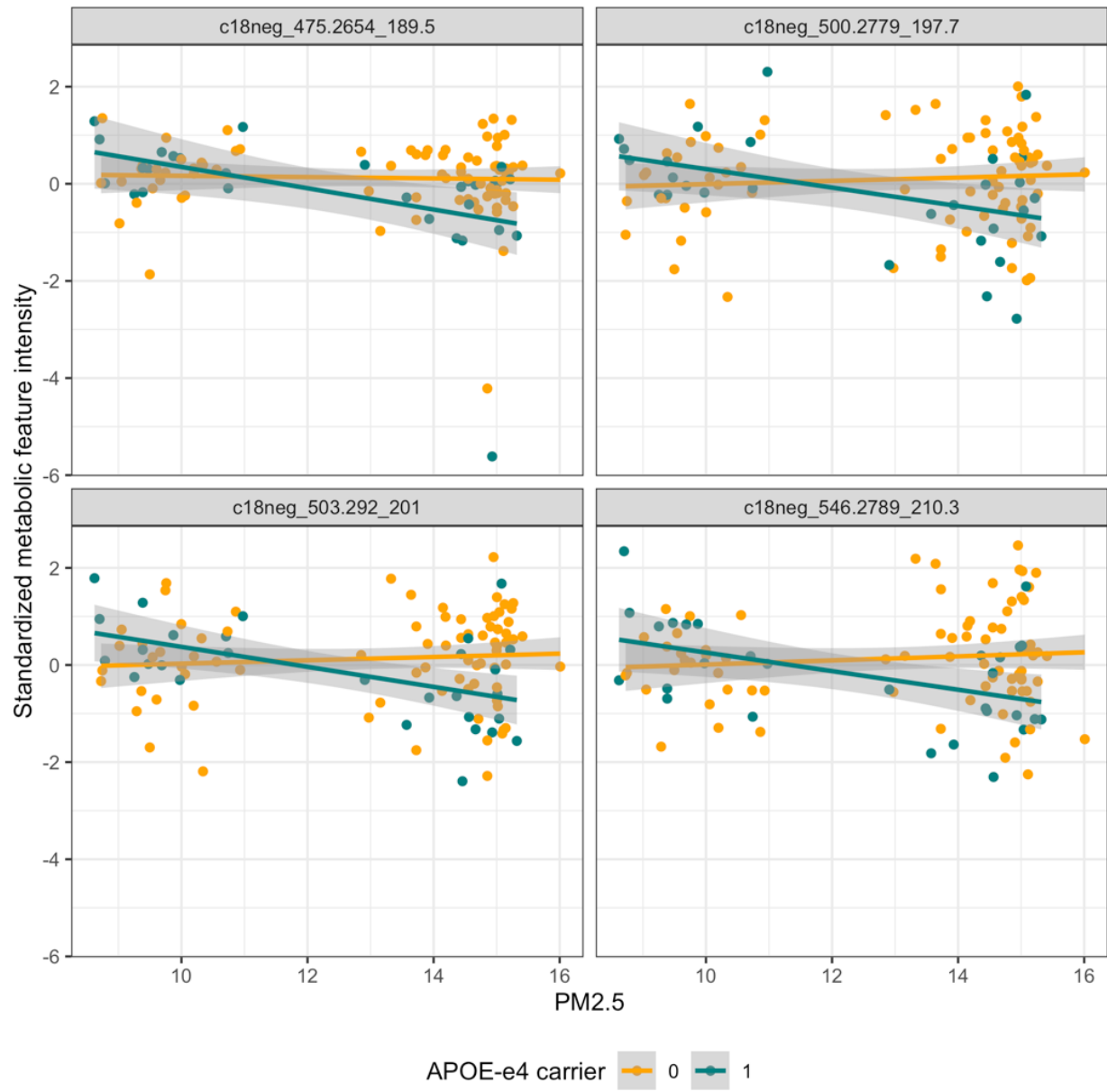
# Supplementary Material

## Linking Air Pollution Exposure to Blood-Based Metabolic Features in a Community-Based Aging Cohort with and without Dementia

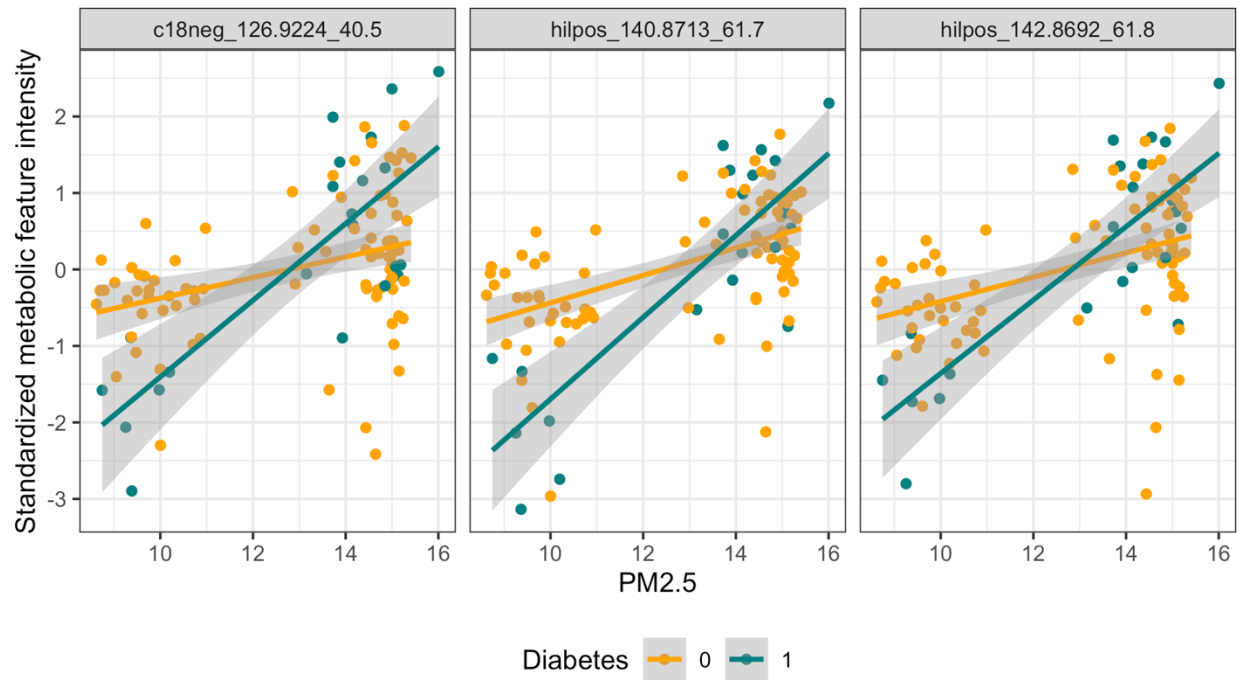
Supplementary Figure 1. Effect modification by Alzheimer's disease



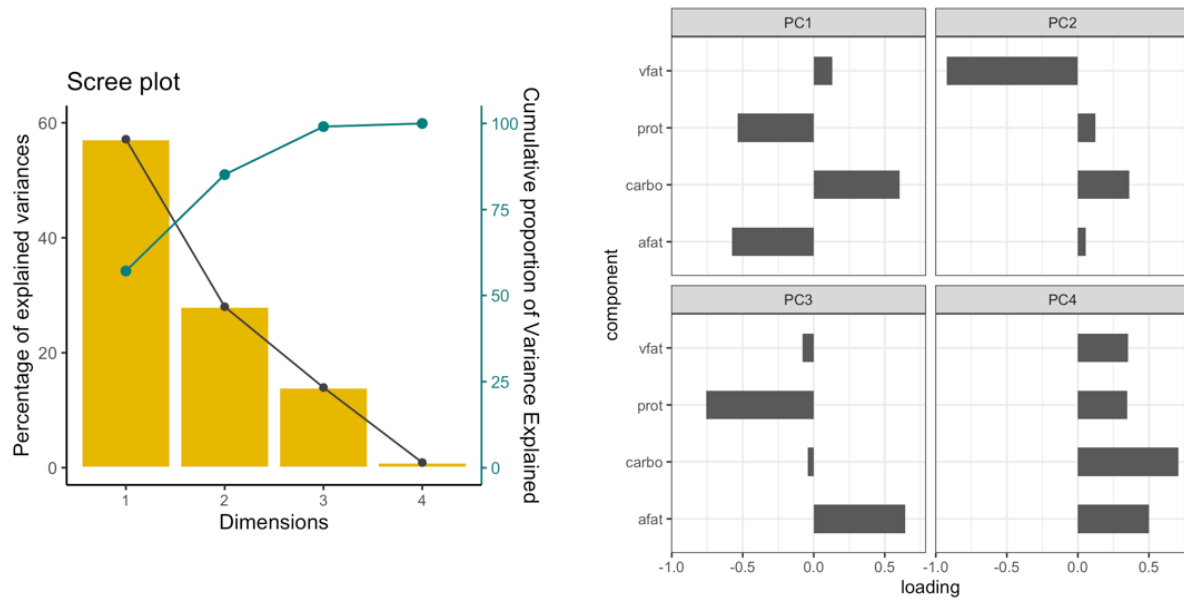
Supplementary Figure 2. Effect modification by *APOE*  $\epsilon 4$  allele status



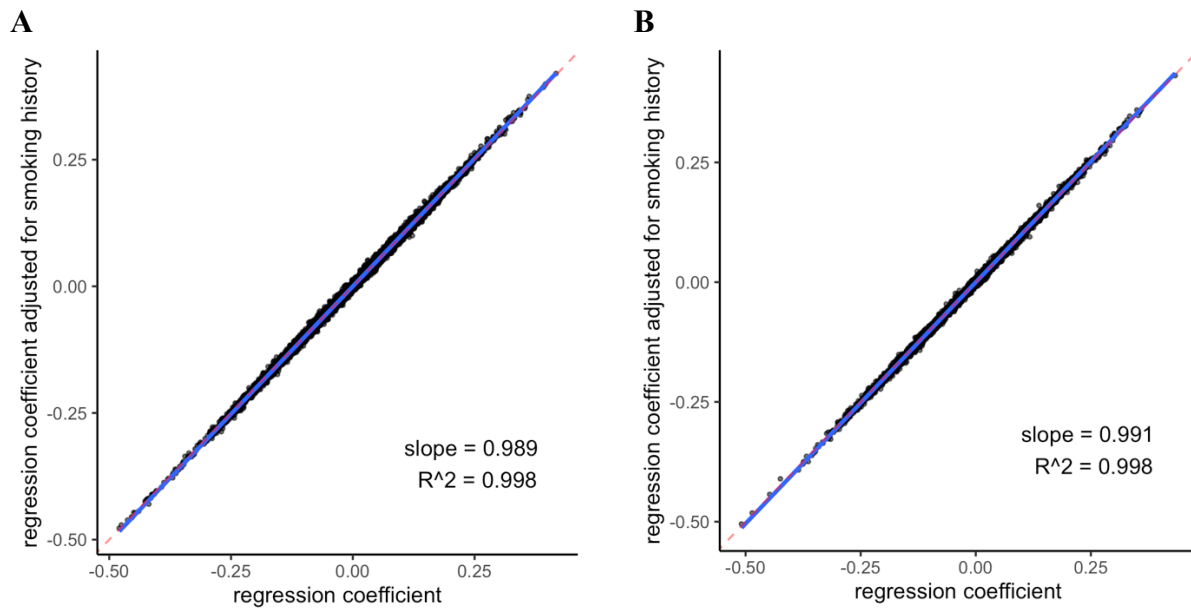
**Supplementary Figure 3.** Effect modification by a history of diabetes



**Supplementary Figure 4.** Principal component analysis of macronutrient dietary data. Vfat, vegetable fat; prot, protein; carbo, carbohydrate; afat, animal fat.



**Supplementary Figure 5.** Sensitivity analysis with smoking history



On the x-axis, regression coefficient for PM<sub>2.5</sub> from model unadjusted for smoking history and on y-axis, regression coefficient for PM<sub>2.5</sub> from model adjusted for smoking history. A) HILIC + data. B) C18 – data.

**Supplementary Table 1.** Characteristics of the study population in the Washington Heights and Inwood Community Aging Project comparing cases and controls of Alzheimer’s disease.

	<b>Case (N=57)</b>	<b>Control (N=50)</b>	<b>Overall (N=107)</b>
<b>Age (y)</b>			
Mean (SD)	86.9 (10.8)	91.7 (2.93)	89.2 (8.44)
<b>Sex</b>			
Women	46 (80.7%)	42 (84.0%)	88 (82.2%)
Men	11 (19.3%)	8 (16.0%)	19 (17.8%)
<b>Racial/Ethnic Group</b>			
Non-Hispanic Black	20 (35.1%)	17 (34.0%)	37 (34.6%)
Non-Hispanic white	19 (33.3%)	17 (34.0%)	36 (33.6%)
Caribbean Hispanic	18 (31.6%)	16 (32.0%)	34 (31.8%)
<b>Education (y)</b>			
Mean (SD)	8.14 (4.66)	10.9 (4.26)	9.42 (4.66)
<b>APOE ε4 carrier</b>			
No ε4 allele	37 (64.9%)	41 (82.0%)	78 (72.9%)
At least one ε4 allele	20 (35.1%)	9 (18.0%)	29 (27.1%)
<b>History of diabetes</b>			
No	42 (73.7%)	43 (86.0%)	85 (79.4%)
Yes	15 (26.3%)	7 (14.0%)	22 (20.6%)
<b>History of heart disease</b>			
No	39 (68.4%)	28 (56.0%)	67 (62.6%)
Yes	18 (31.6%)	22 (44.0%)	40 (37.4%)
<b>History of hypertension</b>			
No	13 (22.8%)	18 (36.0%)	31 (29.0%)
Yes	44 (77.2%)	32 (64.0%)	76 (71.0%)
<b>PM<sub>2.5</sub> (µg/m<sup>3</sup>)</b>			
Mean (SD)	13.0 (2.36)	12.9 (2.48)	12.9 (2.41)
<b>PM<sub>10</sub> (µg/m<sup>3</sup>)</b>			
Mean (SD)	20.7 (7.43)	21.4 (8.12)	21.0 (7.73)
<b>NO<sub>2</sub> (ppb)</b>			
Mean (SD)	31.7 (6.89)	31.7 (7.25)	31.7 (7.03)

**Supplementary Table 2.** Correlation between estimated exposure to air pollutants in this study.

	PM <sub>2.5</sub>	PM <sub>10</sub>	NO <sub>2</sub>
PM <sub>2.5</sub>	1	0.73	0.91
PM <sub>10</sub>		1	0.87
NO <sub>2</sub>			1

**Supplementary Table 3.** Putative annotations of features associated with PM<sub>2.5</sub> through the metabolome-wide association study framework. m/z: mass-to-charge ratio, Time: Retention time, Delta ppm: mass difference in parts per million, ID score: confidence in annotation based on Schymanski scale (1 being the highest and 5 the lowest), ESI: electrospray ionization.

m/z	time	ID score	delta ppm	Putative annotation	Adduct	ESI	$\beta$	q
243.0263	182.7	3	-	Cystine	M+H [+2]	+	-0.473	8.86E-04
300.0478	120.7	3	-	L-Cysteinyglycine disulfide; multiple matches	M+H [+2]	+	-0.486	8.86E-04
149.53	124.3	3	0.47	Cysteinyglycine disulfide	M+2H	+	-0.453	3.80E-03
141.5325	181.9	3	0.14	Cystine	M+ACN+2H	+	-0.427	4.29E-03
298.0517	119	3	2.99	Cysteinyglycine disulfide	M+H	+	-0.425	4.29E-03
774.5957	47.4	3	6.49	A phosphatidylcholine or phosphatidylethanolamine	M+H	+	-0.428	4.29E-03
263.0126	183.2	3	1.79	Cystine	M+Na	+	-0.419	5.73E-03
320.0336	122.2	3	2.91	L-Cysteinyglycine disulfide	M+Na	+	-0.426	5.73E-03
241.0308	181.6	3	1.33	Cystine	M+H	+	-0.395	8.09E-03
324.3257	41.9	3	1.2	N-(14-Methylhexadecanoyl)pyrrolidine	M+H	+	0.352	1.24E-02
170.0128	179.7	3	6.06	Cysteic acid	M+H	+	-0.372	2.15E-02
817.5875	45.6	3	2.54	A phosphatidylethanolamine	M+ACN+H	+	0.354	2.68E-02
122.027	183.9	3	0.25	Cysteine	M+H	+	-0.360	2.77E-02
161.0076	183.1	3	8.26	(2-Furanylmethyl) methyl disulfide	M+H	+	-0.362	2.97E-02
299.0555	124.2	3	1.64	Aflatoxin P1; Multiple matches	M+H	+	-0.368	2.97E-02
265.0197	181.8	3	4	58-Dihydro-6-(4-methyl-3-pentenyl)-1234-tetrathiocin	M+H	+	0.336	3.17E-02
503.2963	49.1	3	-	Fexofenadine; a lysophosphatidylethanolamine	M+H [+1]	+	-0.358	3.80E-02
309.2056	40.5	3	1.42	Multiple matches	M+H	+	0.276	4.77E-02
190.0357	35.6	3	0.05	Isosorbide Mononitrate; gamma-Carboxyglutamic acid	M-H	-	-0.506	4.71E-04
129.0194	36.5	3	0.54	A dicarboxylic acid	M-H	-	-0.488	9.22E-04
177.0041	35.4	3	4.75	Bissulfine; multiple other matches		-	-0.431	4.60E-03
209.0303	35.4	3	0.05	A dicarboxylic acid	M-H	-	-0.446	5.22E-03
475.2654	189.5	3	-	A lysophosphatidylethanolamine	M-H [-1]	-	-0.353	1.66E-02
503.292	201	3	-	A lysophosphatidylethanolamine	M-H [-1]	-	-0.381	1.83E-02
500.2779	197.7	3	0.72	A lysophosphatidylethanolamine	M-H	-	-0.383	2.71E-02
502.2937	205	3	0.42	A lysophosphatidylethanolamine	M-H	-	-0.341	4.94E-02
154.9871	183.3	5	8	Alphachloralose	M+2H	+	-0.454	1.46E-03
355.0733	115.4	5	1.75	norserttraline; multiple matches	M+ACN+Na	+	-0.444	3.86E-03
361.048	121.3	5	8.5	6-Demethylgriseofulvin	M+Na	+	-0.424	4.18E-03
775.6017	48	5	4.32	A diglyceride	M+2ACN+H	+	-0.429	4.18E-03



98.5181	183.4	5	3.25	Diethyl trisulfide, multiple other matches	M+ACN+2H	+	-0.419	5.73E-03
152.9913	182.8	5	1.24	Roxarsone	M+ACN+2H	+	-0.413	5.73E-03
360.0233	98.5	5	0.47	Cefdinir	M+H-2H2O	+	-0.406	5.73E-03
822.5468	54.6	5	3.65	A phosphatidylethanolamine	M+H-H2O	+	0.400	5.85E-03
178.0407	118.6	5	1.35	Methimazole	M+ACN+Na	+	-0.417	6.23E-03
824.5603	55.7	5	1.02	A phosphatidylethanolamine	M+H-H2O	+	0.399	9.80E-03
296.2944	42.1	5		Multiple matches		+	0.319	1.10E-02
132.9872	60.1	5	0	Pyruvic acid, multiple other matches	M+2Na-H	+	-0.395	1.11E-02
195.0259	184.9	5	1.28	Thiocysteine	M+ACN+H	+	-0.388	1.18E-02
130.159	43.8	5	0.23	Decamethonium/Propane	M+2H	+	0.362	1.58E-02
378.7789	61.9	5	7.42	A diglyceride	M+ACN+2H	+	0.332	2.77E-02
586.0316	182.9	5	8.75	Zoledronate	2M+ACN+H	+	-0.371	2.77E-02
98.0164	186.8	5	0.61	Thiocysteine	M+ACN+2H	+	-0.357	2.97E-02
142.0342	182.5	5	2.53	Polyvidone	M+H-2H2O	+	-0.362	2.97E-02
461.3484	48	5	3.97	Solanidine	M+ACN+Na	+	0.307	2.97E-02
242.0344	181.1	5	3.76	Glucosamine 6-sulfate	M+H-H2O	+	-0.359	3.70E-02
130.5333	26.1	5	2.3	Tyrosol 4-sulfate	M+ACN+2H	+	-0.161	4.26E-02
796.5254	57.2	5	0.3	A phosphatidylethanolamine	M+Na	+	0.344	4.26E-02
244.2632	42.7	5	1.19	Pentadecanal; 2-Pentadecanone; Heptyl ketone	M+NH4	+	0.343	4.86E-02
264.0158	183.5	5	5.49	5-Sulfo-13-benzenedicarboxylic acid	M+NH4	+	-0.357	4.86E-02
267.0003	36.7	5	0.94	Cyclobassinone	M+Cl	-	0.367	2.39E-02
605.3636	229.7	5	3.57	A Hericenone	M+Cl	-	-0.390	2.39E-02
265.0024	37.2	5	1.96	Apraclonidine	M+Na-2H	-	0.360	2.55E-02
356.9921	31.7	5	4.82	Cyanidin	M+Cl	-	0.352	4.76E-02
320.0038	182.8			Unknown		+	-0.481	8.86E-04
120.0115	183.7			Unknown		+	-0.450	1.46E-03
162.5474	182.9			Unknown		+	-0.460	1.68E-03
121.0192	186.1			Unknown		+	-0.433	4.18E-03
140.8713	61.7			Unknown		+	0.359	4.29E-03
162.0457	185.1			Unknown		+	-0.421	4.29E-03
288.2889	42.7			Unknown		+	0.419	8.09E-03
587.035	182.7			Unknown		+	-0.406	8.83E-03
156.8449	62			Unknown		+	0.391	9.69E-03
185.5406	273.4			Unknown		+	-0.382	1.38E-02
142.5304	184.8			Unknown		+	-0.372	1.58E-02

181.0193	183.2	<i>Unknown</i>	+	-0.378	1.58E-02
142.8692	61.8	<i>Unknown</i>	+	0.344	1.74E-02
86.1112	57.6	<i>Unknown</i>	+	0.342	2.44E-02
160.506	183.2	<i>Unknown</i>	+	-0.357	2.77E-02
121.5209	183.1	<i>Unknown</i>	+	-0.362	3.10E-02
852.6074	57.8	<i>Unknown</i>	+	0.340	4.74E-02
872.5548	57.2	<i>Unknown</i>	+	0.359	4.74E-02
866.5841	60.4	<i>Unknown</i>	+	0.328	4.86E-02
109.0224	25.8	<i>Unknown</i>	+	-0.335	5.03E-02
126.9224	40.5	<i>Unknown</i>	-	0.437	1.61E-03
168.836	35.3	<i>Unknown</i>	-	0.353	5.22E-03
479.2843	183.6	<i>Unknown</i>	-	-0.367	1.87E-02
280.8711	42.1	<i>Unknown</i>	-	0.364	2.39E-02
546.2789	210.3	<i>Unknown</i>	-	-0.382	2.61E-02
500.4841	197.4	<i>Unknown</i>	-	-0.372	4.94E-02

**Supplementary Table 4.** Putative annotations of features with a non-zero coefficient when predicting PM<sub>2.5</sub> exposure through the elastic net regression. m/z: mass-to-charge ratio, Time: Retention time, Delta ppm: mass difference in parts per million, ID score: confidence in annotation based on Schymanski scale (1 being the highest and 5 the lowest), ESI: electrospray ionization.

m/z	time	ID score	delta ppm	Putative annotation	Adduct	ESI	Elastic net coefficient	$\beta$	q
190.0357	35.6	3	0.05	Isosorbide Mononitrate; gamma-Carboxyglutamic acid	M-H	-	-0.190	-0.51	0.0003
129.0194	36.5	3	0.54	A dicarboxylic acid	M-H	-	-0.068	-0.49	0.0009
354.9404	33.3	3	5.75	Silver sulfadiazine	M-H	-	0.006	0.22	0.2751
387.33	290.9	3	8.13	3-Hydroxy-1-phenyl-1-eicosanone	M-H	-	0.049	0.28	0.1453
149.53	124.3	3	0.47	L-Cysteinylglycine disulfide	M+2H	+	-0.019	-0.45	0.0039
300.0478	120.7	3	-	L-Cysteinylglycine disulfide; Glyzaglabrin; Aflatoxin P1	M+H [+2]	+	-0.047	-0.48	0.0011
167.0825	60.9	3	-	L-Phenylalanine; multiple other matches	M+H [+1]	+	-0.012	-0.29	0.1533
163.1329	22.7	3	0.18	(3R7R)-137-Octanetriol	M+H	+	-0.004	-0.21	0.4118
508.3385	53.8	3	2.5	A lysophosphatidylethanolamine	M+H	+	-0.030	-0.23	0.3093
138.0914	228.7	3	0.43	Tyramine; multiple other matches	M+H	+	-0.021	-0.28	0.2326
205.0171	25.9	3	2.83	O-methoxycatechol-O-sulphate	M+H	+	-0.008	-0.34	0.0494
605.3636	229.7	5	3.57	A Hericenone	M+Cl	-	-0.089	-0.39	0.0309
98.0964	56.2	5	0.31	Ethylene; 3-Nonyl-1H-pyrazole	2M+ACN+H; M+2H	+	-0.003	-0.27	0.1519
130.159	43.8	5	0.23	Decamethonium; Propane	M+2H; 2M+ACN+H	+	0.027	0.35	0.0228
154.9871	183.3	5	8	Alphachloralose	M+2H	+	-0.021	-0.45	0.0015
355.0733	115.4	5	1.75	norserttraline	M+ACN+Na	+	-0.005	-0.44	0.0043
556.4413	40.5	5	3.4	Didodecyl thiobispropanoate	M+ACN+H	+	0.082	0.28	0.2031
775.6017	48	5	4.32	a Diacylglyceride	M+2ACN+H	+	-0.089	-0.42	0.0057
114.9341	144.4	-	-	Unknown		-	-0.006	-0.29	0.1716
126.9224	40.5	-	-	Unknown		-	0.093	0.43	0.0018
137.8919	112.2	-	-	Unknown		-	-0.032	-0.28	0.0632
236.9005	85.7	-	-	Unknown		-	-0.013	-0.28	0.1432
254.9444	45.3	-	-	Unknown		-	-0.055	-0.36	0.0512
279.6142	34.1	-	-	Unknown		-	-0.005	-0.31	0.0956
479.2843	183.6	-	-	Unknown		-	-0.037	-0.37	0.0183
500.4841	197.4	-	-	Unknown		-	-0.009	-0.37	0.0507
546.2789	210.3	-	-	Unknown		-	-0.005	-0.38	0.0261
179.9855	23.6	-	-	Unknown		+	-0.001	-0.29	0.1751

288.2889	42.7	-	-	<i>Unknown</i>	+	0.104	0.42	0.0083
470.9033	73	-	-	<i>Unknown</i>	+	0.042	0.31	0.0757
646.7869	70.4	-	-	<i>Unknown</i>	+	-0.019	-0.32	0.0971
202.9893	288.2			<i>Unknown</i>	+	0.001	0.31	0.1143

**Supplementary Table 5.** Putative annotations of features with high variable importance scores (VIP) in predicting high or low PM<sub>2.5</sub> exposure groups through the partial least square discriminant analysis. m/z: mass-to-charge ratio, Time: Retention time, Delta ppm: mass difference in parts per million, ID score: confidence in annotation based on Schymanski scale (1 being the highest and 5 the lowest), ESI: electrospray ionization. VIP comp1: variable importance score on component 1, VIP comp2: variable importance score on component 1

mz	time	ID score	delta ppm	Putative annotation	Adduct	ESI	$\beta$	q	VIP comp1	VIP comp2
300.0478	120.7	3	-	L-Cysteinylglycine disulfide; multiple matches	M+H [+2]	+	-0.486	8.86E-04	4.18	3.16
243.0263	182.7	3	-	Cystine	M+H [+2]	+	-0.473	8.86E-04	4.14	3.02
177.0041	35.4	3	4.75	Bissulfine; multiple other matches		-	-0.431	4.60E-03	3.93	2.96
129.0194	36.5	3	0.54	A dicarboxylic acid	M-H	-	-0.488	9.22E-04	3.71	2.72
149.53	124.3	3	0.47	Cysteinylglycine disulfide	M+2H	+	-0.453	3.80E-03	3.70	2.77
320.0336	122.2	3	2.91	L-Cysteinylglycine disulfide	M+Na	+	-0.426	5.73E-03	3.44	2.59
263.0126	183.2	3	1.79	Cystine	M+Na	+	-0.419	5.73E-03	3.36	2.41
276.1114	44.2	3	4.31	Queuine	M-H	-	0.266	1.28E-01	3.28	2.68
241.0308	181.6	3	1.33	Cystine	M+H	+	-0.395	8.09E-03	3.27	2.38
298.0517	119	3	2.99	Cysteinylglycine disulfide	M+H	+	-0.425	4.29E-03	3.22	2.43
209.0303	35.4	3	0.05	A dicarboxylic acid	M-H	-	-0.446	5.22E-03	3.10	2.25
214.0513	253.3	3	0.33	Cysteineglutathione disulfide	M+2H	+	-0.335	6.47E-02	3.09	2.34
141.5325	181.9	3	0.14	Cystine	M+ACN+2H	+	-0.427	4.29E-03	3.06	2.19
299.0555	124.2	3	1.64	Aflatoxin P1; Multiple matches	M+H	+	-0.368	2.97E-02	3.02	2.24
301.0511	119.9	3	-	L-Cysteinylglycine disulfide; multiple other matches	M+H [+3]	+	-0.342	5.99E-02	3.00	2.36
236.0894	286.7	3	9.87	3-Oxo-carbofuran	M+H	+	0.133	6.18E-01	2.97	2.51
355.0733	115.4	5	1.75	norsertaline; multiple matches	M+ACN+Na	+	-0.444	3.86E-03	4.21	3.30
361.048	121.3	5	8.5	6-Demethylgriseofulvin	M+Na	+	-0.424	4.18E-03	4.00	3.00
178.0407	118.6	5	1.35	Methimazole	M+ACN+Na	+	-0.417	6.23E-03	3.96	3.20
195.0259	184.9	5	1.28	Thiocysteine	M+ACN+H	+	-0.388	1.18E-02	3.51	2.56
775.6017	48	5	4.32	A diglyceride	M+2ACN+H	+	-0.429	4.18E-03	3.35	2.54
154.9871	183.3	5	8	Alphachloralose	M+2H	+	-0.454	1.46E-03	3.26	2.34
98.0164	186.8	5	0.61	Thiocysteine	M+ACN+2H	+	-0.357	2.97E-02	3.18	2.29
98.5181	183.4	5	3.25	Diethyl trisulfide, multiple other matches	M+ACN+2H	+	-0.419	5.73E-03	3.12	2.23
152.9913	182.8	5	1.24	Roxarsone	M+ACN+2H	+	-0.413	5.73E-03	3.08	2.22
264.0158	183.5	5	5.49	5-Sulfo-13-benzenedicarboxylic acid	M+NH4	+	-0.357	4.86E-02	3.05	2.18

826.685	71.8	5	3.5	N-Glycoloylganglioside GM2	M+2ACN+H	+	-0.248	2.91E-01	3.03	2.35
120.0115	183.7			<i>Unknown</i>		+	-0.450	1.46E-03	4.17	3.06
320.0038	182.8			<i>Unknown</i>		+	-0.481	8.86E-04	4.16	3.04
162.0457	185.1			<i>Unknown</i>		+	-0.421	4.29E-03	3.71	2.67
181.0193	183.2			<i>Unknown</i>		+	-0.378	1.58E-02	3.41	2.45
162.5474	182.9			<i>Unknown</i>		+	-0.460	1.68E-03	3.28	2.36
121.0192	186.1			<i>Unknown</i>		+	-0.433	4.18E-03	3.27	2.35
160.506	183.2			<i>Unknown</i>		+	-0.357	2.77E-02	3.20	2.29
185.5406	273.4			<i>Unknown</i>		+	-0.382	1.38E-02	3.13	2.24
181.5296	121.4			<i>Unknown</i>		+	-0.309	6.94E-02	3.11	2.38

**Supplementary Table 6.** Effect modification. The relationship between several metabolic features and PM<sub>2.5</sub> was modified by Alzheimer's disease diagnosis, *APOE* ε4 allele, history of diabetes, and diet. #A noteworthy interaction was defined at an FDR < 0.2. LR, Likelihood ratio test; m/z, mass-to-charge ratio; Time, retention time; Delta ppm, mass difference in parts per million; ID score, confidence in annotation based on Schymanski scale (1 being the highest and 5 the lowest); ESI, electrospray ionization.

Modifier	Number of features <sup>#</sup>	m/z	Time (s)	FDR from LR test	Putative annotation	Adduct	Delta ppm	ID score*	ESI
<i>APOE</i> ε4 allele status	4	546.2789	210.3	0.101	<i>Unknown</i>				-
History of diabetes	3	126.9224	40.5	0.0003	<i>Unknown</i>				-
		140.8713	61.7	0.0002	<i>Unknown</i>				+
		142.8692	61.8	0.004	<i>Unknown</i>				+
Diet: PC1 ↑ carbohydrate, vegetable fat ↓ protein, animal fat	1	126.9224	40.5	0.158	<i>Unknown</i>				-
Diet: PC4 ↑ carbohydrates, animal fat, protein and vegetable fat	39	86.1112	57.6	0.058	<i>Unknown</i>				+
		120.0115	183.7	0.058	<i>Unknown</i>				+
		121.0192	186.1	0.063	<i>Unknown</i>				+
		121.5209	183.1	0.09	<i>Unknown</i>				+
		140.8713	61.7	0.127	<i>Unknown</i>				+
		142.5304	184.8	0.102	<i>Unknown</i>				+
		142.8692	61.8	0.092	<i>Unknown</i>				+
		156.8449	62	0.092	<i>Unknown</i>				+
		160.506	183.2	0.063	<i>Unknown</i>				+
		162.0457	185.1	0.063	<i>Unknown</i>				+
		162.5474	182.9	0.063	<i>Unknown</i>				+
181.0193	183.2	0.063	<i>Unknown</i>				+		

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320.0038	182.8	0.063	<i>Unknown</i>	+
587.035	182.7	0.109	<i>Unknown</i>	+
866.5841	60.4	0.07	<i>Unknown</i>	+
168.836	35.3	0.195	<i>Unknown</i>	-

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