

## Supporting Information

### **Metabolomics Profiles of Smokers from Two Ethnic Groups with Differing Lung Cancer Risk**

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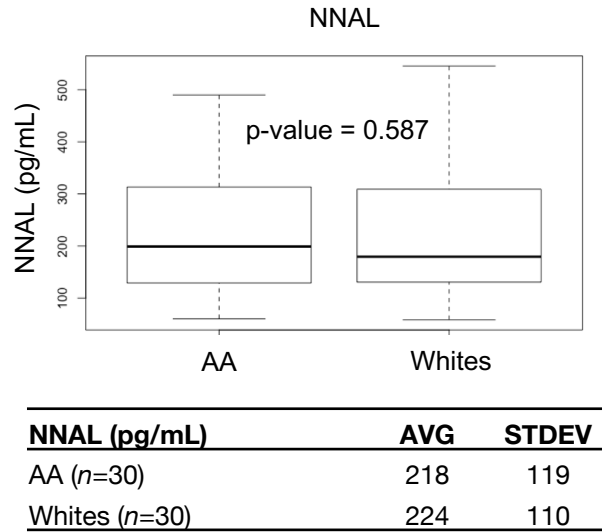
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**Figure S1**



**Fig. S1.** Levels of NNAL (pg/mL) in urine of the 60 subjects used in the metabolomics analysis.

Figure S2

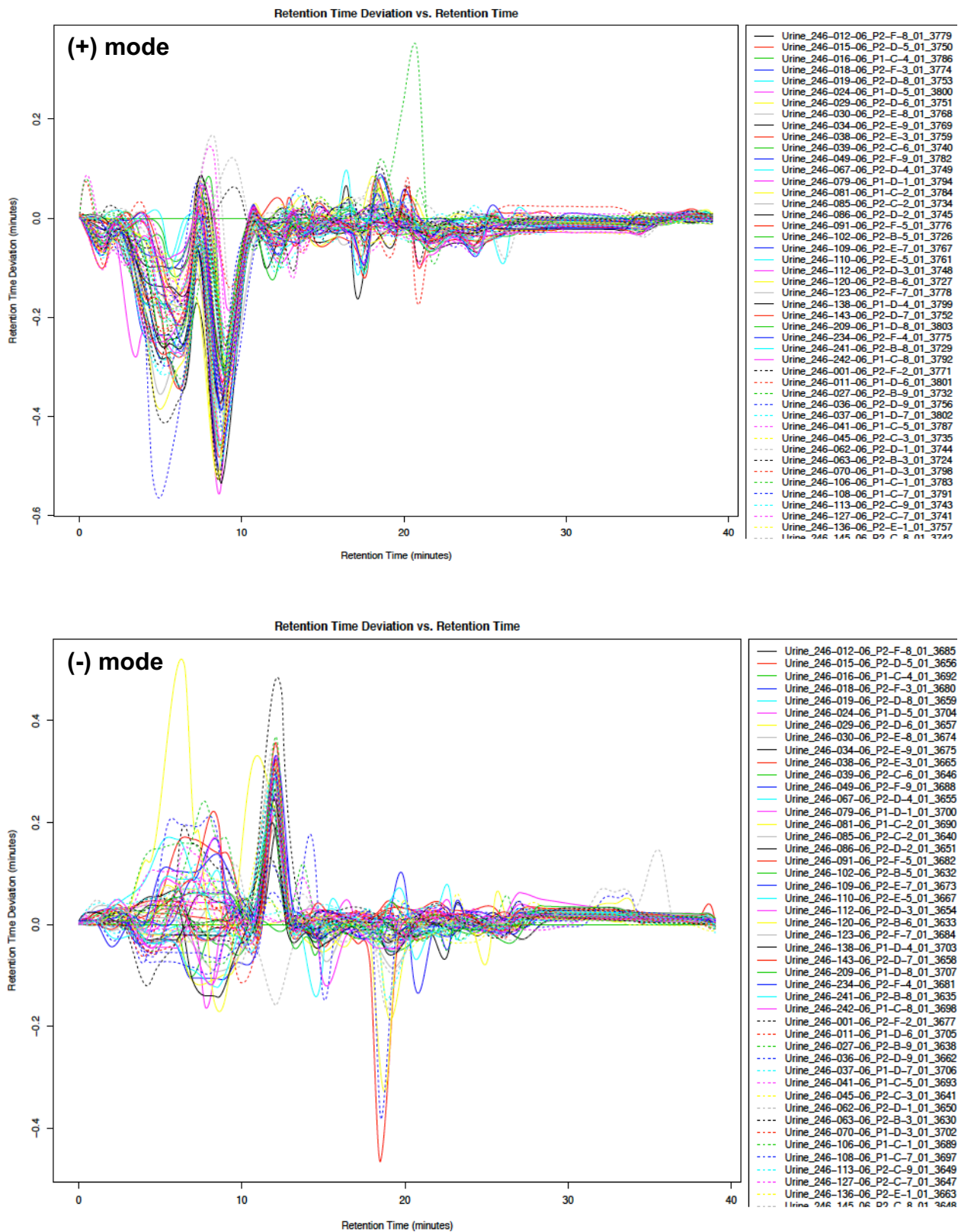


Fig. S2. Retention time deviation versus retention time of the 60 samples in positive (top panel) and negative mode data acquisition (bottom panel).

Figure S3

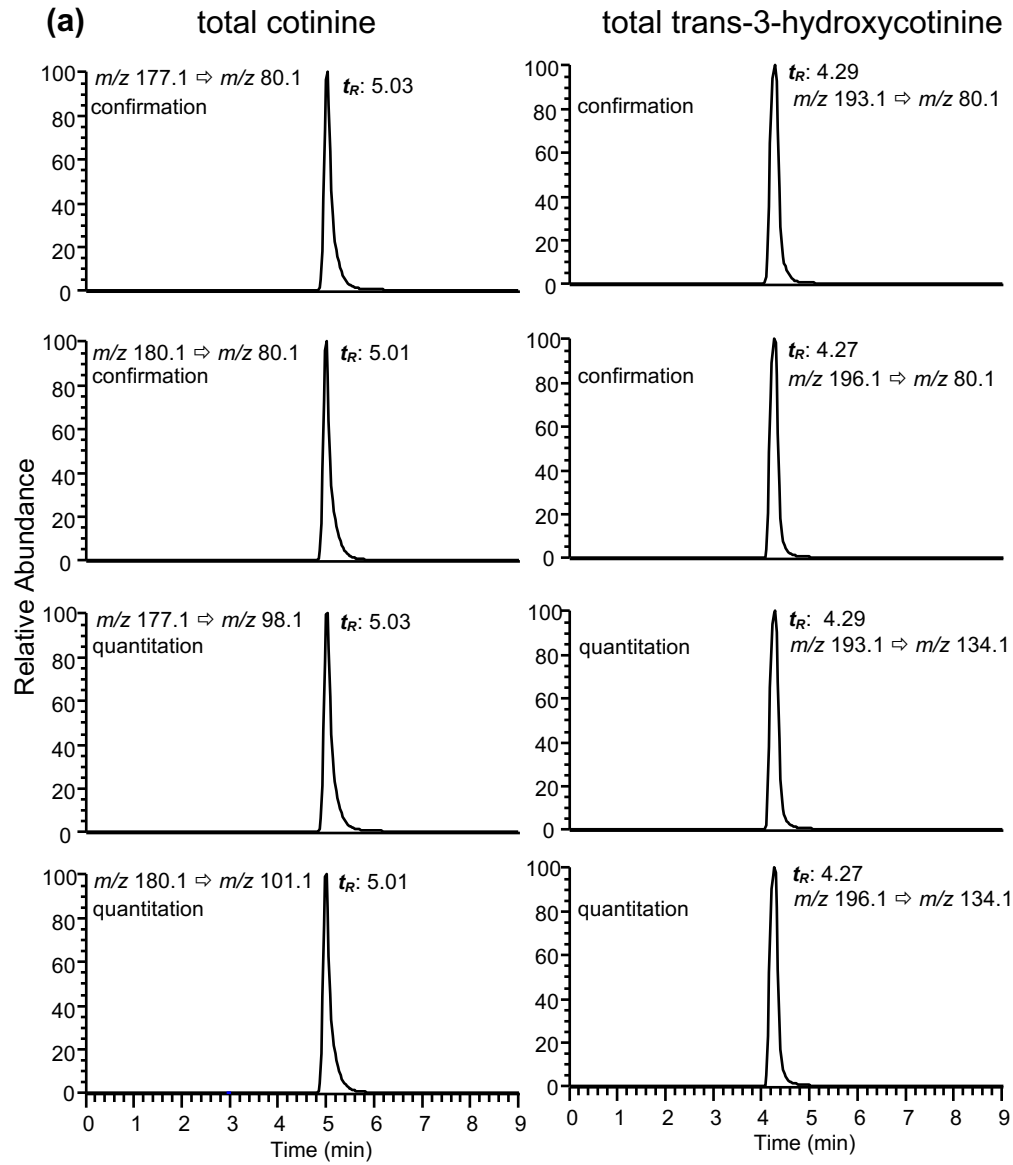


Figure S3 (cont.)

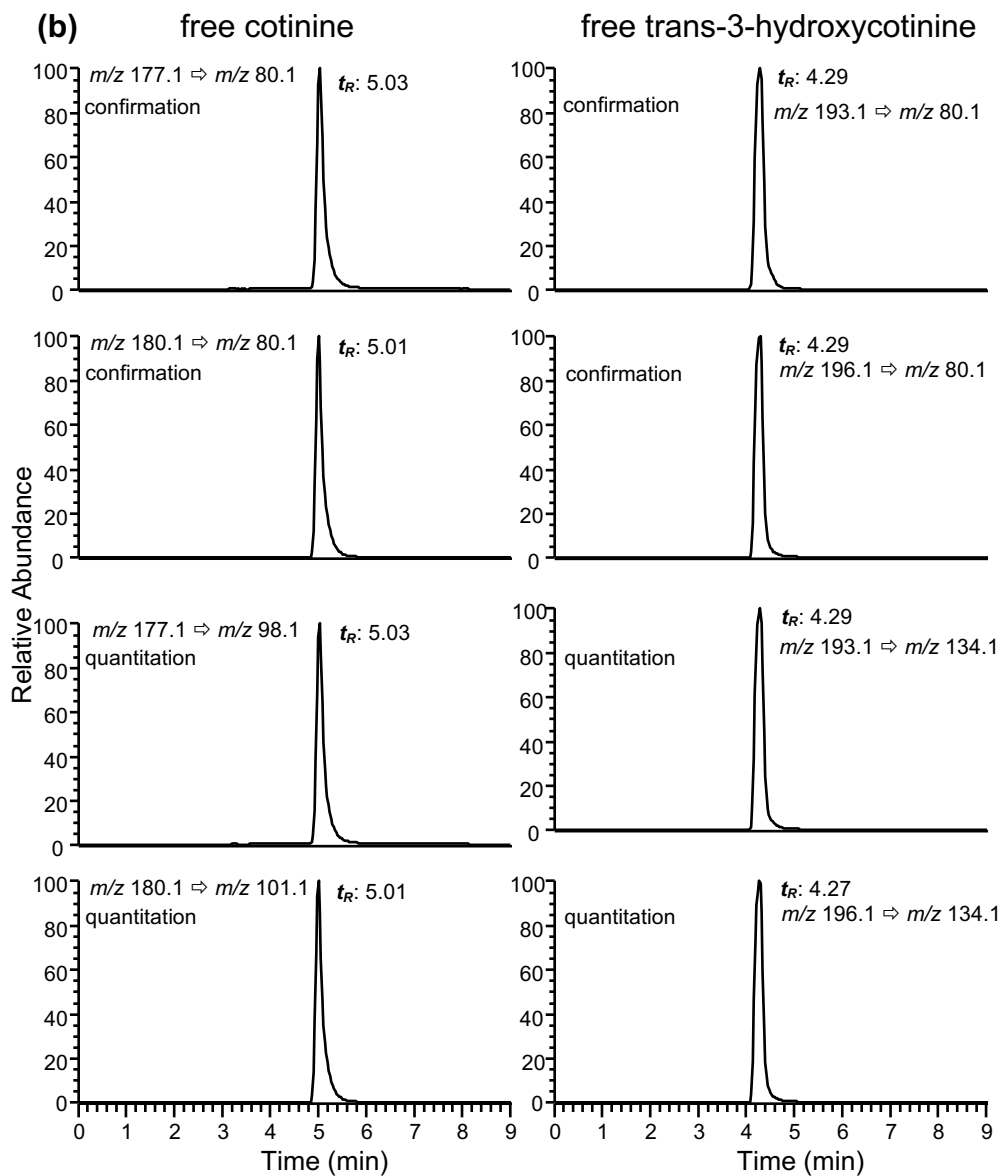
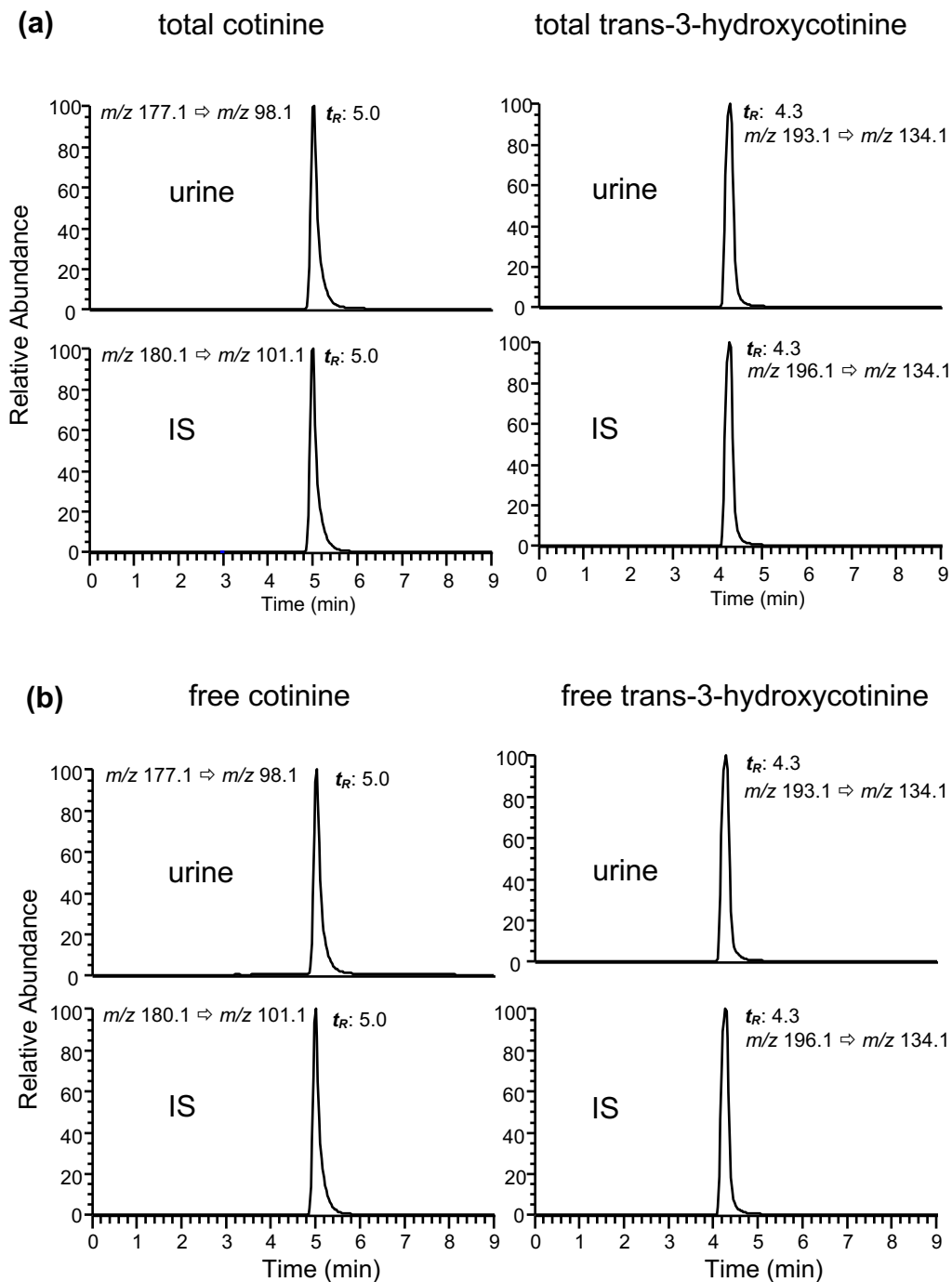


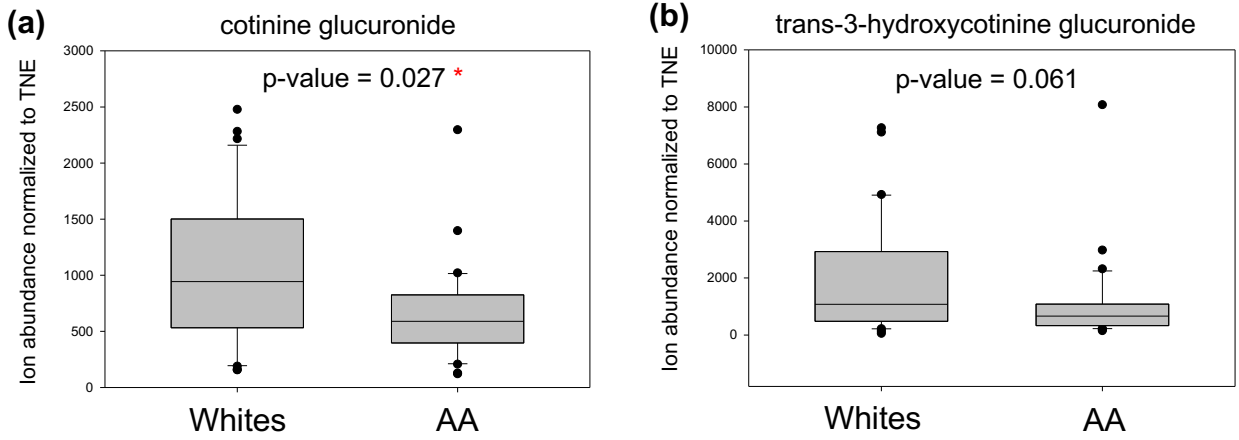
Fig. S3. (a) Extracted ion chromatograms (EICs) of the SRM transitions of total cotinine and trans-3-hydroxycotinine; (b) EICs of the SRM transitions of free cotinine and trans-3-hydroxycotinine.

**Figure S4**



**Fig. S4.** Representative EICs of the SRM transitions of (a) total cotinine and trans-3-hydroxycotinine; (b) free cotinine and trans-3-hydroxycotinine in urine samples with corresponding  $d_3$ -labeled IS.

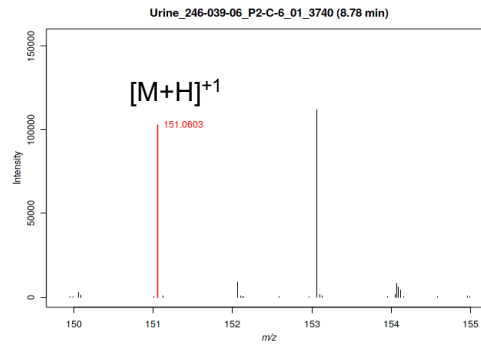
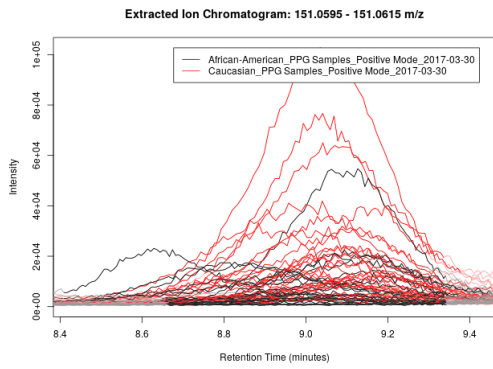
**Figure S5**



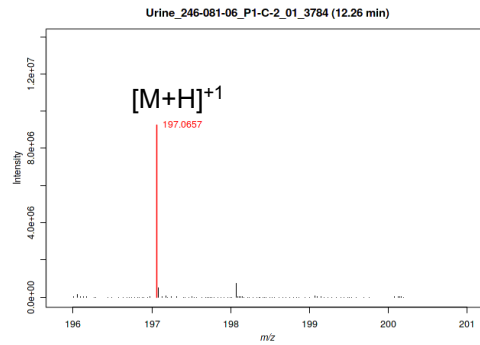
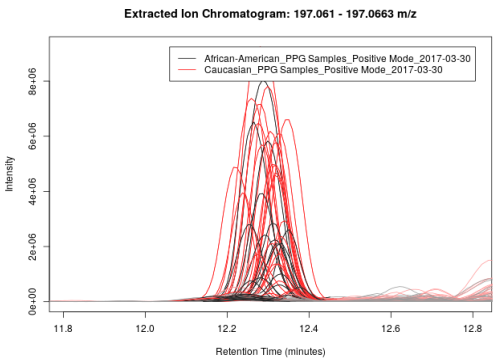
**Fig. S5.** (a) Ion abundance of cotinine glucuronide adjusted to TNE; (b) Ion abundance of trans-3-hydroxycotinine glucuronide adjusted to TNE in the metabolomics analysis.

# Figure S6

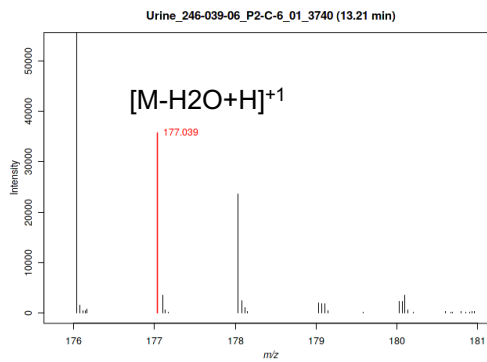
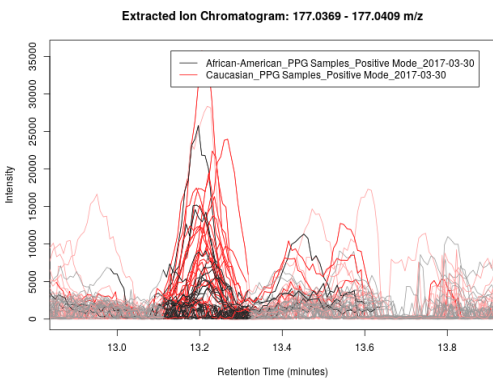
## (a) L-xylulose



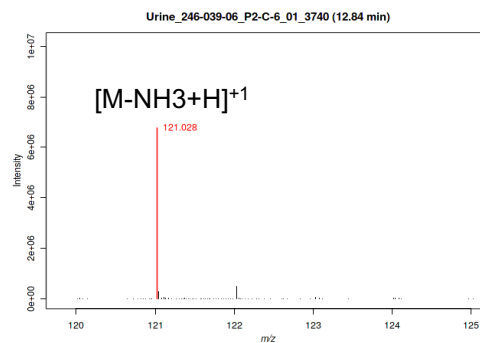
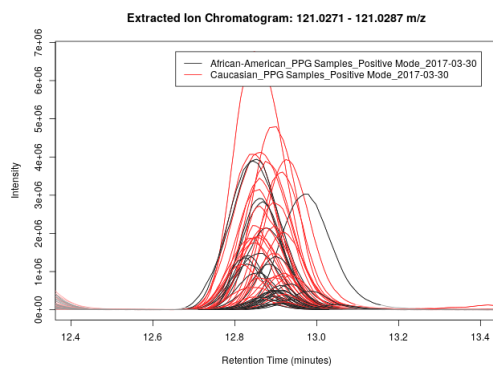
## (b) L-gulonate



## (c) aldehydo-D-glucuronate/3-keto-L-gulonate



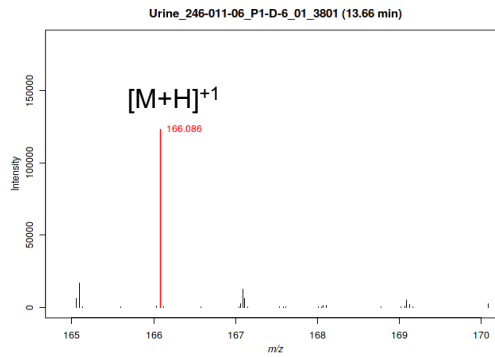
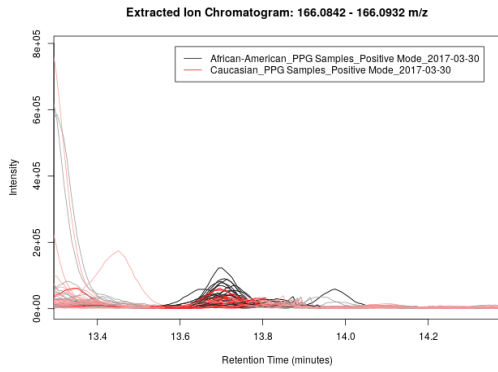
## (d) 3-pyridylacetate



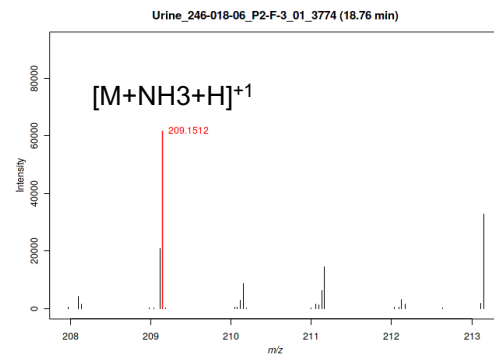
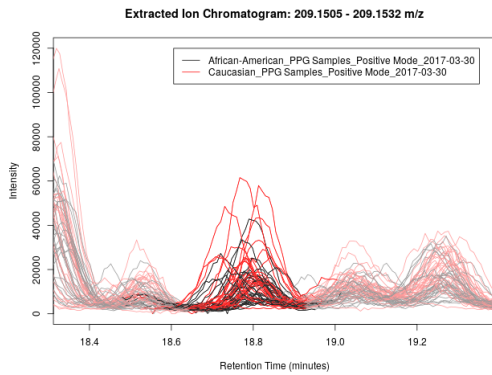


# Figure S6 (cont.)

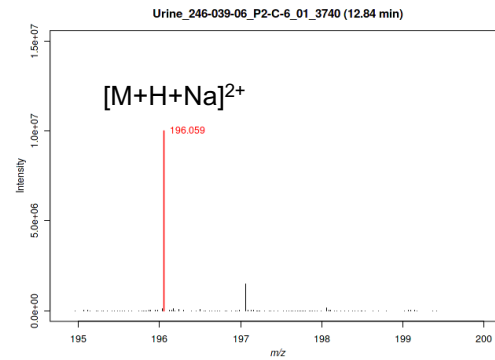
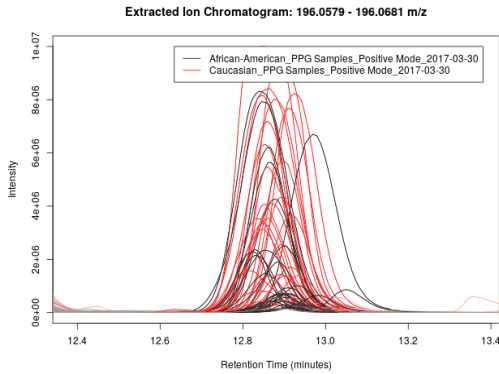
## (e) 4-(3-pyridyl)-butanoate



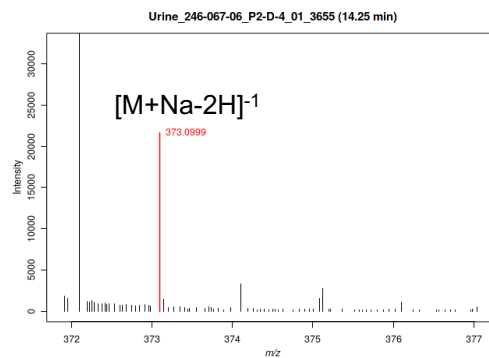
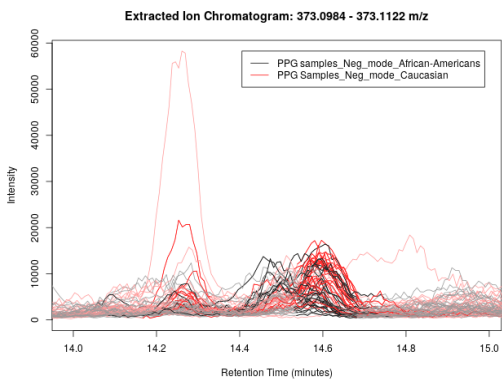
## (f) cotinine methonium ion



## (g) trans-3-hydroxycotinine-glucuronide

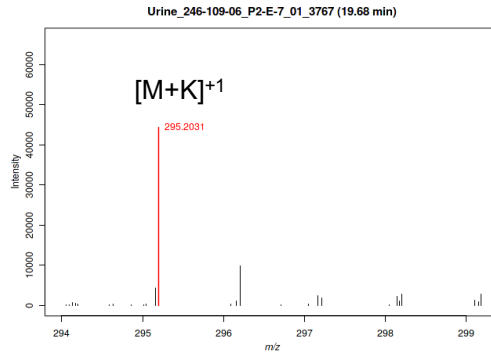
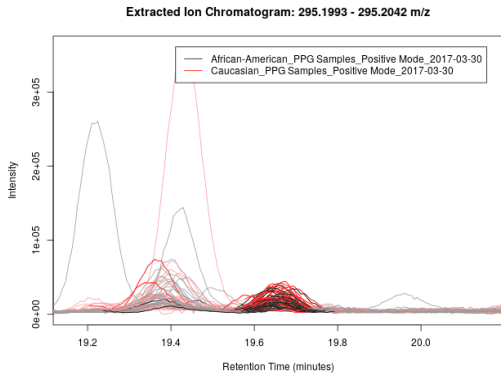


## (h) cotinine-glucuronide

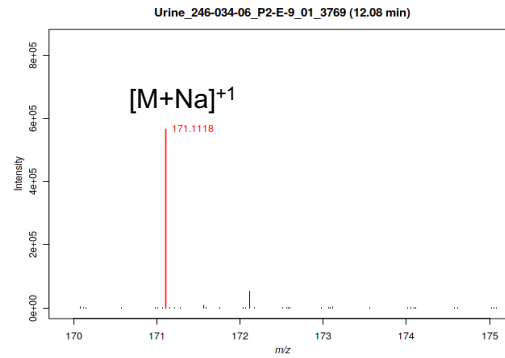
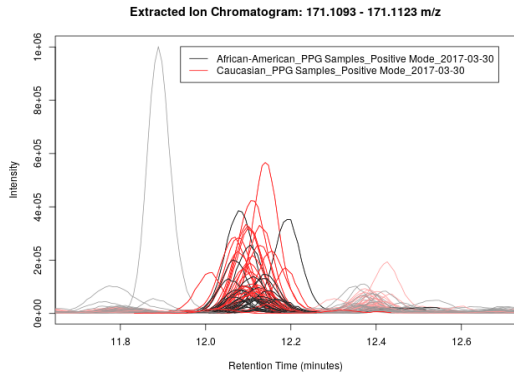


# Figure S6 (cont.)

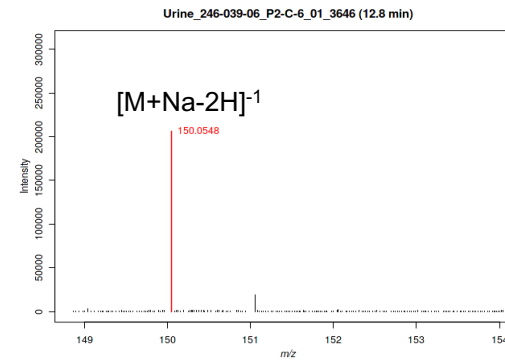
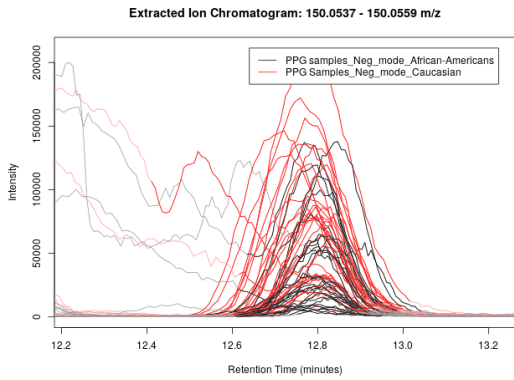
## (i) palmitate



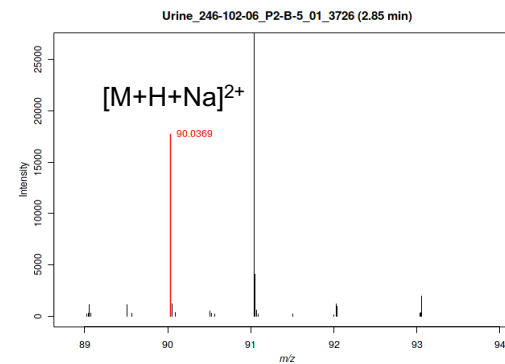
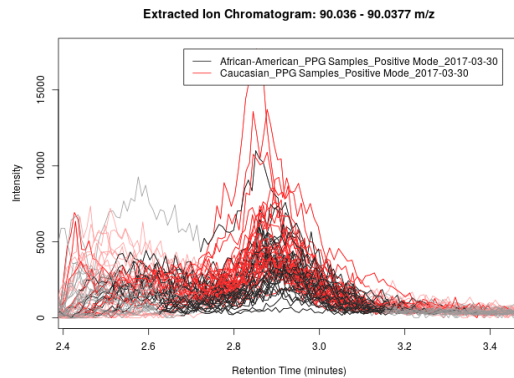
## (j) L-lysine



## (k) L-pipecolate

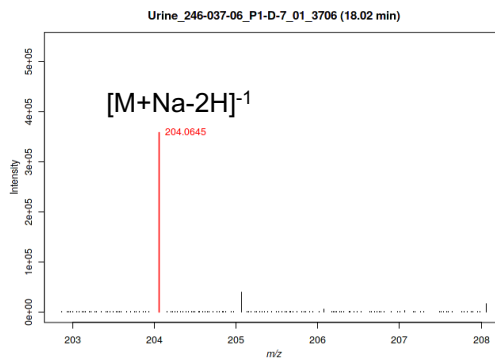
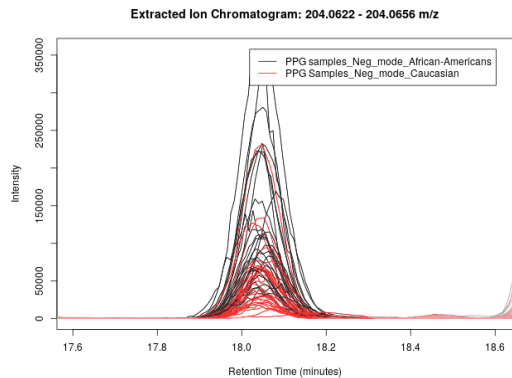


## (l) L-histidine

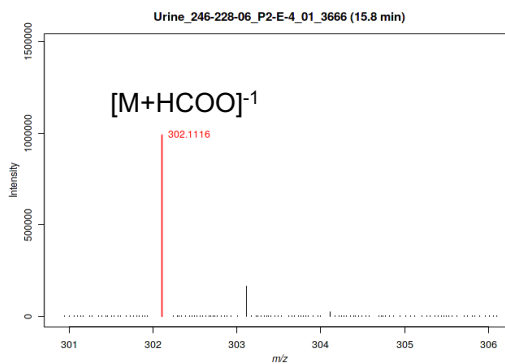
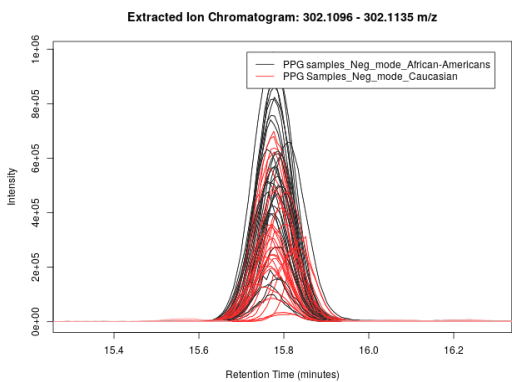


# Figure S6 (cont.)

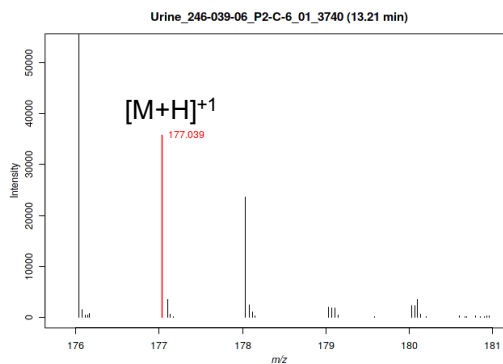
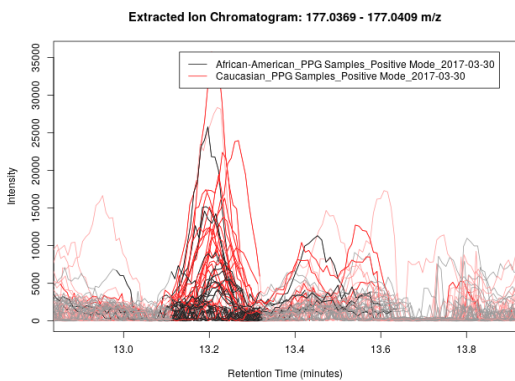
(m) (R)-adrenaline



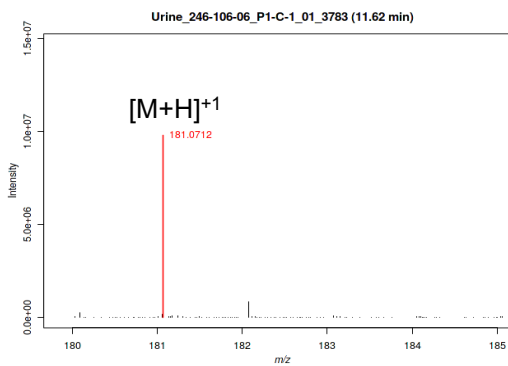
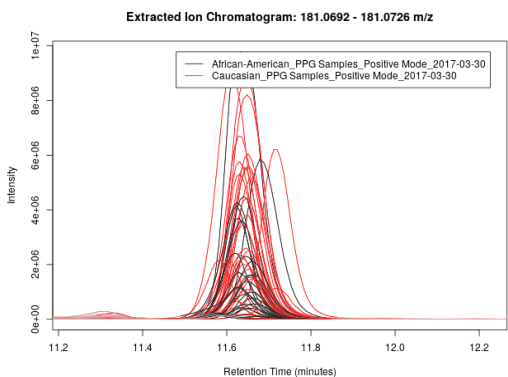
(n) 4 $\alpha$ -hydroxy-tetrahydrobiopterin



(o) L-ascorbate

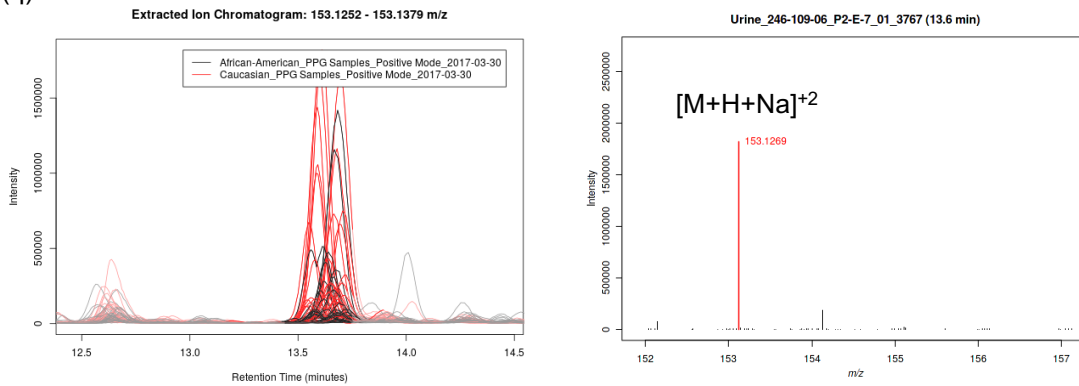


(p)  $\beta$ -D-glucose/ $\alpha$ -D-glucose/ $\beta$ -D-fructofuranose/ $\beta$ -D-galactose/ $\alpha$ -D-galactose



## Figure S6 (cont.)

(q) oleate



**Fig. S6.** Representative extracted ion chromatograms (EIC) and zoomed precursor ion full scan MS spectra of putative metabolites associated with differentially regulated pathways identified in the multi-modal pathway analysis.

**Table S1. Demographics of subjects, NNAL levels, and nicotine metabolites data.**

Subject	TNE (nmol/mL)	Creatinine (mg/mL)	NNAL (pg/mL)	Age	Total COT (ng/mL)	Total 3-HCOT (ng/mL)	Free COT (ng/mL)	Free 3-HCOT (ng/mL)	COT-gluc (ng/mL)
<b>African American</b>									
S001	59	1.9	106	50	4519	2798	1674	2128	2845
S002	83	1.5	158	45	4880	3411	2554	3097	2326
S003	67	1.1	167	46	2617	2894	1668	2365	950
S004	113	2.5	317	50	3836	7838	2102	5572	1734
S005	102	1.5	213	53	5034	15019	4789	12846	245
S006	89	1.8	285	57	3604	9790	1844	5582	1761
S007	32	0.7	151	50	2064	1463	1609	1031	455
S008	36	1.2	192	52	1484	7788	991	4500	493
S009	54	0.7	125	40	2508	3477	1608	2417	900
S010	51	1.4	125	33	3201	7071	2425	6265	776
S011	102	1.2	298	43	5103	18300	4425	12057	678
S012	130	2.2	242	52	4053	18198	2709	12989	1344
S013	75	1.0	152	44	5467	11218	2651	7514	2816
S014	80	1.1	206	50	7968	6655	2008	5355	5961
S015	83	0.8	340	50	2403	11138	1313	9045	1090
S016	50	0.6	164	50	3382	10100	3226	8176	155
S017	159	1.2	380	49	11671	26943	3756	20744	7915
S018	93	1.8	325	41	6064	16659	3337	11567	2727
S019	68	1.4	313	29	3728	8669	3259	7612	470
S020	100	1.0	304	44	3677	1225	2045	687	1632
S021	77	1.8	490	49	7473	12778	4364	10122	3109
S022	30	0.4	140	49	2382	2545	1703	2175	679
S023	33	1.0	129	43	1669	5159	618	4020	1051
S024	47	1.0	102	54	3341	5927	1826	4728	1515
S025	28	1.6	60	28	1432	4665	1236	2566	196
S026	51	1.1	114	54	2889	5478	1408	4458	1481
S027	91	1.8	257	54	5184	9870	2455	6262	2729
S028	69	3.5	367	40	5947	7893	3671	5879	2276
S029	60	1.6	91	55	2763	13200	1631	8504	1132
S030	77	1.5	410	26	5653	8781	3052	5944	2601
<b>White</b>									
S031	53	1.3	132	52	3624	6591	1429	4491	2195
S032	69	0.4	215	62	4172	12031	2483	8933	1689
S033	124	1.3	467	58	8103	18639	2499	12177	5604
S034	95	1.0	153	20	8594	10321	2624	7898	5970
S035	30	2.5	193	18	1665	4961	794	4273	871
S036	79	1.6	58	26	6616	3809	1975	2693	4641
S037	70	1.3	219	21	8278	18385	2217	14307	6062
S038	98	1.9	319	31	8412	12639	2430	9856	5982
S039	77	1.7	157	30	7139	12240	2581	8089	4558
S040	47	0.9	179	26	2379	8787	1221	7088	1159
S041	131	1.3	314	51	5456	19850	2985	16222	2472
S042	95	1.4	276	54	4237	17637	1544	12718	2694
S043	90	1.5	179	42	5087	8346	1931	5985	3156
S044	76	0.5	159	36	6165	8487	2612	6157	3553
S045	29	0.5	108	43	1500	4660	898	3363	601
S046	173	2.3	545	45	9920	35479	2287	30064	7633
S047	153	1.9	357	28	8050	23859	3378	18891	4673
S048	73	1.5	309	36	2961	18336	2246	14788	715
S049	115	1.2	276	53	7661	9743	2574	8036	5086
S050	62	1.2	110	43	5075	6346	1652	5203	3424
S051	75	0.8	227	48	5270	11624	2382	7603	2887
S052	20	0.3	131	52	1078	785	607	638	471
S053	40	0.9	112	50	2239	4492	657	3185	1582
S054	132	1.2	337	37	8999	12145	2585	8587	6414
S055	74	1.1	178	24	4680	10503	1819	7528	2861
S056	107	1.5	389	47	6343	19174	1678	13373	4664
S057	53	0.8	61	41	1620	9067	1527	5580	93
S058	64	0.4	119	60	5801	6887	3037	5342	2764
S059	63	0.9	172	47	5629	11248	2183	8653	3445
S060	41	0.4	92	29	3176	6824	1212	5519	1965

**Table S2. Levels of nicotine metabolites normalized to TNE.**

<b>(a) cotinine glucuronide</b>	<b>AVG</b>	<b>STDEV</b>
Whites ( <i>n</i> =30)	40	18
AA ( <i>n</i> =30)	24	16

<b>(b) trans-3-hydroxycotinine glucuronide</b>	<b>AVG</b>	<b>STDEV</b>
Whites ( <i>n</i> =30)	36	15
AA ( <i>n</i> =30)	33	22

<b>(c) free cotinine</b>	<b>AVG</b>	<b>STDEV</b>
Whites ( <i>n</i> =30)	27	7
AA ( <i>n</i> =30)	35	13

<b>(d) free trans-3-hydroxycotinine</b>	<b>AVG</b>	<b>STDEV</b>
Whites ( <i>n</i> =30)	109	41
AA ( <i>n</i> =30)	89	39

<b>(e) total cotinine</b>	<b>AVG</b>	<b>STDEV</b>
Whites ( <i>n</i> =30)	67	19
AA ( <i>n</i> =30)	59	19

<b>(f) total trans-3-hydroxycotinine</b>	<b>AVG</b>	<b>STDEV</b>
Whites ( <i>n</i> =30)	145	51
AA ( <i>n</i> =30)	122	55

**Table S3. Differentially regulated metabolic pathways determined in the autonomous multi-modal pathway analysis with p-value =0.01 and 5 ppm mass tolerance.**

Pathway	Overlapping putative metabolites <sup>1</sup>	% Overlapping putative metabolites <sup>1</sup>	All metabolites <sup>2</sup>	p-value
D-glucuronate degradation	5	83.3%	6	0.0002
bupropion degradation	4	80.0%	5	0.0002
nicotine degradation V	5	27.8%	18	0.0002
sucrose degradation	3	60.0%	5	0.0002
lysine degradation I (saccharopine pathway)	3	42.9%	7	0.0002
lactose degradation III	2	100.0%	2	0.0002
D-galactose degradation V (Leloir pathway)	2	100.0%	2	0.0002
lysine degradation II (pipecolate pathway)	3	30.0%	10	0.0002
dermatan sulfate degradation (metazoa)	2	66.7%	3	0.0002
trehalose degradation	2	66.7%	3	0.0002
thyroid hormone metabolism II (via conjugation and/or degradation)	3	75.0%	4	0.0002
myo-inositol de novo biosynthesis	1	100.0%	1	0.0003
sulfite oxidation	1	100.0%	1	0.0003
oleate biosynthesis	1	100.0%	1	0.0003
D-myo-inositol (1,4,5)-trisphosphate biosynthesis	1	100.0%	1	0.0003
D-myo-inositol (1,4,5)-trisphosphate degradation	1	100.0%	1	0.0003
thiamin salvage III	1	100.0%	1	0.0003
glycogenolysis	1	100.0%	1	0.0003
3-phosphoinositide biosynthesis	1	100.0%	1	0.0003
phosphatidylserine biosynthesis I	1	100.0%	1	0.0003
tRNA charging	2	15.4%	13	0.0003
α-tocopherol degradation	1	50.0%	2	0.0003
UDP-N-acetyl-D-galactosamine biosynthesis II	1	50.0%	2	0.0003
sorbitol degradation I	1	50.0%	2	0.0003
chondroitin sulfate degradation (metazoa)	1	50.0%	2	0.0003
sulfate activation for sulfonation	1	50.0%	2	0.0003
phospholipases	1	50.0%	2	0.0003
palmitate biosynthesis	1	50.0%	2	0.0003
histamine biosynthesis	1	50.0%	2	0.0003
stearate biosynthesis	1	50.0%	2	0.0003
carnosine biosynthesis	1	50.0%	2	0.0003
pyrimidine deoxyribonucleotide phosphorylation	1	33.3%	3	0.0004
pyrimidine deoxyribonucleotides biosynthesis from CTP	1	33.3%	3	0.0004
phosphatidylcholine biosynthesis	1	33.3%	3	0.0004
homocarnosine biosynthesis	1	33.3%	3	0.0004
nicotine degradation IV	2	11.8%	17	0.0004
hydrogen sulfide biosynthesis (trans-sulfuration)	1	25.0%	4	0.0005
choline degradation	1	25.0%	4	0.0005
tetrapyrrole biosynthesis	1	25.0%	4	0.0005
proline degradation	1	20.0%	5	0.0007
proline biosynthesis	1	20.0%	5	0.0007
ornithine de novo biosynthesis	1	20.0%	5	0.0007
pyrimidine deoxyribonucleotides de novo biosynthesis	1	20.0%	5	0.0007
histidine degradation	2	40.0%	5	0.0007
ascorbate recycling (cytosolic)	1	20.0%	5	0.0007
estradiol biosynthesis I	1	20.0%	5	0.0007
tryptophan degradation to 2-amino-3-carboxymuconate semialdehyde	1	20.0%	5	0.0007
thyronamine and iodothyronamine metabolism	1	16.7%	6	0.0009
adenine and adenosine salvage III	2	33.3%	6	0.0009
adenosine nucleotides degradation	1	16.7%	6	0.0009
4-hydroxyproline degradation	1	14.3%	7	0.0012
purine ribonucleosides degradation to ribose-1-phosphate	1	12.5%	8	0.0017
serotonin degradation	1	11.1%	9	0.0022
androgen biosynthesis	2	22.2%	9	0.0022
catecholamine biosynthesis	3	30.0%	10	0.0029

1) Number of significantly dysregulated metabolites found in pathway

2) Total number of putative metabolites found in the pathway using the entire LC-MS analysis results

**Table S4. Differentially regulated metabolic pathways and the associated metabolites determined in the autonomous multi-modal pathway analysis ( p-value =0.01 and 5 ppm mass tolerance).**

Pathway	METLIN ID	Dysregulation*	Fold Change	p-value	m/z	t <sub>R</sub> (min)	Adduct Form
<b>D-glucuronate degradation</b>							
L-xylulose	139	DOWN	2.2	3.00E-03	151.0604	9.08	M+H[1+]
L-gulonate	63144	DOWN	2.4	2.40E-03	197.0652	12.29	M+H[1+]
L-gulonate	63144	DOWN	3	1.50E-04	195.0503	11.99	M-H[-]
aldehydo-D-glucuronate <sup>a</sup>	NA	DOWN	2	1.70E-03	177.0392	13.23	M-H <sub>2</sub> O+H[1+]
3-keto-L-gulonate <sup>a</sup>	58394	DOWN	2	1.70E-03	177.0392	13.23	M-H <sub>2</sub> O+H[1+]
<b>nicotine degradation V<sup>b</sup></b>							
3-pyridylacetate	NA	DOWN	2.1	4.50E-03	121.0279	12.88	M-NH <sub>3</sub> +H[1+]
4-(3-pyridyl)-butanoate	NA	UP	1.7	6.60E-03	166.0855	13.71	M+H[1+]
cotinine-glucuronide	NA	DOWN	1.5	7.20E-03	373.1022	14.59	M+Na-2H[-]
cotinine methonium ion	NA	DOWN	1.5	5.00E-03	209.1516	18.8	M+NH <sub>3</sub> +H[1+]
trans-3-hydroxycotinine-glucuronide	NA	DOWN	2.1	6.00E-03	196.0593	12.85	M+H+Na[2+]
<b>nicotine degradation IV<sup>b</sup></b>							
3-pyridylacetate	NA	DOWN	2.1	4.50E-03	121.0279	12.88	M-NH <sub>3</sub> +H[1+]
4-(3-pyridyl)-butanoate	NA	UP	1.7	6.60E-03	166.0855	13.71	M+H[1+]
<b>sucrose degradation<sup>c</sup></b>							
β-D-glucose	3755	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
β-D-glucose	3755	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
β-D-glucose	3755	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
β-D-glucose	3755	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
α-D-glucose	133	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
α-D-glucose	133	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
α-D-glucose	133	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
α-D-glucose	133	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
β-D-fructofuranose	63197	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
β-D-fructofuranose	63197	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
β-D-fructofuranose	63197	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
β-D-fructofuranose	63197	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
<b>lactose degradation III<sup>c</sup></b>							
β-D-galactose	NA	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
β-D-galactose	NA	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
β-D-galactose	NA	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
β-D-galactose	NA	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
β-D-glucose	3755	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
β-D-glucose	3755	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
β-D-glucose	3755	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
β-D-glucose	3755	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
<b>D-galactose degradation V (Leloir pathway)<sup>c</sup></b>							
β-D-galactose	NA	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
β-D-galactose	NA	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
β-D-galactose	NA	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
β-D-galactose	NA	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
α-D-galactose	NA	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
α-D-galactose	NA	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
α-D-galactose	NA	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
α-D-galactose	NA	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
<b>trehalose degradation<sup>c</sup></b>							
β-D-glucose	3755	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
β-D-glucose	3755	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
β-D-glucose	3755	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
β-D-glucose	3755	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
α-D-glucose	133	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
α-D-glucose	133	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
α-D-glucose	133	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
α-D-glucose	133	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
<b>myo-inositol de novo biosynthesis<sup>c</sup></b>							
myo-inositol	144	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
myo-inositol	144	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
myo-inositol	144	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
myo-inositol	144	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
<b>D-myo-inositol (1,4,5)-trisphosphate biosynthesis<sup>c</sup></b>							
myo-inositol	144	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
myo-inositol	144	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
myo-inositol	144	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
myo-inositol	144	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
<b>glycogenolysis<sup>c</sup></b>							
β-D-glucose	3755	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
β-D-glucose	3755	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
β-D-glucose	3755	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
β-D-glucose	3755	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]



Table S4 (cont.)

Pathway	METLIN ID	Dysregulation*	Fold Change	p-value	m/z	t <sub>R</sub> (min)	Adduct Form
<b>UDP-N-acetyl-D-galactosamine biosynthesis II<sup>c</sup></b>							
β-D-glucose	3755	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
β-D-glucose	3755	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
β-D-glucose	3755	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
β-D-glucose	3755	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
<b>sorbitol degradation I<sup>c</sup></b>							
keto-D-fructose	NA	DOWN	1.8	5.30E-03	179.0558	11.39	M-H[-]
keto-D-fructose	NA	DOWN	3.6	1.80E-04	181.0704	2.79	M+H[1+]
keto-D-fructose	NA	DOWN	3.2	3.40E-04	181.0709	2.44	M+H[1+]
keto-D-fructose	NA	DOWN	2	5.60E-03	181.0706	11.65	M+H[1+]
<b>lysine degradation I (saccharopine pathway)<sup>d</sup></b>							
L-saccharopine	383	DOWN	1.9	4.90E-03	301.1362	10.38	M+Na[1+]
L-2-aminoadipate	3271	DOWN	2.2	5.40E-03	185.0652	2.47	M+Na[1+]
L-2-aminoadipate	3271	DOWN	2.6	5.00E-03	185.0651	2.8	M+Na[1+]
L-lysine	25	DOWN	1.9	3.70E-03	171.1112	12.12	M+Na[1+]
<b>lysine degradation II (pipecolate pathway)<sup>d</sup></b>							
L-2-aminoadipate	3271	DOWN	2.2	5.40E-03	185.0652	2.47	M+Na[1+]
L-2-aminoadipate	3271	DOWN	2.6	5.00E-03	185.0651	2.8	M+Na[1+]
L-pipecolate	50	DOWN	2	2.40E-03	150.0546	12.8	M+Na-2H[-]
L-lysine	25	DOWN	1.9	3.70E-03	171.1112	12.12	M+Na[1+]
<b>tRNA charging<sup>e</sup></b>							
L-histidine	21	DOWN	1.5	4.90E-03	90.0367	2.89	M+H+Na[2+]
L-lysine	25	DOWN	1.9	3.70E-03	171.1112	12.12	M+Na[1+]
<b>histidine degradation<sup>e</sup></b>							
urocanate	298	DOWN	1.8	5.40E-03	183.0397	9.61	M+HCOO[-]
L-histidine	21	DOWN	1.5	4.90E-03	90.0367	2.89	M+H+Na[2+]
<b>pyrimidine deoxyribonucleotide phosphorylation<sup>f</sup></b>							
dTTP	3577	DOWN	1.7	1.50E-04	504.9796	10.04	M+Na[1+]
<b>pyrimidine deoxyribonucleotides biosynthesis from CTP<sup>f</sup></b>							
dTTP	3577	DOWN	1.7	1.50E-04	504.9796	10.04	M+Na[1+]
<b>pyrimidine deoxyribonucleotides de novo biosynthesis<sup>f</sup></b>							
dTTP	3577	DOWN	1.7	1.50E-04	504.9796	10.04	M+Na[1+]
<b>dermatan sulfate degradation (metazoa)</b>							
α-L-iduronate <sup>a</sup>	NA	DOWN	2	1.70E-03	177.0392	13.23	M-H <sub>2</sub> O+H[1+]
sulfate	3235	DOWN	2.1	6.80E-03	136.9301	1.89	M+K[1+]
<b>oleate biosynthesis</b>							
oleate	190	DOWN	3.8	6.70E-03	153.1264	13.58	M+H+Na[2+]
<b>palmitate biosynthesis<sup>g</sup></b>							
palmitate	187	DOWN	1.5	4.20E-03	295.2024	19.65	M+K[1+]
<b>stearate biosynthesis<sup>g</sup></b>							
palmitate	187	DOWN	1.5	4.20E-03	295.2024	19.65	M+K[1+]
<b>α-tocopherol degradation</b>							
α-carboxyethylhydroxychroman	NA	DOWN	1.6	3.60E-05	151.0743	18.18	M+H+Na[2+]
<b>tetrapyrrole biosynthesis</b>							
5-aminolevulinic acid	75	DOWN	2	4.90E-03	155.0554	9.87	M+Na[1+]
<b>proline degradation<sup>h</sup></b>							
L-glutamate-5-semialdehyde	295	DOWN	2	4.90E-03	155.0554	9.87	M+Na[1+]
<b>proline biosynthesis<sup>h</sup></b>							
L-glutamate-5-semialdehyde	295	DOWN	2	4.90E-03	155.0554	9.87	M+Na[1+]
<b>ornithine de novo biosynthesis<sup>h</sup></b>							
L-glutamate-5-semialdehyde	295	DOWN	2	4.90E-03	155.0554	9.87	M+Na[1+]
<b>catecholamine biosynthesis</b>							
(R)-adrenaline	62	UP	2.3	3.10E-04	204.0641	18.04	M+Na-2H[-]
4α-hydroxy-tetrahydrobiopterin	64413	UP	1.7	1.90E-04	302.1112	15.78	M+HCOO[-]
L-ascorbate <sup>a</sup>	249	DOWN	2	1.70E-03	177.0392	13.23	M+H[1+]
<b>ascorbate recycling (cytosolic)</b>							
L-ascorbate <sup>a</sup>	249	DOWN	2	1.70E-03	177.0392	13.23	M+H[1+]

\*Dysregulation (fold change) relative to Whites; NA: not applicable

a) Isobaric putative metabolite/metabolites

b) Pathways with overlapping metabolite/metabolites-1

c) Pathways with overlapping metabolite/metabolites-2

d) Pathways with overlapping metabolite/metabolites-3

e) Pathways with overlapping metabolite/metabolites-4

f) Pathways with overlapping metabolite/metabolites-5

g) Pathways with overlapping metabolite/metabolites-6

h) Pathways with overlapping metabolite/metabolites-7