eTable 1.	Metabolic	changes ir	n smoking	habits
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HMDB_ID	Vetabolite name Men						Women							HMDB_ID	Metabolite name				
		Cigarette smokers vs. never smokers			Past smokers vs. never smokers				Cigarette smokers vs. never smokers			Past smokers vs. never smokers			_				
		Age adujsted		Fully adjusted		Age adujsted	F	ully adjusted		Age adujsted		Fully adjusted		Age adujsted		Fully adjusted			
		Fold change (ref: Never)	FDR <i>P</i> value	Fold change (ref: Never)	FDR <i>P</i> value	Fold change (ref: Never)	FDR P value	old change ref: Never)	FDR P value	Fold change (ref: Never)	FDR <i>P</i> value	Fold change (ref: Never)	FDR P value	Fold change (ref: Never)	DR P value	Fold change (ref: Never)	FDR <i>P</i> value		
1 HMDB0000094	Citrate	0.89	5.2.E-34	0.92	1.4.E-18	0.96	4.8.E-06	0.98	7.0.E-02	0.90	5.8.E-12	0.93	3 2.2.E-05	0.97	7.9.E-02	1.00	9.0.E-0	1 HMDB0000094	Citrate
2 HMDB0000148	3 Glu	1.17	1.8.E-18	1.14	1.6.E-16	1.11	8.7.E-09	1.05	1.8.E-02	1.19	1.1.E-07	1.12	2 1.6.E-04	1.13	8.3.E-07	1.06	4.2.E-0	2 HMDB0000148	Glu
3 HMDB000008	3 2-Hydroxybutyrate	0.89	6.1.E-12	0.89	3.1.E-11	1.03	2.0.E-01	1.00	9.4.E-01	0.89	4.6.E-05	0.92	2 8.9.E-03	0.97	5.3.E-01	0.96	4.4.E-0	1 HMDB000008	2-Hydroxybutyrate
4 HMDB0003157	Guanidinosuccinate	0.69	1.2.E-13	0.74	9.6.E-09	0.81	1.0.E-05	0.87	2.6.E-02	0.77	2.4.E-03	0.81	3.6.E-02	0.89	1.2.E-01	0.94	6.0.E-0	1 HMDB0003157	Guanidinosuccinate
5 HMDB0000875	Trigonelline	1.77	1.2.E-13	1.56	9.6.E-09	1.08	4.3.E-01	1.13	2.9.E-01	2.01	3.7 E-08	1.71	4.9.E-05	1.14	2.9.E-01	1.11	5.9.E-0	1 HMDB0000875	Trigonelline
6 HMDB0000517	' Arg	1.04	1.8.E-07	1.05	9.6.E-09	0.99	1.9.E-01	1.00	8.0.E-01	1.04	8.5.E-03	1.05	6.8.E-03	1.00	8.3.E-01	1.00	9.9.E-0	1 HMDB0000517	Arg
7 HMDB0000296	6 Uridine	0.96	3.4.E-10	0.96	9.6.E-09	0.99	4.3.E-01	0.99	3.9.E-01	0.97	9.9.E-03	0.97	4.4.E-02	0.99	4.4.E-01	0.99	7.8.E-0	1 HMDB0000296	Uridine
8 HMDB0000162	Pro Pro	1.06	1.6.E-06	1.07	2.5.E-07	1.03	5.4.E-02	1.02	2.0.E-01	1.08	2.6.E-04	1.08	5.9.E-04	1.02	2.3.E-01	1.02	5.8.E-0	1 HMDB0000162	Pro
9 HMDB0000639	Mucate	0.89	6.1.E-12	0.92	1.3.E-06	0.94	2.2.E-04	0.96	8.4.E-02	0.91	2.1.E-06	0.93	8.2.E-04	0.97	3.3.E-01	0.99	9.0.E-0	1 HMDB0000639	Mucate
10 HMDB0000214	Ornithine	1.03	3.1.E-03	1.05	1.5.E-06	0.98	1.5.E-01	1.00	8.0.E-01	1.11	1.2.E-08	1.11	4.3.E-09	1.01	4.9.E-01	1.01	5.9.E-0	1 HMDB0000214	Ornithine
11 HMDB0000011	. 3-Hydroxybutyrate	0.79	9.2.E-15	0.86	1.6.E-06	0.95	1.0.E-01	0.98	7.5.E-01	0.74	8.4.E-08	0.85	5 1.1.E-02	0.90	7.0.E-02	0.94	7.6.E-0	1 HMDB0000011	3-Hydroxybutyrate
12 HMDB0000943	8 threonate	0.93	1.1.E-09	0.94	1.0.E-05	0.95	7.7.E-05	0.97	5.9.E-02	0.95	1.4.E-03	0.96	6 4.8.E-02	0.99	9.4.E-01	1.01	9.0.E-0	1 HMDB0000943	threonate
13 HMDB0000187	' Ser	1.01	3.1.E-01	1.04	1.6.E-05	0.99	5.8.E-01	1.02	1.8.E-01	1.02	3.8.E-01	1.05	5 3.7.E-03	0.97	1.8.E-02	0.99	5.9.E-0	1 HMDB0000187	Ser
14 HMDB0000167	'Thr	1.05	5.1.E-08	1.04	2.4.E-05	1.01	1.8.E-01	1.01	5.7.E-01	1.04	1.0.E-02	1.04	3.6.E-02	1.01	4.0.E-01	1.01	7.8.E-0	1 HMDB0000167	Thr
15 HMDB0000092	N,N-Dimethylglycine	1.05	3.3.E-03	1.07	7.6.E-05	1.00	9.3.E-01	1.01	5.7.E-01	1.09	8.5.E-04	1.10) 3.5.E-04	1.01	5.8.E-01	1.02	5.9.E-0	1 HMDB0000092	N,N-Dimethylglycine
16 HMDB0000904	Citrulline	1.02	1.4.E-02	1.04	2.1.E-04	0.99	5.8.E-01	1.01	5.3.E-01	1.02	2.1.E-01	1.04	4.4.E-02	0.99	4.4.E-01	1.00	9.9.E-0	1 HMDB0000904	Citrulline
17 HMDB0000172	? lle	1.02	1.4.E-02	1.03	2.5.E-04	1.00	9.3.E-01	1.00	7.2.E-01	1.05	3.7.E-04	1.05	5 7.7.E-04	1.02	1.8.E-01	1.01	5.9.E-0	1 HMDB0000172	lle
18 HMDB0000158	3 Tyr	1.03	1.5.E-03	1.03	1.0.E-03	1.02	3.6.E-03	1.01	3.0.E-01	1.05	1.3.E-03	1.03	3 4.9.E-02	1.02	1.1.E-01	1.00	9.6.E-0	1 HMDB0000158	Tyr
19 HMDB0000005	5 2-Oxobutyrate	0.75	1.1.E-08	0.83	1.1.E-03	0.93	2.0.E-01	0.98	7.8.E-01	0.70	2.4.E-05	0.81	2.0.E-02	0.95	8.3.E-01	0.99	9.0.E-0	1 HMDB0000005	2-Oxobutyrate
20 HMDB0000684	Kynurenine	0.93	1.3.E-03	0.93	1.2.E-03	0.98	4.2.E-01	0.97	4.2.E-01	0.94	1.8.E-01	0.91	5.0.E-02	1.00	9.3.E-01	0.99	8.9.E-0	1 HMDB0000684	Kynurenine
21 HMDB0000687	' Leu	1.02	4.0.E-02	1.02	2.5.E-03	1.00	9.3.E-01	1.00	6.5.E-01	1.04	7.2.E-04	1.03	3 4.4.E-02	1.02	4.1.E-02	1.01	7.8.E-0	1 HMDB0000687	Leu
22 HMDB0000243	8 Pyruvate	1.06	3.6.E-04	1.04	2.6.E-02	1.05	1.0.E-02	1.02	5.7.E-01	1.06	2.7.E-02	1.06	4.8.E-02	1.02	6.7.E-01	1.01	9.0.E-0	1 HMDB0000243	Pyruvate
23 HMDB0000156	o Malate	0.95	1.9.E-04	0.94	5.5.E-07	1.01	6.7.E-01	0.99	7.2.E-01	0.96	6.7.E-02	0.98	4.3.E-01	1.01	9.4.E-01	1.01	9.0.E-0	1 HMDB0000156	Malate
24 HMDB0000725	Hydroxyproline	1.06	2.1.E-05	1.08	2.5.E-06	1.00	9.3.E-01	1.00	8.6.E-01	1.05	6.2.E-02	1.04	+ 1.7.E-UI	1.04	8.5.E-UZ	1.02	5.4.E-U	1 HMDB0000725	Hydroxyproline
25 HMDB0000656) CSSG Dinesclate	0.80	1.0 E-13	0.87	3.2.E-06	0.86	2.0.E-07	1.02	1.8.E-01	0.89	3.2.E-03	0.93	5 8.2.E-UZ	0.89	2.0.E-04	0.94	I./.E-U	1 HMDB0000656	Disecclete
26 HMDB0000070	Corpiting	1.18	1.0.E-12	1.11	5.U.E-06	1.07	3.0.E-U3	1.03	4.7.E-UI	1.11	2.0.E-03	1.06	0 1.4.E-UI	1.08	4.2.E-U3	1.04	5.4.E-U 7.9.E.0	1 HMDB0000070	Correiting
27 HMDB000002	Croatinina	1.00	E 1 E 00	1.04	1.6E.06	1.04	2.0.E-07	1.02	47E 01	1.01	0.2.E-01	1.00	9 7.2.E-01	1.01	0 2 E 01	1.00	7.0.L-U	1 HMDB000002	Creatinina
28 HMDB0000302	Aca	1.02	1.0 E-03	1.03	2.6 E-05	1.00	2.4.C-01 8.0.E-01	1.01	4.7.E-01	1.00	8.5.L-01	1.00	2 82 F-02	1.00	3.0 E-01	1.00	5.9.L-U 5.8.E-0	1 HMDB0000302	Asn
30 HMDB0000100	Asin Bi Ghu	1.02	66E-03	1.03	2.0.E 05	0.98	1.4 E-02	1.01	7.8 E-01	1.02	5.1 E-01	1.02	2 2 2 E - 01	0.00	1.1 E-02	0.55	17E-0	1 HMDB0000100	Asii
31 HMDB0000123	2-Oxoisopentanoate	0.97	9.4 E-05	0.97	1.7 E-04	1.01	5.0 E-01	0.99	7.2 E-01	0.98	2.5 E-01	0.99	49F-01	1.00	9.4 F-01	0.99	9.0 E-0	1 HMDB0000125	2-Oxoisonentanoate
32 HMDB0003072	2 Ouinate	1.37	6.0 E-07	1 24	1.1 E-03	1.01	1.6 E-01	1 11	2.6 E-01	1.43	1.6 E-03	1.13	42 F-01	1.00	3 3 E-01	1.07	9.0 E-0	1 HMDB0003072	Quinate
33 HMDB0000128	Guanidinoacetate	1.05	2.6.E-05	1.04	1.5.F-03	1.02	1.5.E-01	1.01	4.7.E-01	1.02	3.4.F-01	1.02	2.6.F-01	1.01	4.9.E-01	1.02	5.9.E-0	1 HMDB0000128	Guanidinoacetate
34 HMDB0000224	Ethanolamine phosphate	0.87	1.8.E-03	0.87	2.2.E-03	0.96	3.6.E-01	0.95	5.7.E-01	0.92	2.6.E-01	0.93	4.3.E-01	0.96	8.3.E-01	0.98	9.0.E-0	1 HMDB0000224	Ethanolamine phosphate
35 HMDB0000043	Betaine	1.03	9.0.E-03	1.03	6.6.E-03	1.01	5.5.E-01	1.02	3.0.E-01	1.01	6.0.E-01	1.03	3 2.2.E-01	0.99	4.6.E-01	1.00	8.9.E-0	1 HMDB0000043	Betaine
36 HMDB0000634	Citraconate	1.23	4.4.E-04	1.19	6.9.E-03	1.05	4.5.E-01	1.06	5.7.E-01	1.01	9.4.E-01	1.03	8.2.E-01	0.99	9.4.E-01	0.99	9.4.E-0	1 HMDB0000634	Citraconate
37 HMDB0000958	trans-Aconitate	0.89	5.5.E-03	0.89	7.1.E-03	0.97	4.5.E-01	0.96	5.7.E-01	1.13	8.7.E-02	1.10	2.6.E-01	1.01	9.4.E-01	1.00	9.4.E-0	1 HMDB0000958	trans-Aconitate
38 HMDB0003911	3-Aminoisobutyrate	0.86	2.2.E-04	0.89	9.1.E-03	0.95	3.2.E-01	0.97	6.5.E-01	0.97	7.5.E-01	1.04	6.1.E-01	0.96	4.9.E-01	1.00	9.9.E-0	1 HMDB0003911	3-Aminoisobutyrate
39 HMDB0000182	2 Lys	0.98	1.0.E-03	0.98	1.2.E-02	0.98	3.7.E-02	0.99	2.0.E-01	1.00	7.5.E-01	0.99	6.9.E-01	1.01	5.5.E-01	1.00	9.9.E-0	1 HMDB0000182	Lys
40 HMDB0000650	2AB	0.96	1.5.E-03	0.97	1.5.E-02	1.02	4.0.E-01	1.00	8.0.E-01	0.95	3.9.E-02	0.96	6 8.3.E-02	0.99	5.8.E-01	0.97	1.7.E-0	1 HMDB0000650	2AB
41 HMDB0000072	cis-Aconitate	0.97	5.5.E-03	0.97	1.6.E-02	1.02	2.0.E-01	1.01	7.2.E-01	0.97	1.9.E-01	0.99	9 7.6.E-01	1.00	9.9.E-01	1.00	9.0.E-0	1 HMDB0000072	cis-Aconitate
42 HMDB0000695	6 4-Methyl-2-oxopentanoate	0.98	1.3.E-01	0.98	1.9.E-02	1.01	2.3.E-01	0.99	7.2.E-01	1.02	1.9.E-01	1.01	5.3.E-01	1.01	9.4.E-01	0.99	9.0.E-0	1 HMDB0000695	4-Methyl-2-oxopentanoate
43 HMDB0000682	? 3-Indoxyl sulfate	0.89	1.9.E-03	0.91	1.9.E-02	0.94	1.0.E-01	0.95	5.7.E-01	0.92	2.0.E-01	0.91	2.2.E-01	1.03	9.4.E-01	1.03	9.0.E-0	1 HMDB0000682	3-Indoxyl sulfate
44 HMDB0000157	' Hypoxanthine	1.05	3.4.E-01	1.12	2.2.E-02	1.03	5.8.E-01	1.05	4.7.E-01	0.98	7.8.E-01	1.01	9.2.E-01	0.99	9.1.E-01	1.00	9.9.E-0	1 HMDB0000157	Hypoxanthine
45 HMDB0003903	8 Isethionate	0.97	4.7.E-02	0.96	2.4.E-02	0.99	7.1.E-01	1.00	9.2.E-01	0.97	4.0.E-01	0.96	5 3.1.E-01	1.00	9.9.E-01	1.00	9.4.E-0	1 HMDB0003903	Isethionate
46 HMDB0000511	. Decanoate	0.95	2.6.E-02	0.94	3.0.E-02	0.99	6.8.E-01	0.99	7.5.E-01	0.98	6.6.E-01	0.98	3 7.6.E-01	0.99	9.4.E-01	0.99	9.0.E-0	1 HMDB0000511	Decanoate
47 HMDB0000086	Glycerophosphorylcholine	0.98	5.9.E-01	0.94	3.6.E-02	0.99	7.1.E-01	0.97	4.7.E-01	0.98	7.2.E-01	0.96	5 4.1.E-01	0.99	9.1.E-01	0.99	8.9.E-0	1 HMDB0000086	Glycerophosphorylcholine
48 HMDB0002428	3 Terephthalate	0.97	1.2.E-01	0.97	4.2.E-02	0.99	5.8.E-01	0.99	7.2.E-01	0.96	1.7.E-01	0.96	6 2.6.E-01	1.01	9.4.E-01	1.01	9.0.E-0	1 HMDB0002428	Terephthalate
49 HMDB0004827	′ proline betaine	0.90	1.2.E-02	0.91	5.1.E-02	0.91	5.4.E-02	0.92	2.2.E-01	0.88	1.5.E-01	0.89	2.0.E-01	0.97	6.8.E-01	0.98	8.9.E-0	1 HMDB0004827	proline betaine
50 HMDB0000161	. Ala	1.03	1.2.E-03	1.02	6.7.E-02	1.02	7.6.E-02	1.00	8.4.E-01	1.07	1.1.E-04	1.04	2.4.E-02	1.03	4.0.E-02	1.01	7.8.E-0	1 HMDB0000161	Ala
51 HMDB0000177	' His	1.02	1.5.E-03	1.01	7.5.E-02	1.01	5.3.E-01	1.00	8.0.E-01	1.03	2.6.E-03	1.01	2.0.E-01	1.02	5.5.E-03	1.01	5.4.E-0	1 HMDB0000177	His
52 HMDB0000191	. Asp	1.04	3.0.E-02	1.04	7.8 E-02	1.03	1.5.E-01	1.01	7.2.E-01	1.10	9.9.E-03	1.09	3.8.E-02	1.09	4.2.E-03	1.06	1.4.E-0	1 HMDB0000191	Asp
53 HMDB0000254	Succinate	0.99	2.1.E-01	0.98	8.9.E-02	0.99	1.9.E-01	0.99	5.7.E-01	0.99	7.1.E-01	1.00	9.1.E-01	1.00	9.4.E-01	1.00	9.0.E-0	1 HMDB0000254	Succinate
54 HMDB0001161	gamma-Butyrobetaine	0.97	3.2.E-03	0.98	9.2.E-02	0.98	1.6.E-01	0.99	5.4.E-01	0.99	7.8.E-01	1.01	1 7.1.E-01	0.97	1.1.E-02	0.98	3.4.E-0	1 HMDB0001161	gamma-Butyrobetaine
55 HMDB0000056	beta-Ala	0.96	1.5.E-03	0.98	1.0.E-01	0.99	4.2.E-01	0.99	4.7.E-01	1.01	7.8.E-01	1.01	1 8.6.E-01	1.04	1.2.E-01	1.03	3.9.E-0	T HMDR000026	beta-Ala

56 HMDB0000271	Sarcosine	1.07	2.3.E-02	1.05	1.0.E-01	1.00	9.3 E-01	0.99	8.4.E-01	1.11	5.6.E-02	1.11	7.9.E-02	0.99	9.1.E-01	0.99	8.9.E-01 HMDB0000271 Sarcosine
57 HMDB0001539	ADMA	1.05	7.9.E-02	1.05	1.0.E-01	1.02	5.8.E-01	1.02	5.7.E-01	1.12	3.9.E-02	1.11	7.6.E-02	1.03	4.9.E-01	1.04	6.0.E-01 HMDB0001539 ADMA
58 HMDB0000126	Glycerophosphate	0.98	5.5.E-01	0.96	1.0.E-01	1.03	2.9.E-01	1.00	9.3.E-01	0.93	7.2.E-02	0.91	2.3.E-02	1.01	9.4.E-01	1.01	9.0.E-01 HMDB0000126 Glycerophosphate
59 HMDB0000929	Trp	1.02	1.2.E-03	1.01	1.2.E-01	1.00	7.9.E-01	0.99	5.3.E-01	1.05	2.2.E-04	1.02	8.2.E-02	1.01	2.2.E-01	1.00	9.9.E-01 HMDB0000929 Trp
60 HMDB0000699	1-Methylnicotinamide	1.08	8.4.E-02	1.07	1.4.E-01	1.05	4.2.E-01	1.02	7.8.E-01	0.90	1.9.E-01	0.86	5.0.E-02	0.96	5.5.E-01	0.92	4.4.E-01 HMDB0000699 1-Methylnicotinamide
61 HMDB0000208	2-Oxoglutarate	1.00	9.4.E-01	0.98	1.7.E-01	1.03	7.3.E-02	1.01	7.5.E-01	0.99	7.1.E-01	0.99	7.5.E-01	1.02	7.7.E-01	1.01	9.0.E-01 HMDB0000208 2-Oxoglutarate
62 HMDB0000847	Pelargonate	1.02	2.3.E-01	1.02	1.7.E-01	1.01	4.5.E-01	1.01	5.7.E-01	1.00	1.0.E+00	1.01	7.7.E-01	1.01	9.4.E-01	1.01	9.0.E-01 HMDB0000847 Pelargonate
63 HMDB0000201	o-Acetylcarnitine	1.07	9.1.E-02	1.06	1.7.E-01	1.08	7.1.E-02	1.04	4.7.E-01	0.97	7.5.E-01	0.98	7.9.E-01	1.03	5.8.E-01	1.02	8.9.E-01 HMDB0000201 o-Acetylcarnitine
64 HMDB0000925	Trimethylamine N-oxide	0.94	1.8.E-01	0.94	1.9.E-01	0.96	4.6.E-01	0.95	4.7.E-01	1.03	7.5.E-01	1.01	8.8.E-01	1.12	4.1.E-02	1.09	3.9.E-01 HMDB0000925 Trimethylamine N-oxide
65 HMDB0000159	Phe	1.00	9.2.E-01	1.01	2.1.E-01	1.00	6.1.E-01	0.99	4.7.E-01	1.02	5.6.E-02	1.02	1.3.E-01	1.01	2.3.E-01	1.01	7.8.E-01 HMDB0000159 Phe
66 HMDB0000192	Cystine	0.98	1.2.E-02	0.99	2.1.E-01	1.00	5.8.E-01	1.00	6.5.E-01	1.00	8.0.E-01	0.99	6.7 E-01	1.00	8.3.E-01	0.99	5.9.E-01 HMDB0000192 Cystine
67 HMDB0000479	3-Methylhistidine	0.96	6.8.E-02	0.97	2.4.E-01	0.96	1.5.E-01	0.96	2.7.E-01	0.94	1.9.E-01	0.95	2.8.E-01	0.99	8.3.E-01	0.99	8.9.E-01 HMDB0000479 3-Methylhistidine
68 HMDB0000883	Val	1.00	8.6.E-01	1.01	2.4.E-01	1.00	7.0.E-01	0.99	4.7.E-01	1.02	8.7.E-02	1.01	2.7.E-01	1.01	2.2.E-01	1.00	8.9.E-01 HMDB0000883 Val
69 HMDB0000064	Creatine	1.01	7.9.E-01	0.97	2.4.E-01	0.99	7.0.E-01	0.96	1.8.E-01	0.99	7.2.E-01	0.98	4.8.E-01	0.96	8.5.E-02	0.94	4.2.E-02 HMDB0000064 Creatine
70 HMDB0000134	Fumarate	0.98	5.8.E-01	0.97	2.7.E-01	1.05	1.0.E-01	1.04	4.6.E-01	1.03	5.4.E-01	1.04	4.3.E-01	0.99	9.4.E-01	1.00	9.4.E-01 HMDB0000134 Fumarate
71 HMDB0000731	Cysteine S-sulfate	0.96	2.9.E-01	0.96	2.7.E-01	0.98	5.8.E-01	0.98	7.5.E-01	1.11	9.8.E-02	1.10	1.8 E-01	1.07	3.3.E-01	1.07	6.2.E-01 HMDB0000731 Cysteine S-sulfate
72 HMDB0000510	alpha-Aminoadipate	0.96	1.6.E-01	0.97	2.7.E-01	1.00	9.3 E-01	0.99	8.0.E-01	1.00	9.4.E-01	0.97	6.3.E-01	1.04	4.5.E-01	1.01	8.9.E-01 HMDB0000510 alpha-Aminoadipate
73 HMDB0000190	Lactate	1.03	2.2.E-02	1.01	2.9.E-01	1.03	2.6.E-02	1.01	7.2.E-01	1.04	1.3.E-01	1.04	1.6.E-01	1.00	9.4.E-01	1.00	9.0.E-01 HMDB0000190 Lactate
74 HMDB0000251	Taurine	0.99	4.2.E-01	0.99	3.0.E-01	0.99	5.8.E-01	1.00	8.0.E-01	1.01	5.1.E-01	1.00	8.4.E-01	1.01	3.8.E-01	1.01	5.9.E-01 HMDB0000251 Taurine
75 HMDB0000641	GIn	0.99	3.0.E-02	1.01	3.4.E-01	0.98	6.0.E-04	1.00	6.5.E-01	1.01	6.5.E-01	1.01	2.8.E-01	0.99	4.8.E-02	0.99	5.4.E-01 HMDB0000641 GIn
76 HMDB0032538	Triethanolamine	1.03	6.4.E-01	1.05	3.9.E-01	1.04	5.8.E-01	1.05	5.7.E-01	0.95	7.2.E-01	0.97	7.7.E-01	0.95	4.9.E-01	0.95	7.8.E-01 HMDB0032538 Triethanolamine
77 HMDB0003334	SDMA	0.97	2.1.E-01	0.98	4.4.E-01	0.98	5.8 E-01	0.99	8.0.E-01	0.93	1.9.E-01	0.92	1.7.E-01	1.00	9.7.E-01	1.00	9.9.E-01 HMDB0003334 SDMA
78 HMDB0000812	N-Acetylaspartate	0.99	6.3.E-01	0.99	4.9.E-01	0.99	7.1.E-01	0.99	7.8.E-01	1.01	8.7.E-01	1.01	7.1.E-01	1.01	9.4.E-01	1.02	9.0.E-01 HMDB0000812 N-Acetylaspartate
79 HMDB0000289	Urate	1.00	9.3.E-01	0.99	4.9.E-01	1.04	8.3.E-05	1.02	7.9.E-02	1.04	8.3.E-02	1.01	7.6.E-01	1.06	8.0.E-05	1.03	4.4.E-01 HMDB0000289 Urate
80 HMDB0000193	Isocitrate	1.01	4.0.E-01	1.01	5.7.E-01	1.04	2.1.E-03	1.02	2.6.E-01	1.00	9.7.E-01	1.01	7.6.E-01	1.02	4.3.E-01	1.02	7.6.E-01 HMDB0000193 Isocitrate
81 HMDB0061881	4-Acetylbutyrate	1.03	5.5.E-01	1.03	5.8.E-01	1.01	7.1.E-01	1.02	7.5.E-01	1.04	6.4.E-01	1.02	7.6.E-01	1.01	9.4.E-01	1.01	9.0.E-01 HMDB0061881 4-Acetylbutyrate
82 HMDB0000784	Azelate	1.01	7.5.E-01	1.01	5.8.E-01	1.01	7.4.E-01	1.01	7.5.E-01	1.03	3.7.E-01	1.03	5.3.E-01	1.00	9.4.E-01	1.01	9.0.E-01 HMDB0000784 Azelate
83 HMDB0000127	Glucuronate	1.00	9.1.E-01	1.02	5.8.E-01	1.02	5.0.E-01	1.01	7.5.E-01	1.06	2.5.E-01	1.05	4.3.E-01	1.03	7.7.E-01	1.02	9.0.E-01 HMDB0000127 Glucuronate
84 HMDB0000097	Choline	1.02	5.4.E-02	1.00	6.0.E-01	1.01	2.6.E-01	1.00	8.0.E-01	1.02	1.2.E-01	1.02	3.4.E-01	1.01	4.0.E-01	1.00	8.9.E-01 HMDB0000097 Choline
85 HMDB0000696	Met	1.00	7.9.E-01	1.01	6.4.E-01	0.99	5.8.E-01	0.99	5.1.E-01	1.04	8.7.E-02	1.03	2.2.E-01	1.01	6.9.E-01	1.00	8.9.E-01 HMDB0000696 Met
86 HMDB0000482	Octanoate	0.99	7.7.E-01	0.98	6.5.E-01	1.00	9.5.E-01	1.00	9.3.E-01	0.91	8.9.E-02	0.93	2.6.E-01	1.00	9.4.E-01	1.02	9.0.E-01 HMDB0000482 Octanoate
87 HMDB0000118	Homovanillate	1.05	3.1.E-01	1.02	6.8.E-01	1.09	3.5.E-02	1.06	3.3.E-01	1.03	7.1.E-01	1.00	9.8 E-01	1.00	9.9.E-01	0.98	9.0.E-01 HMDB0000118 Homovanillate
88 HMDB0000763	Indole-3-acetate	1.00	9.0.E-01	0.99	6.8.E-01	1.00	9.3 E-01	0.99	8.0.E-01	0.98	7.8.E-01	0.95	5.4.E-01	1.04	4.9.E-01	1.04	7.7.E-01 HMDB0000763 Indole-3-acetate
89 HMDB0000661	Glutarate	0.98	4.3.E-01	0.99	8.1.E-01	1.01	6.8.E-01	1.01	7.2.E-01	0.96	2.8.E-01	1.00	9.9.E-01	0.99	9.4.E-01	1.01	9.0.E-01 HMDB0000661 Glutarate
90 HMDB0000691	Malonate	1.00	9.6.E-01	0.99	8.2.E-01	0.99	8.8.E-01	0.99	8.5.E-01	1.05	5.2.E-01	1.05	5.3.E-01	1.01	9.4.E-01	1.02	9.0.E-01 HMDB0000691 Malonate
91 HMDB0000267	5-Oxoproline	0.99	4.3.E-01	1.00	8.2.E-01	0.99	3.2.E-01	1.00	9.3.E-01	1.03	5.7.E-02	1.04	2.0.E-02	1.01	7.7.E-01	1.02	7.6.E-01 HMDB0000267 5-Oxoproline
92 HMDB0000714	Hippurate	0.94	5.2.E-01	0.98	8.2.E-01	0.85	3.5.E-02	0.93	5.7.E-01	0.95	7.1.E-01	0.96	7.6.E-01	0.98	9.4.E-01	1.02	9.0.E-01 HMDB0000714 Hippurate
93 HMDB0000666	Heptanoate	0.97	4.3.E-01	0.99	8.3.E-01	0.97	4.5.E-01	0.98	7.5.E-01	0.99	8.8.E-01	0.97	7.6.E-01	0.94	5.3.E-01	0.93	6.2.E-01 HMDB0000666 Heptanoate
94 HMDB0000535	Hexanoate	0.99	6.4.E-01	1.00	8.7.E-01	0.98	2.1.E-01	0.98	5.7.E-01	0.93	7.1.E-03	0.93	2.0.E-02	0.99	9.4.E-01	0.99	9.0.E-01 HMDB0000535 Hexanoate

FDR, false discovery rate.

	HTP users	Cigarette smokers	Past smokers	Never smokers
N, %	55 (11.9)	119 (25.7)	144 (31.1)	145 (31.3)
Women, n (%)	10 (18.2)	27 (22.7)	30 (20.7)	30 (20.7)
Age, mean (SD)	49.22 (10.57)	54.51 (8.83)	52.72 (10.25)	51.34 (10.08)
Total tobacco products number per day	13.12 (4.82)	14.41 (6.23)		
Cigarette, mean (SD)		14.41 (6.23)		
IQOS, mean (SD)	11.05 (6.41)			
Ploom TECH, mean (SD)	0.27 (2.02)			
glo, mean (SD)	1.80 (5.06)			
Years of using HTPs	1.69 (0.84)			
Cigarette number per day	15.49 (6.14)	16.08 (6.80)		
Years of smoking	27.47	33.00	23.25	
Years after cessation	(10.51)	(10.25)	8.77 (7.65)	
Daily drinking, %	42 (76.4)	90 (75.6)	104 (72.2)	108 (74.5)
Systolic blood pressure, mean (SD) BMI, mean (SD)	128.93 (17.56) 23.00 (3.03)	129.93 (17.99) 23.05 (3.75)	131.51 (16.44) 23.77 (3.66)	128.61 (15.80) 23.86 (3.61)
HbA1c, mean (SD)	5.66 (0.60)	5.71 (0.47)	5.75 (0.59)	5.66 (0.56)
Triglyceride, median (IQR]	94.0 (58.0–134.5)	108.0 (79.5–146.5)	92.0 (65.8–144.3)	95.0 (62.0–132.0)

eTable 2. Characteristics of the participants at the follow-up survey after matching

HTP, heated tobacco products; IQR, interquartile range; SD, standard deviation.



eFigure 1. Glutamate pathway and atherosclerosis development in smokers.

Previous studies reported that the glutamate transporter encoded by SLC7A11 was activated in cigarette smokers, which increased circulating glutamate, arginine, ornithine, and citrulline.^{23,24} In our study, the elevation of these metabolites was confirmed. Previous studies have suggested that elevation of this metabolic pathway can be linked to endothelial cell damage through nitric oxide decline and contribute to atherosclerosis.²⁵⁻²⁷