

## **Supplementary Material**

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**Supplementary Table 1.** Results of heterogeneity test and inverse-variance-weighted model used in mendelian randomization analysis.

<b>ID</b>	<b>Metabolites</b>	<b>Outcome</b>	<b>Q value</b>	<b>P value</b>	<b>Model</b>
met-a-304	Tryptophan	Colorectal cancer	29.26	0.03	random effects
met-a-306	Leucine	Colorectal cancer	5.74	0.89	fixed effects
met-a-314	Mannose	Colorectal cancer	5.22	0.27	fixed effects
met-a-316	Uridine	Colorectal cancer	0.93	0.63	fixed effects
met-a-319	Arachidonate (20:4n6)	Colorectal cancer	7.39	0.12	fixed effects
met-a-325	Tyrosine	Colorectal cancer	0.89	0.64	fixed effects
met-a-339	4-acetamidobutanoate	Colorectal cancer	1.80	0.88	fixed effects
met-a-341	Citrate	Colorectal cancer	1.30	0.97	fixed effects
met-a-345	Urate	Colorectal cancer	1.03	0.90	fixed effects
met-a-355	Proline	Colorectal cancer	4.18	0.52	fixed effects
met-a-356	Citrulline	Colorectal cancer	2.00	0.57	fixed effects
met-a-357	Biliverdin	Colorectal cancer	7.20	0.52	fixed effects
met-a-359	Gamma-glutamylglutamine	Colorectal cancer	2.60	0.27	fixed effects
met-a-360	Gamma-glutamyltyrosine	Colorectal cancer	11.71	0.02	random effects
met-a-362	Betaine	Colorectal cancer	9.89	0.13	fixed effects
met-a-373	X-03094	Colorectal cancer	5.22	0.27	fixed effects
met-a-375	Kynurenine	Colorectal cancer	17.89	$1.30 \times 10^{-3}$	random effects
met-a-379	Carnitine	Colorectal cancer	25.53	0.18	fixed effects
met-a-381	N-acetyloronithine	Colorectal cancer	8.69	0.47	fixed effects
met-a-383	3-methyl-2-oxovalerate	Colorectal cancer	4.68	0.10	fixed effects
met-a-396	X-18601	Colorectal cancer	1.21	0.55	fixed effects

met-a-419	1,5-anhydroglucitol (1,5-AG)	Colorectal cancer	12.17	0.01	random effects
met-a-426	X-08402	Colorectal cancer	4.77	0.44	fixed effects
met-a-427	2-hydroxyisobutyrate	Colorectal cancer	0.30	0.96	fixed effects
met-a-435	X-08988	Colorectal cancer	0.22	0.89	fixed effects
met-a-444	X-10510	Colorectal cancer	0.04	0.98	fixed effects
met-a-449	N-acetylglycine	Colorectal cancer	4.21	0.65	fixed effects
met-a-450	Bilirubin (Z,Z)	Colorectal cancer	3.89	0.79	fixed effects
met-a-460	Androsterone sulfate	Colorectal cancer	10.40	0.17	fixed effects
met-a-464	Serine	Colorectal cancer	0.75	0.69	fixed effects
met-a-467	Hexanoylcarnitine	Colorectal cancer	5.91	0.66	fixed effects
met-a-468	Glycine	Colorectal cancer	4.02	0.86	fixed effects
met-a-476	Butyrylcarnitine	Colorectal cancer	28.56	0.24	fixed effects
met-a-479	Propionylcarnitine	Colorectal cancer	4.93	0.30	fixed effects
met-a-482	10-undecenoate (11:1n1)	Colorectal cancer	0.29	0.87	fixed effects
met-a-484	X-11204	Colorectal cancer	3.41	0.18	fixed effects
met-a-485	X-02269	Colorectal cancer	0.61	0.90	fixed effects
met-a-490	X-11261	Colorectal cancer	7.39	0.19	fixed effects
met-a-491	Bilirubin (E,E)*	Colorectal cancer	4.28	0.64	fixed effects
met-a-495	X-11315	Colorectal cancer	1.12	0.57	fixed effects
met-a-500	3-dehydrocarnitine*	Colorectal cancer	3.98	0.41	fixed effects
met-a-501	Pyroglutamine*	Colorectal cancer	8.45	0.08	fixed effects
met-a-505	X-03056--N-[3-(2-Oxopyrrolidin-1-yl)propyl]acetamide	Colorectal cancer	5.44	0.61	fixed effects
met-a-510	X-09789	Colorectal cancer	3.00	0.22	fixed effects
met-a-513	X-11440	Colorectal cancer	2.88	0.82	fixed effects
met-a-514	X-11441	Colorectal cancer	2.41	0.79	fixed effects
met-a-515	X-11442	Colorectal cancer	3.11	0.79	fixed effects

met-a-516	X-11444	Colorectal cancer	0.50	0.92	fixed effects
met-a-517	X-11445--5-alpha-pregnan-3beta,20alpha-disulfate	Colorectal cancer	2.07	0.36	fixed effects
met-a-519	X-11469	Colorectal cancer	1.01	0.80	fixed effects
met-a-524	X-11491	Colorectal cancer	3.34	0.34	fixed effects
met-a-526	HWESASXX*	Colorectal cancer	2.12	0.35	fixed effects
met-a-528	X-11529	Colorectal cancer	6.00	0.81	fixed effects
met-a-529	X-11530	Colorectal cancer	4.42	0.73	fixed effects
met-a-531	X-11538	Colorectal cancer	6.68	0.46	fixed effects
met-a-536	X-11593--O-methylascorbate*	Colorectal cancer	13.66	0.32	fixed effects
met-a-541	X-11787	Colorectal cancer	5.99	0.54	fixed effects
met-a-542	X-11792	Colorectal cancer	0.05	0.97	fixed effects
met-a-543	X-11793--oxidized bilirubin* 1-	Colorectal cancer	5.26	0.81	fixed effects
met-a-558	arachidonoylglycerophosphocholine*	Colorectal cancer	3.67	0.45	fixed effects
met-a-560	X-11905	Colorectal cancer	0.16	0.92	fixed effects
met-a-570	X-12063	Colorectal cancer	12.80	0.46	fixed effects
met-a-573	Isobutyrylcarnitine	Colorectal cancer	9.08	0.17	fixed effects
met-a-578	Erythronate*	Colorectal cancer	0.85	0.65	fixed effects
met-a-580	X-12092	Colorectal cancer	10.51	0.91	fixed effects
met-a-581	X-12093	Colorectal cancer	2.84	0.59	fixed effects
met-a-596	X-12244--N-acetylcarnosine	Colorectal cancer	5.04	0.41	fixed effects
met-a-613	X-12456	Colorectal cancer	0.96	0.62	fixed effects
met-a-615	Octanoylcarnitine	Colorectal cancer	2.62	0.86	fixed effects

met-a-616	Alpha-hydroxyisovalerate	Colorectal cancer	6.26	0.04	random effects
met-a-618	Decanoylcarnitine	Colorectal cancer	3.30	0.51	fixed effects
met-a-627	Epiandrosterone sulfate	Colorectal cancer	10.35	0.11	fixed effects
met-a-629	X-12510--2-aminooctanoic acid	Colorectal cancer	5.88	0.44	fixed effects
met-a-631	Bilirubin (E,Z or Z,E)*	Colorectal cancer	0.89	0.83	fixed effects
met-a-633	X-12556	Colorectal cancer	1.16	0.76	fixed effects
met-a-634	1-arachidonoylglycerophosphoinositol*	Colorectal cancer	13.11	0.01	random effects
met-a-636	X-12644	Colorectal cancer	6.49	0.04	random effects
met-a-638	Asparagine	Colorectal cancer	0.75	0.69	fixed effects
met-a-640	X-12696	Colorectal cancer	13.54	0.00	random effects
met-a-646	X-12728	Colorectal cancer	2.05	0.96	fixed effects
met-a-652	Isovalerylcarnitine	Colorectal cancer	4.26	0.51	fixed effects
met-a-656	Bradykinin, des-arg(9)	Colorectal cancer	0.55	0.97	fixed effects
met-a-661	X-12798	Colorectal cancer	9.48	0.66	fixed effects
met-a-665	X-12844	Colorectal cancer	3.38	0.34	fixed effects
met-a-667	X-12850	Colorectal cancer	1.16	0.56	fixed effects
met-a-682	1-arachidonoylglycerophosphoethanolamine*	Colorectal cancer	8.11	0.04	random effects
met-a-683	X-13429	Colorectal cancer	1.66	0.64	fixed effects
met-a-684	X-13431--nonanoylcarnitine*	Colorectal cancer	8.27	0.22	fixed effects
met-a-685	X-13435	Colorectal cancer	5.02	0.08	fixed effects

met-a-699	Glutaroyl carnitine	Colorectal cancer	4.92	0.90	fixed effects
met-a-709	Tetradecanedioate	Colorectal cancer	3.43	0.33	fixed effects
met-a-711	Hexadecanedioate	Colorectal cancer	4.43	0.35	fixed effects
met-a-712	Dihomo-linolenate (20:3n3 or n6)	Colorectal cancer	9.49	0.01	random effects
met-a-720	X-14205--alpha- glutamyltyrosine	Colorectal cancer	3.95	0.14	fixed effects
met-a-729	X-14626	Colorectal cancer	0.64	0.73	fixed effects
met-a-735	Octadecanedioate	Colorectal cancer	3.83	0.28	fixed effects
met-a-742	Succinylcarnitine	Colorectal cancer	7.62	0.67	fixed effects
met-a-743	Tryptophan betaine	Colorectal cancer	6.95	0.07	fixed effects
met-a-746	5alpha-androstan- 3beta,17beta-diol disulfate	Colorectal cancer	3.48	0.63	fixed effects
met-a-747	4-androsten- 3beta,17beta-diol disulfate 1*	Colorectal cancer	1.16	0.95	fixed effects
met-a-753	Cis-4-decenoyl carnitine	Colorectal cancer	2.10	0.72	fixed effects

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**Supplementary Table 2.** IVW analyses for 101 human blood metabolites on colorectal cancer.

<b>ID</b>	<b>Metabolites</b>	<b>SNPs</b>	<b>OR</b>	<b>95% CI</b>	<b>P value</b>
met-a-304	Tryptophan	18	0.57	0.08-4.18	0.582
met-a-306	Leucine	12	1.13	0.19-6.76	0.895
met-a-314	Mannose	5	2.09	1.10-3.97	0.024
met-a-316	Uridine	3	0.29	0.04-1.91	0.197
met-a-319	Arachidonate (20:4n6)	5	3.14	1.78-5.53	7.54×10 <sup>-5</sup>
met-a-325	Tyrosine	3	0.08	0.01-0.61	0.014
met-a-339	4-acetamidobutanoate	6	1.03	0.43-2.46	0.952
met-a-341	Citrate	7	1.91	0.60-6.03	0.272
met-a-345	Urate	5	0.25	0.10-0.61	0.003
met-a-355	Proline	6	0.82	0.45-1.49	0.524
met-a-356	Citrulline	4	0.25	0.04-1.43	0.120
met-a-357	Biliverdin	9	0.92	0.72-1.16	0.482
met-a-359	Gamma-glutamylglutamine	3	2.11	0.54-8.24	0.282
met-a-360	Gamma-glutamyltyrosine	5	1.10	0.08-15.27	0.944
met-a-362	Betaine	7	1.88	0.87-4.04	0.106
met-a-373	X-03094	5	0.57	0.21-1.56	0.273
met-a-375	Kynurenine	5	0.51	0.10-2.71	0.433
met-a-379	Carnitine	21	0.44	0.18-1.11	0.081
met-a-381	N-acetylmethionine	10	0.99	0.83-1.18	0.920
met-a-383	3-methyl-2-oxovalerate	3	0.75	0.14-3.92	0.731
met-a-396	X-18601	3	1.28	0.69-2.37	0.425
met-a-419	1,5-anhydroglucitol (1,5-AG)	4	0.32	0.07-1.50	0.148
met-a-426	X-08402	6	0.87	0.52-1.46	0.600
met-a-427	2-hydroxyisobutyrate	4	0.47	0.19-1.16	0.102

met-a-435	X-08988	3	0.67	0.25-1.75	0.409
met-a-444	X-10510	3	0.64	0.27-1.52	0.316
met-a-449	N-acetylglycine	7	0.73	0.54-0.98	0.033
met-a-450	Bilirubin (Z,Z)	8	0.96	0.82-1.13	0.640
met-a-460	Androsterone sulfate	8	0.95	0.82-1.09	0.458
met-a-464	Serine	3	0.40	0.14-1.14	0.088
met-a-467	Hexanoylcarnitine	9	0.89	0.63-1.25	0.485
met-a-468	Glycine	9	0.74	0.52-1.06	0.098
met-a-476	Butyrylcarnitine	25	1.11	0.98-1.26	0.092
met-a-479	Propionylcarnitine	5	0.51	0.20-1.29	0.156
met-a-482	10-undecenoate (11:1n1)	4	1.49	0.80-2.75	0.208
met-a-484	X-11204	3	2.85	0.36-22.31	0.319
met-a-485	X-02269	4	1.16	0.79-1.71	0.443
met-a-490	X-11261	6	0.80	0.53-1.21	0.283
met-a-491	Bilirubin (E,E)*	7	0.95	0.76-1.19	0.652
met-a-495	X-11315	3	1.37	0.55-3.43	0.498
met-a-500	3-dehydrocarnitine*	5	0.45	0.20-1.00	0.050
met-a-501	Pyroglutamine*	5	0.76	0.46-1.24	0.271
met-a-505	X-03056--N-[3-(2- Oxopyrrolidin-1- yl)propyl]acetamide	8	0.92	0.54-1.57	0.752
met-a-510	X-09789	3	0.70	0.41-1.20	0.193
met-a-513	X-11440	7	1.18	0.95-1.46	0.126
met-a-514	X-11441	6	0.95	0.74-1.24	0.721
met-a-515	X-11442	7	0.97	0.75-1.25	0.796
met-a-516	X-11444	4	1.13	0.59-2.17	0.703
met-a-517	X-11445--5-alpha-pregnan- 3beta,20alpha-disulfate	3	0.95	0.66-1.36	0.783
met-a-519	X-11469	4	1.26	0.84-1.89	0.272



met-a-524	X-11491	4	1.04	0.73-1.47	0.833
met-a-526	HWESASXX*	3	0.80	0.48-1.35	0.407
met-a-528	X-11529	11	1.01	0.90-1.12	0.881
met-a-529	X-11530	8	0.95	0.75-1.22	0.694
met-a-531	X-11538	8	1.07	0.84-1.38	0.584
met-a-536	X-11593--O-methylascorbate*	13	1.68	1.04-2.72	0.034
met-a-541	X-11787	8	0.84	0.42-1.70	0.634
met-a-542	X-11792	3	1.06	0.84-1.32	0.639
met-a-543	X-11793--oxidized bilirubin*	10	1.04	0.78-1.39	0.774
met-a-558	1-arachidonoylglycerophosphocholine*	5	4.23	2.51-7.12	6.35×10 <sup>-8</sup>
met-a-560	X-11905	3	0.98	0.65-1.48	0.914
met-a-570	X-12063	14	1.07	0.91-1.27	0.406
met-a-573	Isobutyrylcarnitine	7	0.89	0.64-1.26	0.519
met-a-578	Erythronate*	3	1.81	0.31-10.46	0.508
met-a-580	X-12092	19	0.89	0.81-0.99	0.028
met-a-581	X-12093	5	0.92	0.73-1.17	0.511
met-a-596	X-12244--N-acetylcarnosine	6	1.26	0.60-2.64	0.546
met-a-613	X-12456	3	1.05	0.69-1.58	0.823
met-a-615	Octanoylcarnitine	7	0.98	0.72-1.33	0.902
met-a-616	Alpha-hydroxyisovalerate	3	1.40	0.44-4.42	0.568
met-a-618	Decanoylcarnitine	5	0.96	0.65-1.41	0.827
met-a-627	Epiandrosterone sulfate	7	0.84	0.69-1.03	0.092
met-a-629	X-12510--2-aminooctanoic acid	7	1.08	0.82-1.42	0.606
met-a-631	Bilirubin (E,Z or Z,E)*	4	1.05	0.73-1.50	0.812

met-a-633	X-12556	4	0.97	0.38-2.46	0.950
met-a-634	1-arachidonoylglycerophosphoinositol*	5	2.16	0.64-7.36	0.217
met-a-636	X-12644	3	0.89	0.11-7.39	0.914
met-a-638	Asparagine	3	0.33	0.11-1.00	0.050
met-a-640	X-12696	3	0.37	0.02-5.90	0.483
met-a-646	X-12728	8	1.01	0.97-1.04	0.711
met-a-652	Isovalerylcarnitine	6	0.63	0.37-1.08	0.092
met-a-656	Bradykinin, des-arg(9)	5	1.05	0.91-1.21	0.517
met-a-661	X-12798	12	1.23	0.98-1.55	0.078
met-a-665	X-12844	4	0.77	0.32-1.82	0.545
met-a-667	X-12850	3	1.21	0.83-1.79	0.322
met-a-682	1-arachidonoylglycerophosphoethanolamine*	4	3.99	1.17-13.54	0.027
met-a-683	X-13429	4	1.03	0.81-1.30	0.824
met-a-684	X-13431--nonanoylcarnitine*	7	0.95	0.74-1.23	0.713
met-a-685	X-13435	3	0.79	0.37-1.69	0.545
met-a-699	Glutaroyl carnitine	11	0.99	0.60-1.62	0.964
met-a-709	Tetradecanedioate	4	0.95	0.70-1.30	0.756
met-a-711	Hexadecanedioate	5	1.03	0.75-1.42	0.837
met-a-712	Dihomo-linolenate (20:3n3 or n6)	3	1.30	0.13-12.77	0.821
met-a-720	X-14205--alpha-glutamyltyrosine	3	0.71	0.42-1.21	0.209
met-a-729	X-14626	3	0.94	0.47-1.86	0.850
met-a-735	Octadecanedioate	4	0.91	0.48-1.70	0.760
met-a-742	Succinylcarnitine	11	0.48	0.27-0.83	0.009
met-a-743	Tryptophan betaine	4	0.90	0.69-1.17	0.433

met-a-746	5alpha-androstan- 3beta,17beta-diol disulfate	6	1.06	0.84-1.34	0.607
met-a-747	4-androsten-3beta,17beta- diol disulfate 1*	6	1.15	0.95-1.40	0.155

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Abbreviations: IVW, Inverse-variance weighted; SNP, single-nucleotide polymorphism.

Odds ratios (ORs) with their 95% confidence intervals (CIs) represent the association estimates with the risks of colorectal cancer of per 1-standard deviation increase of metabolite levels .

**Supplementary Table 3.** Characteristics of genetic variants for Mannose.

<b>SNP</b>	<b>Chr</b>	<b>Pos</b>	<b>EA</b>	<b>OA</b>	<b>Beta</b>	<b>SE</b>	<b>EAF</b>	<b>P value</b>
rs1260326	2	27730940	C	T	0.0439	0.0024	0.5912	$1.30 \times 10^{-77}$
rs13000936	2	28418189	A	G	0.0135	0.0024	0.3138	$3.27 \times 10^{-8}$
rs2141371	2	27860258	A	G	-0.0198	0.0024	0.682	$3.27 \times 10^{-16}$
rs6547811	2	28070071	A	T	0.0222	0.0032	0.1583	$7.10 \times 10^{-12}$
rs7583698	2	27712408	T	C	0.0338	0.0049	0.0483	$8.55 \times 10^{-12}$

Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; Pos, Position; EA, effect allele; OA, other allele; EAF, effect allele frequency.

**Supplementary Table 4.** Characteristics of genetic variants for Arachidonate (20:4n6).

<b>SNP</b>	<b>Chr</b>	<b>Pos</b>	<b>EA</b>	<b>OA</b>	<b>Beta</b>	<b>SE</b>	<b>EAF</b>	<b>P value</b>
rs174548	11	61571348	G	C	-0.0488	0.0025	0.2995	1.43×10 <sup>-84</sup>
rs174602	11	61624414	C	T	-0.0353	0.004	0.1298	2.42×10 <sup>-18</sup>
rs17764324	11	61635088	T	G	-0.0241	0.0041	0.086	3.30×10 <sup>-9</sup>
rs412334	11	61560261	T	C	0.022	0.003	0.157	2.24×10 <sup>-13</sup>
rs526126	11	61624885	C	G	0.0249	0.0039	0.8409	2.11×10 <sup>-10</sup>

Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; Pos, Position; EA, effect allele; OA, other allele; EAF, effect allele frequency.

**Supplementary Table 5.** Characteristics of genetic variants for Tyrosine.

<b>SNP</b>	<b>Chr</b>	<b>Pos</b>	<b>EA</b>	<b>OA</b>	<b>Beta</b>	<b>SE</b>	<b>EAF</b>	<b>P value</b>
rs12728678	1	154764715	T	C	-0.0096	0.0017	0.2003	2.19×10 <sup>-8</sup>
rs172650	16	71603912	A	C	0.0102	0.0016	0.6543	2.82×10 <sup>-10</sup>
rs9400467	6	111424015	T	C	-0.0121	0.0016	0.7059	6.54×10 <sup>-14</sup>

Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; Pos, Position; EA, effect allele; OA, other allele; EAF, effect allele frequency.

**Supplementary Table 6.** Characteristics of genetic variants for Urate.

<b>SNP</b>	<b>Chr</b>	<b>Pos</b>	<b>EA</b>	<b>OA</b>	<b>Beta</b>	<b>SE</b>	<b>EAF</b>	<b>P value</b>
rs10939663	4	10032516	G	T	0.0161	0.0017	0.2721	5.57×10 <sup>-22</sup>
rs11731100	4	9767180	T	A	0.0116	0.0016	0.6498	9.97×10 <sup>-13</sup>
rs11737601	4	10488568	G	A	-0.0104	0.0016	0.3153	1.34×10 <sup>-10</sup>
rs4697910	4	9901874	A	G	-0.0124	0.0017	0.2866	8.72×10 <sup>-14</sup>
rs938554	4	9925692	G	C	0.0348	0.0017	0.7744	5.85×10 <sup>-93</sup>

Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; Pos, Position; EA, effect allele; OA, other allele; EAF, effect allele frequency.

**Supplementary Table 7.** Characteristics of genetic variants for N-acetylglycine.

<b>SNP</b>	<b>Chr</b>	<b>Pos</b>	<b>EA</b>	<b>OA</b>	<b>Beta</b>	<b>SE</b>	<b>EAF</b>	<b>P value</b>
rs12328639	2	211676323	G	A	-0.0342	0.0062	0.15	2.75×10 <sup>-8</sup>
rs12468557	2	211495587	T	C	-0.0293	0.0044	0.373	1.84×10 <sup>-11</sup>
rs13021675	2	211661935	T	C	0.0485	0.006	0.1968	5.60×10 <sup>-16</sup>
rs1367053	2	211862097	C	T	-0.0306	0.0044	0.5456	4.88×10 <sup>-12</sup>
rs1990797	2	211641068	C	G	-0.0486	0.0061	0.1707	1.33×10 <sup>-15</sup>
rs715	2	211543055	C	T	0.091	0.0057	0.2904	6.66×10 <sup>-58</sup>
rs7948073	11	67375184	G	T	0.0256	0.0044	0.4298	4.60×10 <sup>-9</sup>

Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; Pos, Position; EA, effect allele; OA, other allele; EAF, effect allele frequency.



**Supplementary Table 8.** Characteristics of genetic variants for X-11593--O-methylascorbate\*.

SNP	Chr	Pos	EA	OA	Beta	SE	EAF	<i>P</i> value
rs10412803	19	46877975	T	C	0.0097	0.0018	0.3119	4.42×10 <sup>-8</sup>
rs11089325	22	19984200	T	C	0.0227	0.004	0.0613	1.19×10 <sup>-8</sup>
rs16982844	22	19947942	A	C	-0.0423	0.0069	0.0627	9.08×10 <sup>-10</sup>
rs2686184	8	11649359	G	A	0.0097	0.0017	0.592	1.89×10 <sup>-8</sup>
rs3804043	22	20052481	A	C	0.0178	0.0018	0.2911	7.76×10 <sup>-24</sup>
rs438798	22	20169499	G	A	-0.0173	0.0017	0.4654	1.55×10 <sup>-23</sup>
rs4597638	22	19902526	C	T	0.0281	0.0043	0.058	6.06×10 <sup>-11</sup>
rs4680	22	19951271	A	G	-0.0486	0.0017	0.5069	4.66×10 <sup>-178</sup>
rs7290062	22	20175473	C	T	0.0168	0.0025	0.1365	2.24×10 <sup>-11</sup>
rs7707010	5	138444877	G	A	-0.0252	0.0044	0.0418	9.61×10 <sup>-9</sup>
rs887200	22	19963666	T	C	-0.0294	0.0026	0.8808	8.02×10 <sup>-30</sup>
rs9318225	13	74491265	C	T	0.0106	0.0018	0.3171	1.95×10 <sup>-9</sup>
rs9606212	22	20015615	A	C	-0.0318	0.005	0.0586	2.67×10 <sup>-10</sup>

Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; Pos, Position; EA, effect allele; OA, other allele; EAF, effect allele frequency.

**Supplementary Table 9.** Characteristics of genetic variants for 1-arachidonoylglycerophosphocholine\*.

<b>SNP</b>	<b>Chr</b>	<b>Pos</b>	<b>EA</b>	<b>OA</b>	<b>Beta</b>	<b>SE</b>	<b>EAF</b>	<b>P value</b>
rs1692120	11	61417472	A	G	0.0188	0.0027	0.4589	5.82×10 <sup>-12</sup>
rs174535	11	61551356	C	T	-0.0561	0.0027	0.3398	1.86×10 <sup>-94</sup>
rs3738544	1	236914576	T	C	0.0203	0.0035	0.8071	8.05×10 <sup>-9</sup>
rs7104849	11	61638044	A	G	0.0343	0.0052	0.9166	3.26×10 <sup>-11</sup>
rs748196	17	17422768	G	T	-0.0152	0.0027	0.5404	1.70×10 <sup>-8</sup>

Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; Pos, Position; EA, effect allele; OA, other allele; EAF, effect allele frequency.

**Supplementary Table 10.** Characteristics of genetic variants for X-12092.

<b>SNP</b>	<b>Chr</b>	<b>Pos</b>	<b>EA</b>	<b>OA</b>	<b>Beta</b>	<b>SE</b>	<b>EAF</b>	<b>P value</b>
rs1061134	10	100189252	A	G	-0.1458	0.0084	0.0946	2.82×10 <sup>-67</sup>
rs1061135	10	100189138	G	A	-0.0689	0.005	0.5396	2.33×10 <sup>-43</sup>
rs10748725	10	100076982	A	G	-0.0505	0.0052	0.3536	2.11×10 <sup>-22</sup>
rs10883057	10	100032037	C	G	-0.0409	0.0054	0.2703	3.25×10 <sup>-14</sup>
rs11189692	10	100344136	C	T	0.0427	0.0061	0.2203	2.25×10 <sup>-12</sup>
rs11595763	10	100193526	C	A	0.0863	0.0061	0.1705	8.34×10 <sup>-46</sup>
rs12415538	10	100273289	T	C	-0.1204	0.0194	0.0188	5.76×10 <sup>-10</sup>
rs12780272	10	100196452	T	C	0.08	0.0134	0.0376	2.55×10 <sup>-9</sup>
rs1365	10	100035666	A	C	0.0752	0.0101	0.9458	1.16×10 <sup>-13</sup>
rs17109581	10	100140636	T	A	-0.274	0.0166	0.0386	1.61×10 <sup>-61</sup>
rs1889459	10	5314043	C	G	-0.0412	0.0067	0.1628	9.94×10 <sup>-10</sup>
rs4917817	10	100085888	A	C	0.0406	0.005	0.6783	6.71×10 <sup>-16</sup>
rs4919221	10	100115027	C	T	0.0685	0.0052	0.2565	2.70×10 <sup>-40</sup>
rs542386	10	100286160	A	C	-0.0671	0.0123	0.0441	4.56×10 <sup>-8</sup>
rs7096654	10	100134036	T	C	0.2537	0.0047	0.6211	1.00×10 <sup>-200</sup>
rs754586	10	100224362	C	T	0.0341	0.005	0.5872	1.35×10 <sup>-11</sup>
rs8101881	19	33364628	T	C	0.0281	0.005	0.6089	2.57×10 <sup>-8</sup>
rs942800	10	100081443	A	C	0.0362	0.0053	0.4265	1.06×10 <sup>-11</sup>
rs942812	10	100153664	A	C	-0.1771	0.0141	0.0293	4.24×10 <sup>-36</sup>

Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; Pos, Position; EA, effect allele; OA, other allele; EAF, effect allele frequency.

**Supplementary Table 11.** Characteristics of genetic variants for 1-arachidonoylglycerophosphoethanolamine\*.

<b>SNP</b>	<b>Chr</b>	<b>Pos</b>	<b>EA</b>	<b>OA</b>	<b>Beta</b>	<b>SE</b>	<b>EAF</b>	<b>P value</b>
rs10468017	15	58678512	T	C	0.0171	0.0027	0.2875	1.29×10 <sup>-10</sup>
rs11045906	12	21408845	G	A	-0.0154	0.0027	0.2517	7.46×10 <sup>-9</sup>
rs174578	11	61605499	A	T	-0.0354	0.0026	0.341	6.12×10 <sup>-42</sup>
rs4149056	12	21331549	C	T	0.0294	0.0034	0.1595	2.66×10 <sup>-18</sup>

Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; Pos, Position; EA, effect allele; OA, other allele; EAF, effect allele frequency.

**Supplementary Table 12.** Characteristics of genetic variants for Succinylcarnitine.

<b>SNP</b>	<b>Chr</b>	<b>Pos</b>	<b>EA</b>	<b>OA</b>	<b>Beta</b>	<b>SE</b>	<b>EAF</b>	<b>P value</b>
rs10988217	9	131888116	G	A	0.0164	0.0019	0.6117	1.36×10 <sup>-18</sup>
rs11637751	15	63643524	A	G	0.0155	0.0027	0.1659	1.77×10 <sup>-8</sup>
rs12899230	15	63369788	C	T	0.0247	0.0036	0.0787	1.39×10 <sup>-11</sup>
rs1472631	15	63423739	G	A	-0.0366	0.0018	0.5081	1.85×10 <sup>-88</sup>
rs17806888	3	67416322	C	T	0.0224	0.0034	0.1194	7.15×10 <sup>-11</sup>
rs2686513	7	22451353	C	T	0.011	0.002	0.448	3.80×10 <sup>-8</sup>
rs2729786	15	63401605	A	C	0.0238	0.0036	0.099	3.97×10 <sup>-11</sup>
rs2729816	15	63413084	C	T	-0.0313	0.0026	0.7807	5.54×10 <sup>-33</sup>
rs6703518	1	186116797	T	G	-0.0108	0.0019	0.4273	5.85×10 <sup>-9</sup>
rs8060756	16	63202385	A	G	0.0102	0.0018	0.3703	4.07×10 <sup>-8</sup>
rs901273	15	63677966	G	A	-0.0107	0.0019	0.4966	7.48×10 <sup>-9</sup>

Abbreviations: SNP, single-nucleotide polymorphism; Chr, chromosome; Pos, Position; EA, effect allele; OA, other allele; EAF, effect allele frequency.