

**SUPPLEMENTARY MATERIAL**

**Supplementary Table SI.** Characteristics of human blood metabolites GWAS (exposure) and breast cancer GWAS (outcome) for the present study

	<b>Study Cohort</b>	<b>Cohort Description</b>	<b>Case/ Control</b>	<b>GWAS Sample Size</b>	<b>Population</b>		<b>Blood metabolites</b>	<b>Available Path</b>
<b>Exposure</b>								
Shin et al. (2014)	Twins UK KORA	An adult twin British registry cohort study Population-based cohort studies	-	7,824	German British	European	453	the IEU GWAS database: <a href="https://gwas.mrcieu.ac.uk">https://gwas.mrcieu.ac.uk</a> ; PMID: 24816252
<b>Outcome</b>								
Sakaue et al. (2021)	UK Biobank Finn Gen	Population-based prospective cohort Disease-based cohorts	134,469/167,873 3,920/72,468	181,342 76,388	British Finnish	European	-	the IEU GWAS database: <a href="https://gwas.mrcieu.ac.uk">https://gwas.mrcieu.ac.uk</a> ; PMID: 34594039

**Supplementary Table SII.** 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	Brest cancer	17.76	0.40	fixed effect model
met-a-306	Leucine	Brest cancer	8.41	0.68	fixed effect model
met-a-314	Mannose	Brest cancer	5.64	0.23	fixed effect model
met-a-316	Uridine	Brest cancer	2.78	0.25	fixed effect model
met-a-319	Arachidonate (20:4n6)	Brest cancer	3.41	0.49	fixed effect model
met-a-325	Tyrosine	Brest cancer	0.88	0.64	fixed effect model
met-a-339	4-acetamidobutanoate	Brest cancer	6.68	0.25	fixed effect model
met-a-341	Citrate	Brest cancer	14.51	0.02	random effect model
met-a-345	Urate	Brest cancer	5.78	0.12	fixed effect model
met-a-355	Proline	Brest cancer	8.94	0.11	fixed effect model
met-a-356	Citrulline	Brest cancer	6.53	0.09	fixed effect model
met-a-357	Biliverdin	Brest cancer	7.59	0.47	fixed effect model
met-a-359	Gamma-glutamylglutamine	Brest cancer	0.79	0.67	fixed effect model
met-a-360	Gamma-glutamyltyrosine	Brest cancer	2.09	0.55	fixed effect model
met-a-362	Betaine	Brest cancer	10.95	0.09	fixed effect model
met-a-373	X-03094	Brest cancer	0.59	0.96	fixed effect model
met-a-375	Kynurenine	Brest cancer	2.24	0.69	fixed effect model
met-a-379	Carnitine	Brest cancer	34.00	0.02	random effect model
met-a-381	N-acetylorithine	Brest cancer	4.62	0.87	fixed effect model
met-a-383	3-methyl-2-oxovalerate	Brest cancer	0.19	0.91	fixed effect model
met-a-396	X-18601	Brest cancer	7.60	0.02	random effect model
met-a-419	1,5-anhydroglucitol (1,5-AG)	Brest cancer	4.61	0.20	fixed effect model
met-a-426	X-08402	Brest cancer	9.51	0.09	fixed effect model
met-a-427	2-hydroxyisobutyrate	Brest cancer	0.34	0.95	fixed effect model

met-a-435	X-08988	Brest cancer	1.85	0.40	fixed effect model
met-a-444	X-10510	Brest cancer	2.01	0.37	fixed effect model
met-a-449	N-acetylglycine	Brest cancer	5.23	0.52	fixed effect model
met-a-450	Bilirubin (Z,Z)	Brest cancer	7.09	0.42	fixed effect model
met-a-460	Androsterone sulfate	Brest cancer	14.99	0.04	random effect model
met-a-464	Serine	Brest cancer	0.67	0.72	fixed effect model
met-a-467	Hexanoylcarnitine	Brest cancer	11.28	0.19	fixed effect model
met-a-468	Glycine	Brest cancer	6.94	0.54	fixed effect model
met-a-476	Butyrylcarnitine	Brest cancer	22.08	0.52	fixed effect model
met-a-479	Propionylcarnitine	Brest cancer	15.84	0.00	random effect model
met-a-482	10-undecenoate (11:1n1)	Brest cancer	0.36	0.95	fixed effect model
met-a-484	X-11204	Brest cancer	1.04	0.60	fixed effect model
met-a-485	X-02269	Brest cancer	4.52	0.21	fixed effect model
met-a-490	X-11261	Brest cancer	4.50	0.48	fixed effect model
met-a-491	Bilirubin (E,E)*	Brest cancer	5.75	0.33	fixed effect model
met-a-495	X-11315	Brest cancer	1.18	0.55	fixed effect model
met-a-500	3-dehydrocarnitine*	Brest cancer	2.75	0.60	fixed effect model
met-a-501	Pyroglutamine*	Brest cancer	3.11	0.54	fixed effect model
met-a-505	X-03056--N-[3-(2-Oxopyrrolidin -1-yl)propyl]acetamide	Brest cancer	22.04	0.00	random effect model
met-a-510	X-09789	Brest cancer	2.73	0.26	fixed effect model
met-a-513	X-11440	Brest cancer	6.08	0.30	fixed effect model
met-a-514	X-11441	Brest cancer	2.60	0.76	fixed effect model
met-a-515	X-11442	Brest cancer	5.91	0.43	fixed effect model
met-a-516	X-11444	Brest cancer	9.64	0.02	random effect model
met-a-517	X-11445--5-alpha-pregnan-3beta,20alpha-disulfate	Brest cancer	8.63	0.01	random effect model

met-a-519	X-11469	Brest cancer	5.20	0.16	fixed effect model
met-a-524	X-11491	Brest cancer	5.29	0.15	fixed effect model
met-a-526	HWESASXX*	Brest cancer	0.23	0.89	fixed effect model
met-a-528	X-11529	Brest cancer	11.97	0.29	fixed effect model
met-a-529	X-11530	Brest cancer	8.04	0.33	fixed effect model
met-a-531	X-11538	Brest cancer	10.65	0.15	fixed effect model
met-a-536	X-11593--O-methylascorbate*	Brest cancer	9.52	0.66	fixed effect model
met-a-541	X-11787	Brest cancer	5.06	0.65	fixed effect model
met-a-542	X-11792	Brest cancer	4.16	0.13	fixed effect model
met-a-543	X-11793--oxidized bilirubin*	Brest cancer	9.06	0.43	fixed effect model
met-a-558	1-arachidonoylglycero-phosphocholine*	Brest cancer	0.04	1.00	fixed effect model
met-a-560	X-11905	Brest cancer	3.74	0.15	fixed effect model
met-a-570	X-12063	Brest cancer	22.66	0.05	random effect model
met-a-573	Isobutyrylcarnitine	Brest cancer	7.79	0.25	fixed effect model
met-a-578	Erythronate*	Brest cancer	3.59	0.17	fixed effect model
met-a-580	X-12092	Brest cancer	22.10	0.23	fixed effect model
met-a-581	X-12093	Brest cancer	4.81	0.31	fixed effect model
met-a-596	X-12244--N-acetylcarnosine	Brest cancer	8.83	0.12	fixed effect model
met-a-613	X-12456	Brest cancer	8.18	0.02	random effect model
met-a-615	Octanoylcarnitine	Brest cancer	9.61	0.14	fixed effect model
met-a-616	Alpha-hydroxyisovalerate	Brest cancer	0.60	0.74	fixed effect model
met-a-618	Decanoylcarnitine	Brest cancer	2.76	0.60	fixed effect model
met-a-627	Epiandrosterone sulfate	Brest cancer	10.39	0.11	fixed effect model
met-a-629	X-12510--2-aminooctanoic acid	Brest cancer	3.83	0.70	fixed effect model
met-a-631	Bilirubin (E,Z or Z,E)*	Brest cancer	2.50	0.48	fixed effect model

met-a-633	X-12556	Brest cancer	1.13	0.77	fixed effect model
met-a-634	1-arachidonoylglycero-phosphoinositol*	Brest cancer	7.05	0.13	fixed effect model
met-a-636	X-12644	Brest cancer	4.70	0.10	fixed effect model
met-a-640	X-12696	Brest cancer	0.67	0.72	fixed effect model
met-a-646	X-12728	Brest cancer	14.61	0.04	random effect model
met-a-652	Isovalerylcarnitine	Brest cancer	14.43	0.01	random effect model
met-a-656	Bradykinin, des-arg(9)	Brest cancer	6.50	0.16	fixed effect model
met-a-661	X-12798	Brest cancer	17.51	0.13	fixed effect model
met-a-665	X-12844	Brest cancer	2.13	0.55	fixed effect model
met-a-667	X-12850	Brest cancer	4.34	0.11	fixed effect model
met-a-682	1-arachidonoylglycero-phosphoethanolamine*	Brest cancer	0.74	0.86	fixed effect model
met-a-683	X-13429	Brest cancer	11.16	0.01	random effect model
met-a-684	X-13431--nonanoylcarnitine*	Brest cancer	9.01	0.17	fixed effect model
met-a-685	X-13435	Brest cancer	0.24	0.89	fixed effect model
met-a-699	Glutaroyl carnitine	Brest cancer	12.10	0.28	fixed effect model
met-a-709	Tetradecanedioate	Brest cancer	9.09	0.03	random effect model
met-a-711	Hexadecanedioate	Brest cancer	9.62	0.05	random effect model
met-a-712	Dihomo-linolenate (20:3n3 or n6)	Brest cancer	3.12	0.21	fixed effect model
met-a-720	X-14205--alpha-glutamyltyrosine	Brest cancer	1.10	0.58	fixed effect model
met-a-729	X-14626	Brest cancer	1.15	0.56	fixed effect model
met-a-735	Octadecanedioate	Brest cancer	7.96	0.05	random effect model
met-a-742	Succinylcarnitine	Brest cancer	7.30	0.61	fixed effect model
met-a-743	Tryptophan betaine	Brest cancer	13.07	0.00	random effect model
met-a-746	5alpha-androstan-3beta,17beta-diol disulfate	Brest cancer	15.45	0.01	random effect model

met-a-747	4-androsten-3beta,17beta-diol disulfate 1*	Brest cancer	10.08	0.07	fixed effect model
met-a-753	Cis-4-decenoyl carnitine	Brest cancer	4.93	0.29	fixed effect model

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**Supplementary Table SIII.** IVW analyses for 100 human blood metabolites on breast 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	0.80	0.32-2.00	0.637
met-a-306	Leucine	12	1.01	0.35-2.95	0.988
met-a-314	Mannose	5	1.10	0.75-1.59	0.632
met-a-316	Uridine	3	1.81	0.55-5.88	0.326
met-a-319	Arachidonate (20:4n6)	5	1.27	0.92-1.75	0.151
met-a-325	Tyrosine	3	1.68	0.53-5.34	0.381
met-a-339	4-acetamidobutanoate	6	0.76	0.46-1.25	0.282
met-a-341	Citrate	7	0.70	0.24-2.09	0.524
met-a-345	Urate	4	1.39	0.74-2.61	0.304
met-a-355	Proline	6	0.70	0.50-0.98	0.035
met-a-356	Citrulline	4	0.51	0.18-1.48	0.218
met-a-357	Biliverdin	9	0.88	0.76-1.02	0.079
met-a-359	Gamma-glutamylglutamine	3	1.34	0.58-3.11	0.493
met-a-360	Gamma-glutamyltyrosine	4	1.10	0.39-3.13	0.852
met-a-362	Betaine	7	1.13	0.71-1.81	0.611
met-a-373	X-03094	5	0.59	0.33-1.06	0.080
met-a-375	Kynurenine	5	0.73	0.45-1.17	0.186
met-a-379	Carnitine	20	0.93	0.42-2.06	0.867
met-a-381	N-acetylorithine	10	1.00	0.90-1.11	0.992
met-a-383	3-methyl-2-oxovalerate	3	0.71	0.27-1.86	0.484
met-a-396	X-18601	3	1.19	0.57-2.46	0.644
met-a-419	1,5-anhydroglucitol (1,5-AG)	4	1.42	0.88-2.28	0.148
met-a-426	X-08402	6	1.10	0.79-1.54	0.565

met-a-427	2-hydroxyisobutyrate	4	1.33	0.79-2.24	0.287
met-a-435	X-08988	3	1.82	1.00-3.33	0.051
met-a-444	X-10510	3	1.27	0.74-2.16	0.387
met-a-449	N-acetylglycine	7	1.10	0.91-1.32	0.337
met-a-450	Bilirubin (Z,Z)	8	0.95	0.86-1.05	0.319
met-a-460	Androsterone sulfate	8	0.95	0.84-1.07	0.415
met-a-464	Serine	3	2.25	1.18-4.27	0.014
met-a-467	Hexanoylcarnitine	9	0.85	0.68-1.06	0.147
met-a-468	Glycine	9	1.07	0.86-1.35	0.536
met-a-476	Butyrylcarnitine	24	1.03	0.96-1.11	0.388
met-a-479	Propionylcarnitine	5	0.95	0.28-3.27	0.938
met-a-482	10-undecenoate (11:1n1)	4	1.38	1.00-1.90	0.047
met-a-484	X-11204	3	0.89	0.26-3.02	0.855
met-a-485	X-02269	4	0.93	0.73-1.18	0.527
met-a-490	X-11261	6	1.09	0.84-1.42	0.526
met-a-491	Bilirubin (E,E)*	6	0.93	0.81-1.07	0.311
met-a-495	X-11315	3	1.32	0.81-2.15	0.260
met-a-500	3-dehydrocarnitine*	5	0.67	0.40-1.11	0.119
met-a-501	Pyroglutamine*	5	0.91	0.67-1.23	0.545
met-a-505	X-03056--N-[3-(2-Oxopyrrolidin -1-yl)propyl]acetamide	8	0.94	0.52-1.67	0.822
met-a-510	X-09789	3	1.30	0.94-1.79	0.111
met-a-513	X-11440	6	0.82	0.71-0.95	0.008
met-a-514	X-11441	6	0.87	0.74-1.02	0.088
met-a-515	X-11442	7	0.89	0.76-1.04	0.154
met-a-516	X-11444	4	1.18	0.63-2.20	0.599

met-a-517	X-11445--5-alpha-pregnan-3beta,20alpha-disulfate	3	1.06	0.69-1.62	0.796
met-a-519	X-11469	4	0.89	0.69-1.15	0.389
met-a-524	X-11491	4	1.01	0.81-1.26	0.927
met-a-526	HWESASXX*	3	0.86	0.63-1.18	0.347
met-a-528	X-11529	11	1.01	0.95-1.08	0.685
met-a-529	X-11530	8	0.88	0.76-1.03	0.104
met-a-531	X-11538	8	1.04	0.90-1.21	0.595
met-a-536	X-11593--O-methylascorbate*	13	1.03	0.78-1.36	0.855
met-a-541	X-11787	8	1.02	0.65-1.59	0.947
met-a-542	X-11792	3	0.98	0.86-1.12	0.801
met-a-543	X-11793--oxidized bilirubin*	10	0.90	0.76-1.08	0.264
met-a-558	1-arachidonoylglycero- phosphocholine*	5	1.12	0.83-1.52	0.445
met-a-560	X-11905	3	1.01	0.78-1.31	0.919
met-a-570	X-12063	14	0.99	0.88-1.12	0.890
met-a-573	Isobutyrylcarnitine	7	1.09	0.88-1.36	0.418
met-a-578	Erythronate*	3	0.80	0.28-2.24	0.669
met-a-580	X-12092	19	1.00	0.94-1.06	0.999
met-a-581	X-12093	5	1.10	0.95-1.26	0.189
met-a-596	X-12244--N-acetylcarnosine	6	1.33	0.86-2.07	0.201
met-a-613	X-12456	3	0.94	0.55-1.59	0.808
met-a-615	Octanoylcarnitine	7	0.98	0.81-1.19	0.852
met-a-616	Alpha-hydroxyisovalerate	3	1.25	0.85-1.83	0.256
met-a-618	Decanoylcarnitine	5	1.16	0.91-1.48	0.228
met-a-627	Epiandrosterone sulfate	7	0.96	0.85-1.08	0.497
met-a-629	X-12510--2-aminooctanoic acid	7	0.92	0.77-1.10	0.385

met-a-631	Bilirubin (E,Z or Z,E)*	4	0.79	0.63-1.00	0.047
met-a-633	X-12556	4	1.38	0.81-2.33	0.234
met-a-634	1-arachidonoylglycero-phosphoinositol*	5	1.44	0.98-2.12	0.061
met-a-636	X-12644	3	1.39	0.73-2.67	0.317
met-a-640	X-12696	3	2.15	1.14-4.08	0.018
met-a-646	X-12728	8	1.00	0.97-1.03	0.991
met-a-652	Isovalerylcarnitine	6	0.61	0.34-1.10	0.103
met-a-656	Bradykinin, des-arg(9)	5	0.98	0.90-1.07	0.625
met-a-661	X-12798	13	1.02	0.88-1.18	0.809
met-a-665	X-12844	4	1.30	0.79-2.15	0.306
met-a-667	X-12850	3	0.89	0.71-1.11	0.314
met-a-682	1-arachidonoylglycero-phosphoethanolamine*	4	1.32	0.86-2.03	0.206
met-a-683	X-13429	4	1.03	0.79-1.35	0.813
met-a-684	X-13431--nonanoylcarnitine*	7	0.83	0.72-0.96	0.014
met-a-685	X-13435	3	1.01	0.65-1.58	0.965
met-a-699	Glutaroyl carnitine	11	0.77	0.57-1.04	0.087
met-a-709	Tetradecanedioate	4	1.05	0.77-1.44	0.768
met-a-711	Hexadecanedioate	5	1.08	0.80-1.46	0.593
met-a-712	Dihomo-linolenate (20:3n3 or n6)	3	0.39	0.20-0.73	0.004
met-a-720	X-14205--alpha-glutamyltyrosine	3	1.11	0.81-1.52	0.529
met-a-729	X-14626	3	1.68	1.15-2.46	0.007
met-a-735	Octadecanedioate	4	1.12	0.58-2.16	0.734
met-a-742	Succinylcarnitine	10	1.58	1.06-2.34	0.023
met-a-743	Tryptophan betaine	4	1.20	0.87-1.66	0.264

met-a-746	5alpha-androstan-3beta,17beta-diol disulfate	6	0.85	0.67-1.09	0.206
met-a-747	4-androsten-3beta,17beta-diol disulfate 1*	6	0.86	0.76-0.98	0.025
met-a-753	Cis-4-decenoyl carnitine	5	0.91	0.69-1.20	0.509

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 breast cancer of per 1–standard deviation increase of metabolite levels .

**Supplementary Table SIV.** Characteristics of genetic variants for Proline

<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>
rs2518802	22	18975345	C	A	0.0534	0.0033	0.097	4.15E-59
rs5746636	22	18896301	T	G	-0.0319	0.0036	0.1975	3.94E-19
rs5747934	22	18915282	T	C	0.0715	0.0051	0.0468	2.00E-44
rs715544	22	19133605	A	G	-0.0199	0.0036	0.093	2.44E-08
rs9605907	22	18941457	G	A	0.0229	0.0026	0.8377	9.70E-19
rs9680846	22	18965418	T	C	-0.0144	0.0024	0.2825	2.80E-09

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

**Supplementary Table SV.** Characteristics of genetic variants for Serine

<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>
rs1163251	1	120209755	C	T	-0.0188	0.0017	0.4	7.05E-27
rs4947534	7	56079094	C	T	0.0183	0.0024	0.7521	1.96E-14
rs715	2	211543055	C	T	0.0223	0.0024	0.2889	2.69E-21

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

**Supplementary Table SVI.** Characteristics of genetic variants for 10-undecenoate (11:1n1)

<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>
rs2494248	1	47644902	C	T	0.0251	0.0032	0.3291	1.19E-14
rs6077678	20	1069103	A	G	-0.0228	0.0041	0.848	3.38E-08
rs7556052	1	47414851	T	A	0.0346	0.0034	0.3279	5.50E-24
rs9333029	1	47396162	G	A	0.0695	0.0042	0.1331	1.52E-61

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

**Supplementary Table SVII.** Characteristics of genetic variants for X-11440

<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>
rs11670965	19	48468770	G	A	-0.0347	0.0055	0.6873	3.45E-10
rs2932766	19	48390424	T	G	-0.0621	0.0055	0.7073	1.48E-29
rs296381	19	48371102	T	C	0.1636	0.0064	0.8285	5.38E-143
rs3732218	2	234627304	A	G	-0.0532	0.0089	0.0805	2.77E-09
rs4715354	6	52708797	A	G	0.0278	0.0049	0.478	1.66E-08
rs4802397	19	48361912	C	T	0.0559	0.0078	0.1412	9.94E-13

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

**Supplementary Table SVIII.** Characteristics of genetic variants for Bilirubin (E,Z or Z,E)\*

<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>
rs28898590	2	234619422	T	G	-0.059	0.0107	0.0617	4.01E-08
rs4281899	2	234520669	G	T	-0.0341	0.0059	0.2584	6.26E-09
rs6723936	2	234693382	A	G	0.0294	0.0051	0.6407	1.11E-08
rs887829	2	234668570	T	C	0.081	0.0051	0.3243	1.79E-56

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

**Supplementary Table SIX.** Characteristics of genetic variants for X-12696

<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>
rs12465802	2	136381348	A	G	-0.0302	0.0026	0.2879	2.35E-30
rs13005339	2	137321430	G	A	0.0147	0.0027	0.717	2.70E-08
rs3800993	7	141801007	T	C	0.0224	0.0036	0.1701	4.06E-10

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

**Supplementary Table SX.** Characteristics of genetic variants for X-13431--nonanoylcarnitine\*

<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>
rs12566232	1	151839838	C	A	0.0446	0.005	0.2905	5.69E-19
rs1509821	2	211381335	T	C	0.0574	0.0076	0.1091	5.28E-14
rs2302539	2	211000909	A	G	0.0492	0.0044	0.4002	1.37E-28
rs2539861	2	210859726	C	A	-0.057	0.0085	0.0809	2.21E-11
rs3738934	2	210874246	C	T	0.1056	0.0043	0.3769	1.21E-134
rs4672574	2	211240483	C	T	-0.0329	0.0049	0.3639	1.99E-11
rs992029	2	210295506	T	C	-0.0422	0.0077	0.0981	3.93E-08

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

**Supplementary Table SXI.** Characteristics of genetic variants for Dihomo-linolenate (20:3n3 or n6)

<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>
rs174455	11	61656117	A	G	-0.0147	0.0026	0.6459	1.51E-08
rs6498540	16	15130594	G	A	-0.0172	0.0026	0.2958	2.55E-11
rs968567	11	61595564	T	C	0.0329	0.0035	0.1796	2.14E-21

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

**Supplementary Table SXII.** Characteristics of genetic variants for X-14626

<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>
rs10770797	12	21472629	C	T	-0.0181	0.0029	0.3094	3.81E-10
rs11045834	12	21341096	T	C	-0.0232	0.0029	0.2885	8.62E-16
rs12317268	12	21352541	G	A	0.0536	0.0038	0.1572	2.20E-45

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

**Supplementary Table SXIII.** 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	1.36E-18
rs11637751	15	63643524	A	G	0.0155	0.0027	0.1659	1.77E-08
rs12899230	15	63369788	C	T	0.0247	0.0036	0.0787	1.39E-11
rs1472631	15	63423739	G	A	-0.0366	0.0018	0.5081	1.85E-88
rs17806888	3	67416322	C	T	0.0224	0.0034	0.1194	7.15E-11
rs2686513	7	22451353	C	T	0.011	0.002	0.448	3.80E-08
rs2729786	15	63401605	A	C	0.0238	0.0036	0.099	3.97E-11
rs6703518	1	186116797	T	G	-0.0108	0.0019	0.4273	5.85E-09
rs8060756	16	63202385	A	G	0.0102	0.0018	0.3703	4.07E-08
rs901273	15	63677966	G	A	-0.0107	0.0019	0.4966	7.48E-09

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

**Supplementary Table SXIV.** Characteristics of genetic variants for 4-androsten-3beta,17beta-diol disulfate 1\*

<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>
rs11669552	19	48472723	A	G	-0.0395	0.0065	0.5468	1.47E-09
rs11761528	7	99118801	T	C	-0.0696	0.012	0.074	6.27E-09
rs296396	19	48365523	C	T	0.1754	0.0086	0.8349	1.48E-92
rs4149452	19	48377519	T	C	0.0773	0.0078	0.2655	3.01E-23
rs4802397	19	48361912	C	T	0.0621	0.0096	0.1414	1.09E-10
rs7259671	19	48345407	C	T	-0.0435	0.0066	0.6799	3.83E-11

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