

**Twin Research and Human Genetics**

**Supplementary material**

**Associations of Obesity Measurements with Serum Metabolomic Profile: A Chinese Twin Study**

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Supplementary Table 1. Metabolites associated with obesity measurements in negative ion mode

RT_M/Z	Metabolite_ID	Metabolite_Name	Metabolite category	Beta coefficient	P-value	FDR
<b>BMI</b>						
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	1.996	1.15E-08	2.91E-07
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	2.342	2.06E-10	1.54E-08
0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Amino acids and derivatives	1.806	8.52E-10	3.20E-08
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	1.785	1.64E-07	3.08E-06
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	1.505	1.39E-06	2.08E-05
8.63_504.3094m/z	HMDB09295	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-1.703	3.82E-06	4.78E-05
5.38_201.1126m/z	HMDB00792	Sebacic acid	Lipids and lipid-like molecules	1.081	1.05E-04	1.12E-03
5.38_187.0971m/z	HMDB00784	Azelaic acid	Lipids and lipid-like molecules	0.957	1.81E-04	1.70E-03
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	1.218	2.70E-04	2.25E-03
3.75_203.0819m/z	HMDB13609	D-Tryptophan	Organoheterocyclic compounds	1.212	3.09E-04	2.25E-03
4.89_173.0814m/z	HMDB00893	Suberic acid	Lipids and lipid-like molecules	0.934	3.29E-04	2.25E-03
3.75_359.0036m/z	HMDB00288	Uridine 5'-monophosphate	Nucleosides, nucleotides, and analogues	1.256	4.29E-04	2.68E-03
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-1.147	5.28E-04	3.04E-03
5.38_397.1815m/z	HMDB00063	Hydrocortisone	Lipids and lipid-like molecules	0.892	3.14E-03	1.57E-02
9.50_464.3146m/z	LMGP02070002	PE(P-18:0/0:0)	Lipids and lipid-like molecules	-0.732	3.14E-03	1.57E-02
9.46_337.2132m/z	NA	rac-Glycerol 1-myristate	-	0.913	5.08E-03	2.38E-02
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-0.938	6.70E-03	2.95E-02
11.25_722.5123m/z	LMGP02030093	PE(P-16:0/20:4(5Z,8Z,11Z,14Z))	Lipids and lipid-like molecules	-0.661	1.15E-02	4.56E-02
8.35_498.2635m/z	LMGP02050027	PE(20:5(5Z,8Z,11Z,14Z,17Z)/0:0)	Lipids and lipid-like molecules	0.900	1.13E-02	4.56E-02
<b>WC</b>						
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	2.480	3.94E-08	1.50E-06
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	3.058	1.28E-10	9.57E-09

0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Amino acids and derivatives	1.801	2.39E-06	8.95E-05
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	1.866	1.60E-05	2.00E-04
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	1.916	1.38E-05	2.00E-04
8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-2.094	1.04E-05	2.00E-04
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-1.850	1.48E-05	2.00E-04
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	1.479	2.35E-04	2.20E-03
3.75_203.0819m/z	HMDB13609	D-Tryptophan	Organoheterocyclic compounds	1.517	4.76E-04	3.97E-03
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-1.510	7.13E-04	5.35E-03
3.75_359.0036m/z	HMDB00288	Uridine 5'-monophosphate	Nucleosides, nucleotides, and analogues	1.491	1.19E-03	8.12E-03
9.46_337.2132m/z	NA	rac-Glycerol 1-myristate	-	1.306	1.91E-03	1.19E-02
4.89_173.0814m/z	HMDB00893	Suberic acid	Lipids and lipid-like molecules	1.023	2.22E-03	1.28E-02
5.38_187.0971m/z	HMDB00784	Azelaic acid	Lipids and lipid-like molecules	0.951	3.89E-03	2.08E-02
0.62_199.0369m/z	C00586	L-(-)-Fucose	Organic oxygen compounds	-1.307	6.33E-03	2.97E-02
5.38_201.1126m/z	HMDB00792	Sebacic acid	Lipids and lipid-like molecules	0.981	6.27E-03	2.97E-02
4.15_178.0507m/z	HMDB00714	Hippuric acid	Benzenoids	-1.234	9.06E-03	4.00E-02
9.11_466.3294m/z	LMGP02060003	PE(O-18:0/0:0)	Lipids and lipid-like molecules	-1.115	1.03E-02	4.08E-02
9.50_464.3146m/z	LMGP02070002	PE(P-18:0/0:0)	Lipids and lipid-like molecules	-0.822	1.02E-02	4.08E-02
<b>WHR</b>						
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	3.525	6.49E-08	5.07E-06
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	4.848	1.02E-09	7.62E-08
0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Amino acids and derivatives	3.525	6.49E-08	2.43E-06
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	3.634	1.15E-06	2.87E-05
3.75_203.0819m/z	HMDB13609	D-Tryptophan	Organoheterocyclic compounds	2.903	7.25E-05	1.36E-03
4.89_173.0814m/z	HMDB00893	Suberic acid	Lipids and lipid-like molecules	2.096	2.66E-04	3.73E-03
8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-2.858	2.99E-04	3.73E-03

5.38_187.0971m/z	HMDB00784	Azelaic acid	Lipids and lipid-like molecules	2.008	4.00E-04	4.13E-03
5.38_201.1126m/z	HMDB00792	Sebacic acid	Lipids and lipid-like molecules	2.040	9.14E-04	6.86E-03
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-2.364	8.86E-04	6.86E-03
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	2.372	1.09E-03	7.45E-03
3.75_359.0036m/z	HMDB00288	Uridine 5'-monophosphate	Nucleosides, nucleotides, and analogues	2.413	1.62E-03	1.01E-02
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	1.929	4.36E-03	2.52E-02
9.46_337.2132m/z	NA	rac-Glycerol 1-myristate	-	1.972	5.17E-03	2.77E-02
<b>%BF</b>						
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	1.037	2.69E-07	2.04E-05
0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Amino acids and derivatives	0.845	8.10E-07	6.07E-05
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	0.976	4.83E-06	1.81E-04
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	0.754	1.40E-04	2.06E-03
8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-0.799	1.65E-04	2.06E-03
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-0.726	1.44E-04	2.06E-03
4.89_173.0814m/z	HMDB00893	Suberic acid	Lipids and lipid-like molecules	0.546	3.13E-04	3.35E-03
3.75_359.0036m/z	HMDB00288	Uridine 5'-monophosphate	Nucleosides, nucleotides, and analogues	0.718	4.42E-04	4.14E-03
5.38_187.0971m/z	HMDB00784	Azelaic acid	Lipids and lipid-like molecules	0.510	6.30E-04	5.25E-03
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	0.635	7.89E-04	5.92E-03
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-0.643	1.24E-03	8.44E-03
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	0.578	1.38E-03	8.64E-03
0.62_199.0369m/z	C00586	L-(-)-Fucose	Organic oxygen compounds	-0.672	1.84E-03	1.02E-02
5.38_201.1126m/z	HMDB00792	Sebacic acid	Lipids and lipid-like molecules	0.505	1.90E-03	1.02E-02
3.75_203.0819m/z	HMDB13609	D-Tryptophan	Organoheterocyclic compounds	0.599	2.22E-03	1.11E-02
8.97_478.2935m/z	LMGP02050004	PE(18:1(9Z)/0:0)	Lipids and lipid-like molecules	-0.538	6.60E-03	3.09E-02
4.15_178.0507m/z	HMDB00714	Hippuric acid	Benzenoids	-0.555	8.98E-03	3.96E-02

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RT\_M/Z: retention time(min)\_mass-to-charge ratio; BMI: body mass index; WC: waist circumference; WHR: waist to hip ratio; %BF: percent body fat

Beta coefficient indicates regression coefficient, i.e., the effect size of the association

Mixed-effect linear regression models were used. Twins were treated as individuals, but the models accounted for clustering within a pair. Models were adjusted for age, sex, zygosity, study sites, smoking, drinking, diet, physical activity, education, and test batch as fixed effects, family id as random effect

Supplementary Table 2a. Metabolites associated with obesity measurements in negative ion mode additionally adjust for medication use

RT_M/Z	Metabolite_ID	Metabolite_Name	Metabolite category	Beta coefficient	P-value	FDR
<b>BMI</b>						
0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Amino acids and derivatives	1.853	1.66E-10	6.31E-09
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	2.377	1.13E-10	6.31E-09
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	1.973	1.72E-08	4.35E-07
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	1.800	1.41E-07	2.15E-06
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	1.512	1.33E-06	1.69E-05
8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-1.707	3.94E-06	4.27E-05
3.75_203.0819m/z	HMDB13609	D-Tryptophan	Organoheterocyclic compounds	1.269	1.26E-04	1.06E-03
5.38_201.1126m/z	HMDB00792	Sebacic acid	Lipids and lipid-like molecules	1.079	1.13E-04	1.06E-03
5.38_187.0971m/z	HMDB00784	Azelaic acid	Lipids and lipid-like molecules	0.956	1.93E-04	1.47E-03
3.75_359.0036m/z	HMDB00288	Uridine 5'-monophosphate	Nucleosides, nucleotides, and analogues	1.298	2.65E-04	1.83E-03
4.89_173.0814m/z	HMDB00893	Suberic acid	Lipids and lipid-like molecules	0.930	3.62E-04	2.30E-03
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	1.063	5.63E-04	3.06E-03
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-1.147	5.47E-04	3.06E-03
5.38_397.1815m/z	HMDB00063	Hydrocortisone	Lipids and lipid-like molecules	0.886	3.43E-03	1.74E-02
9.50_464.3146m/z	LMGP02070002	PE(P-18:0/0:0)	Lipids and lipid-like molecules	-0.721	3.67E-03	1.74E-02
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-0.953	6.01E-03	2.54E-02
9.46_337.2132m/z	NA	rac-Glycerol 1-myristate	-	0.901	5.77E-03	2.54E-02
11.25_722.5123m/z	LMGP02030093	PE(P-16:0/20:4(5Z,8Z,11Z,14Z))	Lipids and lipid-like molecules	-0.669	1.08E-02	4.33E-02
8.35_498.2635m/z	LMGP02050027	PE(20:5(5Z,8Z,11Z,14Z,17Z)/0:0)	Lipids and lipid-like molecules	0.889	1.25E-02	4.76E-02

<b>WC</b>						
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	3.140	4.68E-11	3.56E-09
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	2.439	7.17E-08	2.73E-06
0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Amino acids and derivatives	1.905	4.38E-07	1.11E-05
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	1.952	1.05E-05	1.59E-04
8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-2.108	1.03E-05	1.59E-04
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-1.859	1.51E-05	1.92E-04
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	1.575	7.91E-05	7.51E-04
3.75_203.0819m/z	HMDB13609	D-Tryptophan	Organoheterocyclic compounds	1.645	1.26E-04	1.07E-03
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	1.496	2.13E-04	1.62E-03
3.75_359.0036m/z	HMDB00288	Uridine 5'-monophosphate	Nucleosides, nucleotides, and analogues	1.583	5.88E-04	3.72E-03
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-1.551	5.52E-04	3.72E-03
4.89_173.0814m/z	HMDB00893	Suberic acid	Lipids and lipid-like molecules	1.015	2.51E-03	1.36E-02
9.46_337.2132m/z	NA	rac-Glycerol 1-myristate	-	1.286	2.35E-03	1.36E-02
5.38_187.0971m/z	HMDB00784	Azelaic acid	Lipids and lipid-like molecules	0.948	4.14E-03	2.10E-02
5.38_201.1126m/z	HMDB00792	Sebacic acid	Lipids and lipid-like molecules	0.978	6.72E-03	3.19E-02
4.15_178.0507m/z	HMDB00714	Hippuric acid	Benzenoids	-1.269	7.60E-03	3.40E-02
0.62_199.0369m/z	C00586	L-(-)-Fucose	Organic oxygen compounds	-1.210	1.15E-02	4.81E-02
13.76_915.7595n	HMDB09739	PE(24:0/24:0)	Lipids and lipid-like molecules	1.153	1.33E-02	4.81E-02
9.11_466.3294m/z	LMGP02060003	PE(O-18:0/0:0)	Lipids and lipid-like molecules	-1.097	1.21E-02	4.81E-02
9.50_464.3146m/z	LMGP02070002	PE(P-18:0/0:0)	Lipids and lipid-like molecules	-0.800	1.27E-02	4.81E-02
<b>WHR</b>						
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	3.783	1.97E-06	1.50E-04
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-2.778	1.09E-04	4.13E-03
8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-2.940	2.29E-04	4.34E-03

1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	2.811	2.00E-04	4.34E-03
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	2.286	6.19E-04	7.84E-03
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	2.215	1.08E-03	1.15E-02
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-2.428	1.21E-03	1.15E-02
9.11_466.3294m/z	LMGP02060003	PE(O-18:0/0:0)	Lipids and lipid-like molecules	-2.291	1.77E-03	1.50E-02
0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Organic acids and derivatives	1.808	4.29E-03	3.26E-02
<b>%BF</b>						
0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Amino acids and derivatives	0.882	1.72E-07	1.31E-05
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	1.024	3.81E-07	1.45E-05
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	0.994	3.30E-06	8.36E-05
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	0.764	1.20E-04	1.90E-03
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-0.724	1.55E-04	1.90E-03
8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-0.798	1.75E-04	1.90E-03
3.75_359.0036m/z	HMDB00288	Uridine 5'-monophosphate	Nucleosides, nucleotides, and analogues	0.741	2.81E-04	2.67E-03
4.89_173.0814m/z	HMDB00893	Suberic acid	Lipids and lipid-like molecules	0.544	3.44E-04	2.90E-03
5.38_187.0971m/z	HMDB00784	Azelaic acid	Lipids and lipid-like molecules	0.510	6.59E-04	5.00E-03
3.75_203.0819m/z	HMDB13609	D-Tryptophan	Organoheterocyclic compounds	0.633	1.04E-03	7.19E-03
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-0.649	1.14E-03	7.23E-03
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	0.582	1.31E-03	7.65E-03
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	0.548	1.56E-03	8.45E-03
5.38_201.1126m/z	HMDB00792	Sebacic acid	Lipids and lipid-like molecules	0.505	2.00E-03	1.01E-02
0.62_199.0369m/z	C00586	L-(-)-Fucose	Organic oxygen compounds	-0.648	2.63E-03	1.25E-02
8.97_478.2935m/z	LMGP02050004	PE(18:1(9Z)/0:0)	Lipids and lipid-like molecules	-0.533	7.19E-03	3.21E-02
4.15_178.0507m/z	HMDB00714	Hippuric acid	Benzenoids	-0.564	8.08E-03	3.41E-02
7.57_407.2797m/z	HMDB00619	Cholic acid	Lipids and lipid-like molecules	0.529	9.33E-03	3.73E-02



RT<sub>M/Z</sub>: retention time(min)\_mass-to-charge ratio; BMI: body mass index; WC: waist circumference; WHR: waist to hip ratio; %BF: percent body fat

Beta coefficient indicates regression coefficient, i.e., the effect size of the association

Mixed-effect linear regression models were used. Twins were treated as individuals, but the models accounted for clustering within a pair. Models were adjusted for age, sex, zygosity, study sites, smoking, drinking, diet, physical activity, education, test batch and hypoglycemic/ hypolipidemic drug uses as fixed effects, family id as random effect.

Supplementary Table 2b. Metabolites associated with obesity measurements in negative ion mode exclude type 2 diabetes individuals

RT_M/Z	Metabolite_ID	Metabolite_Name	Metabolite category	Beta coefficient	P-value	FDR
<b>BMI</b>						
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	2.563	7.35E-10	5.59E-08
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	2.095	1.16E-07	2.94E-06
0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Amino acids and derivatives	1.707	2.40E-07	4.56E-06
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	1.724	6.02E-07	9.15E-06
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	1.948	9.38E-07	1.19E-05
8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-1.899	2.98E-06	3.23E-05
5.38_201.1126m/z	HMDB00792	Sebacic acid	Lipids and lipid-like molecules	1.292	3.88E-05	3.69E-04
5.38_187.0971m/z	HMDB00784	Azelaic acid	Lipids and lipid-like molecules	1.092	8.29E-05	7.00E-04
3.75_203.0819m/z	HMDB13609	D-Tryptophan	Organoheterocyclic compounds	1.368	1.95E-04	1.48E-03
4.89_173.0814m/z	HMDB00893	Suberic acid	Lipids and lipid-like molecules	1.071	2.32E-04	1.61E-03
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-1.307	3.25E-04	2.06E-03
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	0.899	3.99E-04	2.33E-03
3.75_359.0036m/z	HMDB00288	Uridine 5'-monophosphate	Nucleosides, nucleotides, and analogues	1.331	6.11E-04	3.32E-03
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-1.043	6.02E-03	3.05E-02
9.50_464.3146m/z	LMGP02070002	PE(P-18:0/0:0)	Lipids and lipid-like molecules	-0.752	7.01E-03	3.33E-02
11.25_722.5123m/z	LMGP02030093	PE(P-16:0/20:4(5Z,8Z,11Z,14Z))	Lipids and lipid-like molecules	-0.781	9.54E-03	4.27E-02
<b>WC</b>						
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	3.399	1.11E-10	8.47E-09
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	2.469	7.48E-07	2.84E-05

8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-2.318	5.88E-06	1.16E-04
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	2.198	1.06E-05	1.61E-04
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-1.975	1.90E-05	2.40E-04
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	1.281	6.68E-05	6.34E-04
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	1.731	6.41E-05	6.34E-04
3.75_203.0819m/z	HMDB13609	D-Tryptophan	Organoheterocyclic compounds	1.823	8.51E-05	7.19E-04
0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Amino acids and derivatives	1.613	9.83E-05	7.47E-04
4.89_173.0814m/z	HMDB00893	Suberic acid	Lipids and lipid-like molecules	1.253	5.14E-04	3.55E-03
5.38_187.0971m/z	HMDB00784	Azelaic acid	Lipids and lipid-like molecules	1.179	5.94E-04	3.76E-03
3.75_359.0036m/z	HMDB00288	Uridine 5'-monophosphate	Nucleosides, nucleotides, and analogues	1.640	8.39E-04	4.91E-03
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-1.575	1.15E-03	6.25E-03
5.38_201.1126m/z	HMDB00792	Sebacic acid	Lipids and lipid-like molecules	1.212	1.92E-03	9.73E-03
<b>WHR</b>						
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	4.257	1.82E-06	1.38E-04
8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-3.934	6.67E-06	2.53E-04
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-3.120	7.51E-05	1.43E-03
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	2.824	1.41E-04	2.14E-03
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	2.956	4.84E-04	6.13E-03
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-2.685	1.20E-03	1.31E-02
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	2.458	3.77E-03	3.58E-02
<b>%BF</b>						
1.23_180.0660m/z	HMDB00158	L-Tyrosine	Amino acids and derivatives	1.143	1.56E-06	1.18E-04
1.51_130.0871m/z	HMDB00172	L-Isoleucine	Amino acids and derivatives	1.049	3.51E-06	1.33E-04
0.58_146.0456m/z	HMDB02393	N-Methyl-D-aspartic acid	Amino acids and derivatives	0.846	1.19E-05	2.38E-04
8.63_504.3094m/z	LMGP02050021	PE(20:2(11Z,14Z)/0:0)	Lipids and lipid-like molecules	-1.016	1.25E-05	2.38E-04

4.89_173.0814m/z	HMDB00893	Suberic acid	Lipids and lipid-like molecules	0.724	1.98E-05	2.68E-04
8.94_506.3251m/z	LMGP02050020	PE(20:1(11Z)/0:0)	Lipids and lipid-like molecules	-0.894	2.12E-05	2.68E-04
5.38_187.0971m/z	HMDB00784	Azelaic acid	Lipids and lipid-like molecules	0.661	5.01E-05	5.44E-04
3.26_164.0712m/z	HMDB00159	L-Phenylalanine	Organic acids and derivatives	0.876	1.28E-04	1.08E-03
5.38_201.1126m/z	HMDB00792	Sebacic acid	Lipids and lipid-like molecules	0.659	3.45E-04	2.62E-03
8.94_570.2935m/z	LMGP01010693	PC(16:1(9Z)/2:0)	Lipids and lipid-like molecules	-0.769	4.35E-04	3.01E-03
8.97_478.2935m/z	LMGP02050004	PE(18:1(9Z)/0:0)	Lipids and lipid-like molecules	-0.746	7.26E-04	4.60E-03
0.93_167.0205m/z	HMDB00289	Uric acid	Organoheterocyclic compounds	0.658	8.99E-04	5.26E-03
3.75_359.0036m/z	HMDB00288	Uridine 5'-monophosphate	Nucleosides, nucleotides, and analogues	0.679	2.23E-03	1.21E-02
3.75_203.0819m/z	HMDB13609	D-Tryptophan	Organoheterocyclic compounds	0.592	5.18E-03	2.62E-02
0.59_215.0322m/z	-	Galactose/Mannose/Glucose	Hexoses	0.377	9.15E-03	4.35E-02

RT\_M/Z: retention time(min)\_mass-to-charge ratio; BMI: body mass index; WC: waist circumference; WHR: waist to hip ratio; %BF: percent body fat

Beta coefficient indicates regression coefficient, i.e., the effect size of the association

Mixed-effect linear regression models were used. Twins were treated as individuals, but the models accounted for clustering within a pair. Models were adjusted for age, sex, zygosity, study sites, smoking, drinking, diet, physical activity, education, test batch as fixed effects, family id as random effect.

Supplementary Table 3: Distribution of physical and clinical blood biochemical indicators between obesity-discordant monozygotic twin pairs

Indicators(Mean±SE)	Number of twin pair	Non-obese	Obese	Paired P
Body mass index(kg/m <sup>2</sup> )	15	23.4±1.5	29±1.4	0.000
Waist circumference(cm)	15	83.7±7.2	96.1±5.4	0.000
Waist to hip ratio	15	0.88±0.06	0.93±0.05	0.029
Percent body fat	15	29.7±7.3	35.5±7.9	0.014
TC(mmol/L)	15	4.9±0.9	5.2±1.1	0.324
TG(mmol/L)	15	1.8±2.3	1.7±0.9	0.845
HDL_C(mmol/L)	15	1.6±0.4	1.5±0.3	0.311
LDL-C(mmol/L)	15	2.2±0.4	2.5±0.6	0.096
Glucose(mmol/L)	15	5.3±0.5	5.5±0.7	0.136
Insulin(pmol/L)	14	66.5±34.6	113.7±70.9	0.019
HbA1c(%)	15	5.5±0.3	5.7±0.5	0.089
HOMA-IR	14	2.7±1.2	3.7±3.0	0.239
SBP(mmHg)	15	126.5±17.0	126.5±14.5	0.988
DBP(mmHg)	15	76.6±9.8	76.5±9.8	0.971

TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Supplementary Table 4: Metabolites associated with obesity measurements in positive ion mode

<b>RT_M/Z</b>	<b>Metabolite_ID</b>	<b>Metabolite_Name</b>	<b>Metabolite category</b>	<b>Beta coefficient</b>	<b>P-value</b>	<b>FDR</b>
<b>BMI</b>						
8.60_519.3354 n	LMGP01050035/LMGP010 50034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E, 4E)/0:0)	Lipids and lipid- like molecules	-1.050	4.69E-06	0.000
0.66_164.0468 n	HMDB02035	p-Coumaric acid	-	1.248	8.80E-04	0.032
0.65_130.0859 m/z	HMDB00070	Pipecolinic acid		-1.087	1.64E-03	0.040
<b>WC</b>						
8.60_519.3354 n	LMGP01050035/LMGP010 50034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E, 4E)/0:0)	Lipids and lipid- like molecules	-1.348	5.11E-06	0.000
0.66_164.0468 n	HMDB02035	p-Coumaric acid		1.750	3.05E-04	0.011
<b>WHR</b>						
8.60_519.3354 n	LMGP01050035/LMGP010 50034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E, 4E)/0:0)	Lipids and lipid- like molecules	-1.806	2.40E-04	0.017
<b>%BF</b>						
8.60_519.3354 n	LMGP01050035/LMGP010 50034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E, 4E)/0:0)	Lipids and lipid- like molecules	-0.556	2.63E-05	0.002

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RT\_M/Z: retention time(min)\_mass-to-charge ratio; BMI: body mass index; WC: waist circumference; WHR: waist to hip ratio; %BF: percent body fat

Beta coefficient indicates regression coefficient, i.e., the effect size of the association

Mixed-effect linear regression models were used. Twins were treated as individuals, but the models accounted for clustering within a pair.

Models were adjusted for age, sex, zygosity, study sites, smoking, drinking, diet, physical activity, education, and test batch as fixed effects, family id as random effect

Supplementary Table 5a: Metabolites associated with obesity measurements in positive ion mode additionally adjust for medication use

RT_M/Z	Metabolite_ID	Metabolite_Name	Metabolite category	Beta coefficient	P-value	FDR
<b>BMI</b>						
8.60_519.3354n	LMGP01050035/LMGP0105034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E,4E)/0:0)	Lipids and lipid-like molecules	-1.045	5.41E-06	0.000
0.66_164.0468n	HMDB02035	p-Coumaric acid	-	1.246	9.21E-04	0.025
0.65_130.0859 m/z	HMDB00070	Pipecolinic acid	Organic acids and derivatives	-1.128	1.04E-03	0.025
<b>WC</b>						
8.60_519.3354n	LMGP01050035/LMGP0105034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E,4E)/0:0)	Lipids and lipid-like molecules	-1.342	6.25E-06	0.000
0.66_164.0468n	HMDB02035	p-Coumaric acid	-	1.754	3.20E-04	0.012
<b>WHR</b>						
8.60_519.3354n	LMGP01050035/LMGP0105034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E,4E)/0:0)	Lipids and lipid-like molecules	-0.553	2.97E-05	0.002
<b>%BF</b>						
8.60_519.3354n	LMGP01050035/LMGP0105034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E,4E)/0:0)	Lipids and lipid-like molecules	-1.791	2.89E-04	0.021



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RT\_M/Z: retention time(min)\_mass-to-charge ratio; BMI: body mass index; WC: waist circumference; WHR: waist to hip ratio; %BF: percent body fat

Beta coefficient indicates regression coefficient, i.e., the effect size of the association

Mixed-effect linear regression models were used. Twins were treated as individuals, but the models accounted for clustering within a pair. Models were adjusted for age, sex, zygosity, study sites, smoking, drinking, diet, physical activity, education, test batch and hypoglycemic/ hypolipidemic drug uses as fixed effects, family id as random effect.

Supplementary Table 5b: Metabolites associated with obesity measurements in positive ion mode exclude type 2 diabetes individuals

RT_M/Z	Metabolite_ID	Metabolite_Name	Metabolite category	Beta coefficient	P-value	FDR
BMI						
8.60_519.3354n	LMGP01050035/LMGP01050034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E,4E)/0:0)	Lipids and lipid-like molecules	-1.189	5.57E-07	4.06E-05
0.66_164.0468n	HMDB02035	p-Coumaric acid	-	1.305	1.03E-03	3.77E-02
WC						
8.60_519.3354n	LMGP01050035/LMGP01050034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E,4E)/0:0)	Lipids and lipid-like molecules	-1.509	9.50E-07	6.93E-05
0.66_164.0468n	HMDB02035	p-Coumaric acid	-	1.897	2.56E-04	9.34E-03
WHR						
8.60_519.3354n	LMGP01050035/LMGP01050034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E,4E)/0:0)	Lipids and lipid-like molecules	-2.159	3.04E-05	2.22E-03
%BF						
8.60_519.3354n	LMGP01050035/LMGP01050034	PC(18:2(9Z,12Z)/0:0)/PC(18:2(2E,4E)/0:0)	Lipids and lipid-like molecules	-0.706	3.69E-07	2.69E-05
5.38_180.0320m/z	HMDB29415	S-Carboxymethyl-L-cysteine	Organic acids and derivatives	0.658	1.00E-03	3.65E-02

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RT\_M/Z: retention time(min)\_mass-to-charge ratio; BMI: body mass index; WC: waist circumference; WHR: waist to hip ratio; %BF: percent body fat

Beta coefficient indicates regression coefficient, i.e., the effect size of the association

Mixed-effect linear regression models were used. Twins were treated as individuals, but the models accounted for clustering within a pair. Models were adjusted for age, sex, zygosity, study sites, smoking, drinking, diet, physical activity, education, test batch as fixed effects, family id as random effect.

Supplementary Table 6: Pathway analysis of metabolic changes associated with BMI

KEGG Pathway	Match Status	Impact	<i>P-value</i>	FDR
Phenylalanine metabolism	2/45	0.12	8.11E-21	5.68E-20
Tyrosine metabolism	1/76	0.05	2.67E-09	5.44E-09
Valine, leucine and isoleucine biosynthesis	1/27	0.01	1.02E-08	1.58E-08
Purine metabolism	2/92	0.01	2.72E-09	5.44E-09
Phenylalanine, tyrosine and tryptophan biosynthesis	2/27	0.01	8.11E-21	5.68E-20
Aminoacyl-tRNA biosynthesis	4/75	0.00	1.64E-09	5.44E-09
Ubiquinone and other terpenoid-quinone biosynthesis	1/36	0.00	2.67E-09	5.44E-09
Thiamine metabolism	1/24	0.00	2.67E-09	5.44E-09
Valine, leucine and isoleucine degradation	1/40	0.00	1.02E-08	1.58E-08
Nitrogen metabolism	3/39	0.00	4.39E-08	6.14E-08

Supplementary Table 7: Pathway enrichment of metabolic changes associated with BMI

Pathway from SMPDB	Total	<i>P-value</i>	FDR
Phenylalanine and Tyrosine Metabolism	2/28	8.11E-21	1.54E-19
Tyrosine Metabolism	1/72	2.67E-09	1.03E-08
Catecholamine Biosynthesis	1/20	2.67E-09	1.03E-08
Thyroid hormone synthesis	1/13	2.67E-09	1.03E-08
Purine Metabolism	2/74	2.72E-09	1.03E-08
Valine, Leucine and Isoleucine Degradation	1/60	1.02E-08	3.21E-08
Nucleotide Sugars Metabolism	1/20	5.32E-03	1.01E-02
Sphingolipid Metabolism	1/40	5.32E-03	1.01E-02
Galactose Metabolism	1/38	5.32E-03	1.01E-02
Lactose Degradation	1/9	5.32E-03	1.01E-02