

Supplementary Tables

STable 1. List of metabolites, annotations, units, and groups.

Annotations	Biomarker name	Unit	Group
Total_C	Total cholesterol	mmol/l	Cholesterol
non_HDL_C	Total cholesterol minus HDL-C	mmol/l	Cholesterol
Remnant_C	Remnant cholesterol (non-HDL, non-LDL - cholesterol)	mmol/l	Cholesterol
VLDL_C	VLDL cholesterol	mmol/l	Cholesterol
Clinical_LDL_C	Clinical LDL cholesterol	mmol/l	Cholesterol
LDL_C	LDL cholesterol	mmol/l	Cholesterol
HDL_C	HDL cholesterol	mmol/l	Cholesterol
Total_TG	Total triglycerides	mmol/l	Triglycerides
VLDL_TG	Triglycerides in VLDL	mmol/l	Triglycerides
LDL_TG	Triglycerides in LDL	mmol/l	Triglycerides
HDL_TG	Triglycerides in HDL	mmol/l	Triglycerides
Total_PL	Total phospholipids in lipoprotein particles	mmol/l	Phospholipids
VLDL_PL	Phospholipids in VLDL	mmol/l	Phospholipids
LDL_PL	Phospholipids in LDL	mmol/l	Phospholipids
HDL_PL	Phospholipids in HDL	mmol/l	Phospholipids
Total_CE	Total esterified cholesterol	mmol/l	Cholesteryl esters
VLDL_CE	Cholesteryl esters in VLDL	mmol/l	Cholesteryl esters
LDL_CE	Cholesteryl esters in LDL	mmol/l	Cholesteryl esters
HDL_CE	Cholesteryl esters in HDL	mmol/l	Cholesteryl esters
Total_FC	Total free cholesterol	mmol/l	Free cholesterol
VLDL_FC	Free cholesterol in VLDL	mmol/l	Free cholesterol
LDL_FC	Free cholesterol in LDL	mmol/l	Free cholesterol
HDL_FC	Free cholesterol in HDL	mmol/l	Free cholesterol
Total_L	Total lipids in lipoprotein particles	mmol/l	Total lipids
VLDL_L	Total lipids in VLDL	mmol/l	Total lipids
LDL_L	Total lipids in LDL	mmol/l	Total lipids
HDL_L	Total lipids in HDL	mmol/l	Total lipids
Total_P	Total concentration of lipoprotein particles	mmol/l	Lipoprotein particle concentrations
VLDL_P	Concentration of VLDL particles	mmol/l	Lipoprotein particle concentrations
LDL_P	Concentration of LDL particles	mmol/l	Lipoprotein particle concentrations
HDL_P	Concentration of HDL particles	mmol/l	Lipoprotein particle concentrations
VLDL_size	Average diameter for VLDL particles	nm	Lipoprotein particle sizes
LDL_size	Average diameter for LDL particles	nm	Lipoprotein particle sizes
HDL_size	Average diameter for HDL particles	nm	Lipoprotein particle sizes
Phosphoglyc	Phosphoglycerides	mmol/l	Other lipids
TG_by_PG	Ratio of triglycerides to phosphoglycerides	ratio	Other lipids
Cholines	Total cholines	mmol/l	Other lipids
Phosphatidylc	Phosphatidylcholines	mmol/l	Other lipids
Sphingomyelins	Sphingomyelins	mmol/l	Other lipids
ApoB	Apolipoprotein B	g/l	Apolipoproteins

ApoA1	Apolipoprotein A1	g/l	Apolipoproteins
ApoB_by_ApoA1	Ratio of apolipoprotein B to apolipoprotein A1	ratio	Apolipoproteins
Total_FA	Total fatty acids	mmol/l	Fatty acids
Unsaturation	Degree of unsaturation	degree	Fatty acids
Omega_3_pct	Ratio of omega-3 fatty acids to total fatty acids	%	Fatty acids
Omega_6_pct	Ratio of omega-6 fatty acids to total fatty acids	%	Fatty acids
PUFA_pct	Ratio of polyunsaturated fatty acids to total fatty acids	%	Fatty acids
MUFA_pct	Ratio of monounsaturated fatty acids to total fatty acids	%	Fatty acids
SFA_pct	Ratio of saturated fatty acids to total fatty acids	%	Fatty acids
LA_pct	Ratio of linoleic acid to total fatty acids	%	Fatty acids
DHA_pct	Ratio of docosahexaenoic acid to total fatty acids	%	Fatty acids
PUFA_by_MUFA	Ratio of polyunsaturated fatty acids to monounsaturated fatty acids	ratio	Fatty acids
Omega_6_by_Omega_3	Ratio of omega-6 fatty acids to omega-3 fatty acids	ratio	Fatty acids
Ala	Alanine	mmol/l	Amino acids
Gln	Glutamine	mmol/l	Amino acids
Gly	Glycine	mmol/l	Amino acids
His	Histidine	mmol/l	Amino acids
Total_BCAA	Total concentration of branched-chain amino acids (leucine + isoleucine + valine)	mmol/l	Amino acids
Ile	Isoleucine	mmol/l	Amino acids
Leu	Leucine	mmol/l	Amino acids
Val	Valine	mmol/l	Amino acids
Phe	Phenylalanine	mmol/l	Amino acids
Tyr	Tyrosine	mmol/l	Amino acids
Glucose	Glucose	mmol/l	Glycolysis related metabolites
Lactate	Lactate	mmol/l	Glycolysis related metabolites
Pyruvate	Pyruvate	mmol/l	Glycolysis related metabolites
Citrate	Citrate	mmol/l	Glycolysis related metabolites
Glycerol	Glycerol	mmol/l	Glycolysis related metabolites
bOHbutyrate	3-Hydroxybutyrate	mmol/l	Ketone bodies
Acetate	Acetate	mmol/l	Ketone bodies
Acetoacetate	Acetoacetate	mmol/l	Ketone bodies
Acetone	Acetone	mmol/l	Ketone bodies
Creatinine	Creatinine	μmol/l	Fluid balance
Albumin	Albumin	g/l	Fluid balance
GlycA	Glycoprotein acetyls	mmol/l	Inflammation
XXL_VLDL_P	Concentration of chylomicrons and extremely large VLDL particles	mmol/l	Lipoprotein subclasses
XXL_VLDL_L	Total lipids in chylomicrons and extremely large VLDL	mmol/l	Lipoprotein subclasses
XXL_VLDL_PL	Phospholipids in chylomicrons and extremely large VLDL	mmol/l	Lipoprotein subclasses
XXL_VLDL_C	Cholesterol in chylomicrons and extremely large VLDL	mmol/l	Lipoprotein subclasses
XXL_VLDL_CE	Cholesteryl esters in chylomicrons and extremely large VLDL	mmol/l	Lipoprotein subclasses

XXL_VLDL_FC	Free cholesterol in chylomicrons and extremely large VLDL	mmol/l	Lipoprotein subclasses
XXL_VLDL_TG	Triglycerides in chylomicrons and extremely large VLDL	mmol/l	Lipoprotein subclasses
XL_VLDL_P	Concentration of very large VLDL particles	mmol/l	Lipoprotein subclasses
XL_VLDL_L	Total lipids in very large VLDL	mmol/l	Lipoprotein subclasses
XL_VLDL_PL	Phospholipids in very large VLDL	mmol/l	Lipoprotein subclasses
XL_VLDL_C	Cholesterol in very large VLDL	mmol/l	Lipoprotein subclasses
XL_VLDL_CE	Cholesteryl esters in very large VLDL	mmol/l	Lipoprotein subclasses
XL_VLDL_FC	Free cholesterol in very large VLDL	mmol/l	Lipoprotein subclasses
XL_VLDL_TG	Triglycerides in very large VLDL	mmol/l	Lipoprotein subclasses
L_VLDL_P	Concentration of large VLDL particles	mmol/l	Lipoprotein subclasses
L_VLDL_L	Total lipids in large VLDL	mmol/l	Lipoprotein subclasses
L_VLDL_PL	Phospholipids in large VLDL	mmol/l	Lipoprotein subclasses
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L_VLDL_FC	Free cholesterol in large VLDL	mmol/l	Lipoprotein subclasses
L_VLDL_TG	Triglycerides in large VLDL	mmol/l	Lipoprotein subclasses
M_VLDL_P	Concentration of medium VLDL particles	mmol/l	Lipoprotein subclasses
M_VLDL_L	Total lipids in medium VLDL	mmol/l	Lipoprotein subclasses
M_VLDL_PL	Phospholipids in medium VLDL	mmol/l	Lipoprotein subclasses
M_VLDL_C	Cholesterol in medium VLDL	mmol/l	Lipoprotein subclasses
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M_VLDL_FC	Free cholesterol in medium VLDL	mmol/l	Lipoprotein subclasses
M_VLDL_TG	Triglycerides in medium VLDL	mmol/l	Lipoprotein subclasses
S_VLDL_P	Concentration of small VLDL particles	mmol/l	Lipoprotein subclasses
S_VLDL_L	Total lipids in small VLDL	mmol/l	Lipoprotein subclasses
S_VLDL_PL	Phospholipids in small VLDL	mmol/l	Lipoprotein subclasses
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IDL_P	Concentration of IDL particles	mmol/l	Lipoprotein subclasses
IDL_L	Total lipids in IDL	mmol/l	Lipoprotein subclasses
IDL_PL	Phospholipids in IDL	mmol/l	Lipoprotein subclasses
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L_LDL_P	Concentration of large LDL particles	mmol/l	Lipoprotein subclasses
L_LDL_L	Total lipids in large LDL	mmol/l	Lipoprotein subclasses
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S_HDL_CE	Cholesteryl esters in small HDL	mmol/l	Lipoprotein subclasses
S_HDL_FC	Free cholesterol in small HDL	mmol/l	Lipoprotein subclasses
S_HDL_TG	Triglycerides in small HDL	mmol/l	Lipoprotein subclasses

Stable 2. Circulating microRNA modules from WGCNA.

Black	Blue	Brown	Green	Green-yellow	Grey	Magenta	Pink	Purple	Red	Turquoise	Yellow
hsa-let-7a-5p	hsa-let-7d-5p	hsa-miR-11400	hsa-let-7d-3p	hsa-miR-483-3p	hsa-miR-10527-5p	hsa-miR-122-5p	hsa-miR-101-3p	hsa-miR-126-3p	hsa-miR-132-3p	hsa-let-7c-5p	hsa-miR-125b-5p
hsa-let-7b-5p	hsa-let-7g-5p	hsa-miR-134-5p	hsa-miR-128-3p	hsa-miR-365a-3p	hsa-miR-106b-3p	hsa-miR-148a-3p	hsa-miR-182-5p	hsa-miR-148b-3p	hsa-miR-181a-5p	hsa-let-7e-5p	hsa-miR-126-5p
hsa-let-7f-5p	hsa-let-7i-3p	hsa-miR-139-3p	hsa-miR-1306-5p	hsa-miR-365b-3p	hsa-miR-1277-3p	hsa-miR-192-5p	hsa-miR-183-5p	hsa-miR-151a-3p	hsa-miR-181b-5p	hsa-miR-103a-3p	hsa-miR-1277-5p
hsa-let-7i-5p	hsa-miR-106a-5p	hsa-miR-146a-5p	hsa-miR-150-5p	hsa-let-7b-3p	hsa-miR-1294	hsa-miR-193a-5p	hsa-miR-25-3p	hsa-miR-181a-2-3p	hsa-miR-181c-5p	hsa-miR-10a-5p	hsa-miR-142-5p
hsa-miR-142-3p	hsa-miR-106b-5p	hsa-miR-221-5p	hsa-miR-191-5p	hsa-miR-885-5p	hsa-miR-1299	hsa-miR-193b-5p	hsa-miR-4732-3p	hsa-miR-28-3p	hsa-miR-1908-5p	hsa-miR-10b-5p	hsa-miR-144-5p
hsa-miR-181d-5p	hsa-miR-107	hsa-miR-337-5p	hsa-miR-199b-5p		hsa-miR-1307-5p	hsa-miR-194-5p	hsa-miR-532-5p	hsa-miR-99b-5p	hsa-miR-204-5p	hsa-miR-125a-5p	hsa-miR-200a-3p
hsa-miR-200c-3p	hsa-miR-1180-3p	hsa-miR-370-3p	hsa-miR-223-3p		hsa-miR-1-3p	hsa-miR-34a-5p	hsa-miR-660-5p		hsa-miR-205-5p	hsa-miR-1301-3p	hsa-miR-21-5p
hsa-miR-28-5p	hsa-miR-1255b-5p	hsa-miR-381-3p	hsa-miR-30b-5p		hsa-miR-141-3p	hsa-miR-483-5p	hsa-miR-7-5p		hsa-miR-22-5p	hsa-miR-1304-3p	hsa-miR-27a-3p
hsa-miR-423-5p	hsa-miR-130b-3p	hsa-miR-382-5p	hsa-miR-331-3p		hsa-miR-146b-3p	hsa-miR-885-3p	hsa-miR-93-5p		hsa-miR-320b	hsa-miR-1307-3p	hsa-miR-27b-3p
hsa-miR-454-3p	hsa-miR-140-3p	hsa-miR-409-3p	hsa-miR-335-5p		hsa-miR-150-3p				hsa-miR-324-3p	hsa-miR-130a-3p	hsa-miR-29a-3p
hsa-miR-98-5p	hsa-miR-144-3p	hsa-miR-432-5p	hsa-miR-339-3p		hsa-miR-17-3p				hsa-miR-335-3p	hsa-miR-140-5p	hsa-miR-29c-3p
	hsa-miR-145-5p	hsa-miR-485-5p	hsa-miR-339-5p		hsa-miR-190a-5p				hsa-miR-423-3p	hsa-miR-143-3p	hsa-miR-30a-3p
	hsa-miR-15a-5p	hsa-miR-493-5p	hsa-miR-361-3p		hsa-miR-190b-5p				hsa-miR-425-5p	hsa-miR-146b-5p	hsa-miR-30a-5p
	hsa-miR-15b-3p	hsa-miR-5187-5p	hsa-miR-424-5p		hsa-miR-196a-5p				hsa-miR-548e-3p	hsa-miR-151a-5p	hsa-miR-30e-3p
	hsa-miR-15b-5p	hsa-miR-127-3p	hsa-miR-505-5p		hsa-miR-196b-5p				hsa-miR-100-5p	hsa-miR-152-3p	hsa-miR-30e-5p
	hsa-miR-16-5p	hsa-miR-323b-3p	hsa-miR-574-3p		hsa-miR-200b-3p				hsa-miR-148a-5p	hsa-miR-155-5p	hsa-miR-338-3p
	hsa-miR-17-5p	hsa-miR-369-3p	hsa-miR-500a-3p		hsa-miR-206					hsa-miR-181a-3p	hsa-miR-340-5p
	hsa-miR-185-5p	hsa-miR-369-5p			hsa-miR-215-5p					hsa-miR-185-3p	hsa-miR-374a-5p
	hsa-miR-186-5p	hsa-miR-379-5p			hsa-miR-2355-3p					hsa-miR-195-5p	hsa-miR-378a-3p
	hsa-miR-18a-3p	hsa-miR-411-5p			hsa-miR-26b-3p					hsa-miR-197-3p	hsa-miR-590-3p
	hsa-miR-18a-5p	hsa-miR-431-5p			hsa-miR-29c-5p					hsa-miR-199a-3p	hsa-miR-95-3p
	hsa-miR-19a-3p	hsa-miR-485-3p			hsa-miR-3065-5p					hsa-miR-199a-5p	hsa-miR-99a-5p
	hsa-miR-19b-3p	hsa-miR-654-3p			hsa-miR-340-3p					hsa-miR-199b-3p	hsa-miR-582-3p
	hsa-miR-20a-5p	hsa-miR-136-3p			hsa-miR-374a-3p					hsa-miR-221-3p	
	hsa-miR-20b-5p	hsa-miR-323a-3p			hsa-miR-378c					hsa-miR-223-5p	
	hsa-miR-2110	hsa-miR-493-3p			hsa-miR-3960					hsa-miR-224-5p	
	hsa-miR-222-3p	hsa-miR-136-5p			hsa-miR-429					hsa-miR-23a-3p	
	hsa-miR-22-3p	hsa-miR-376a-3p			hsa-miR-4446-3p					hsa-miR-23b-3p	
	hsa-miR-26b-5p	hsa-miR-889-3p			hsa-miR-497-5p					hsa-miR-24-3p	
	hsa-miR-29b-3p	hsa-miR-376b-3p			hsa-miR-542-3p					hsa-miR-26a-1-3p	

[illegible]

STable 3. Lasso Cox regression included cmiRs (modules pink and purple).

hsa.miR.101.3p	hsa.miR.182.5p	hsa.miR.183.5p	hsa.miR.25.3p
hsa.miR.4732.3p	hsa.miR.532.5p	hsa.miR.660.5p	hsa.miR.7.5p
hsa.miR.93.5p	hsa.miR.126.3p	hsa.miR.148b.3p	hsa.miR.151a.3p
hsa.miR.181a.2.3p	hsa.miR.28.3p	hsa.miR.99b.5p	

STable 4. Lasso Cox regression included metabolites.

Total_C	VLDL_C	LDL_C	HDL_C	Total_TG	VLDL_TG	HDL_TG	LDL_TG
Total_PL	VLDL_PL	HDL_PL	LDL_PL	VLDL_CE	HDL_CE	LDL_CE	Total_FC
VLDL_FC	HDL_FC	LDL_FC	VLDL_P	HDL_P	LDL_P	VLDL_size	HDL_size
LDL_size	Phosphoglyc	Cholines	Phosphatidylc	Sphingomyelins	ApoB	ApoA1	Omega_3_pct
Omega_6_pct	PUFA_pct	MUFA_pct	SFA_pct	LA_pct	DHA_pct	Ala	Gln
Gly	His	Ile	Leu	Phe	Tyr	Glucose	Pyruvate
Acetate	Acetoacetate	Acetone	Creatinine	Albumin	GlycA	Citrate	bOHbutyrate
Val	S_HDL_P	S_HDL_PL	S_HDL_C	S_HDL_CE	S_HDL_FC	S_HDL_TG	

STable 5. CmiR WGCNA module mean difference within gene variants using Tukey's multiple comparisons. The upper value indicates the difference and the value below the significance (adj.p-value).

Module eigengene (ME)	MSH2-MLH1	MSH6-MLH1	MSH2-MSH6
MEpink	0.01016988 (0.9143948)	0.03770672 (0.2795425)	0.02753684 (0.6687522)
MEpurple	0.00624331 (0.9661112)	-0.04618971 (0.1440606)	-0.05243302 (0.2299122)
MEmagenta	0.034624722 (0.3686426)	-0.007218965 (0.9548694)	-0.041843687 (0.4072116)
MEyellow	0.015130891 (0.8269541)	0.005036238 (0.9780570)	-0.010094653 (0.9491772)
MEblue	0.031329825 (0.4415067)	0.022469887 (0.6412003)	-0.008859939 (0.9601601)
MEgreen	0.04099181 (0.2404544)	-0.01505006 0.8144737	-0.05604187 0.1948082
MEgreenyellow	0.050041333 (0.1232450)	-0.005433753 (0.9737021)	-0.055475085 0.2031136
MEblack	-0.008662855 (0.9395274)	0.009985939 (0.9165389)	0.018648794 (0.8371829)
MEbrown	-0.021201668 (0.6836205)	0.001516794 (0.9979447)	0.022718462 (0.7639468)
MEred	2.207994e-02 (0.6678631)	-8.028222e-05 (0.9999944)	-2.216022e-02 (0.7781561)
MEturquoise	0.01972570 (0.7203488)	-0.00798402 (0.9448624)	-0.02770972 (0.6715545)

STable 6. Circulating metabolite modules from WGCNA.

Blue	Brown	Green	Grey	Red	Turquoise	Yellow
Total_TG	LDL_size	Total_PL	Gln	Unsaturation	non_HDL_C	HDL_C
VLDL_TG	HDL_size	Total_P	Gly	Omega_3_pct	Remnant_C	HDL_PL
LDL_TG	XL_HDL_P	Phosphoglyc	His	Omega_6_pct	VLDL_C	HDL_CE
HDL_TG	XL_HDL_L	Cholines	Phe	PUFA_pct	Clinical_LDL_C	HDL_FC
VLDL_PL	XL_HDL_PL	Phosphatidylc	Tyr	LA_pct	LDL_C	HDL_L
VLDL_FC	XL_HDL_C	S_HDL_P	Glucose	DHA_pct	LDL_PL	HDL_P
VLDL_L	XL_HDL_CE	S_HDL_L	Pyruvate	PUFA_by_MUFA	Total_CE	ApoA1
VLDL_size	XL_HDL_FC	S_HDL_PL	Acetate		VLDL_CE	L_HDL_TG
TG_by_PG	L_HDL_P	S_HDL_C	Acetoacetate		LDL_CE	M_HDL_P
MUFA_pct	L_HDL_L	S_HDL_CE	Acetone		Total_FC	M_HDL_L
SFA_pct	L_HDL_PL	S_HDL_FC	Creatinine		LDL_FC	M_HDL_PL
Ala	L_HDL_C		Albumin		Total_L	M_HDL_C
Ile	L_HDL_CE		Citrate		LDL_L	M_HDL_CE
Leu	L_HDL_FC		Omega_6_by_Omega_3		VLDL_P	M_HDL_FC
GlycA			bOHbutyrate		LDL_P	
XXL_VLDL_L					Sphingomyelins	
XXL_VLDL_PL					ApoB	
XXL_VLDL_C					ApoB_by_ApoA1	
XXL_VLDL_CE					Total_FA	
XXL_VLDL_FC					M_VLDL_P	
XL_VLDL_L					M_VLDL_L	
XL_VLDL_PL					M_VLDL_PL	
XL_VLDL_C					M_VLDL_C	
XL_VLDL_CE					M_VLDL_CE	
XL_VLDL_FC					M_VLDL_FC	
XL_VLDL_TG					S_VLDL_PL	
L_VLDL_P					S_VLDL_C	
L_VLDL_L					S_VLDL_CE	
L_VLDL_PL					S_VLDL_FC	
L_VLDL_C					XS_VLDL_P	
L_VLDL_CE					XS_VLDL_L	
L_VLDL_FC					XS_VLDL_PL	
L_VLDL_TG					XS_VLDL_C	
M_VLDL_TG					XS_VLDL_CE	
S_VLDL_P					XS_VLDL_FC	
S_VLDL_L					IDL_P	
S_VLDL_TG					IDL_L	
XS_VLDL_TG					IDL_PL	
IDL_TG					IDL_C	
L_LDL_TG					IDL_CE	
M_LDL_TG					IDL_FC	
S_LDL_TG					L_LDL_P	
XL_HDL_TG					L_LDL_L	
M_HDL_TG					L_LDL_PL	
S_HDL_TG					L_LDL_C	
Total_BCAA					L_LDL_CE	
Val					L_LDL_FC	
XXL_VLDL_TG					M_LDL_P	
XL_VLDL_P					M_LDL_L	
					M_LDL_PL	
					M_LDL_C	
					M_LDL_CE	
					M_LDL_FC	
					S_LDL_P	
					S_LDL_L	
					S_LDL_PL	
					S_LDL_C	
					S_LDL_CE	
					S_LDL_FC	
					Total_C	