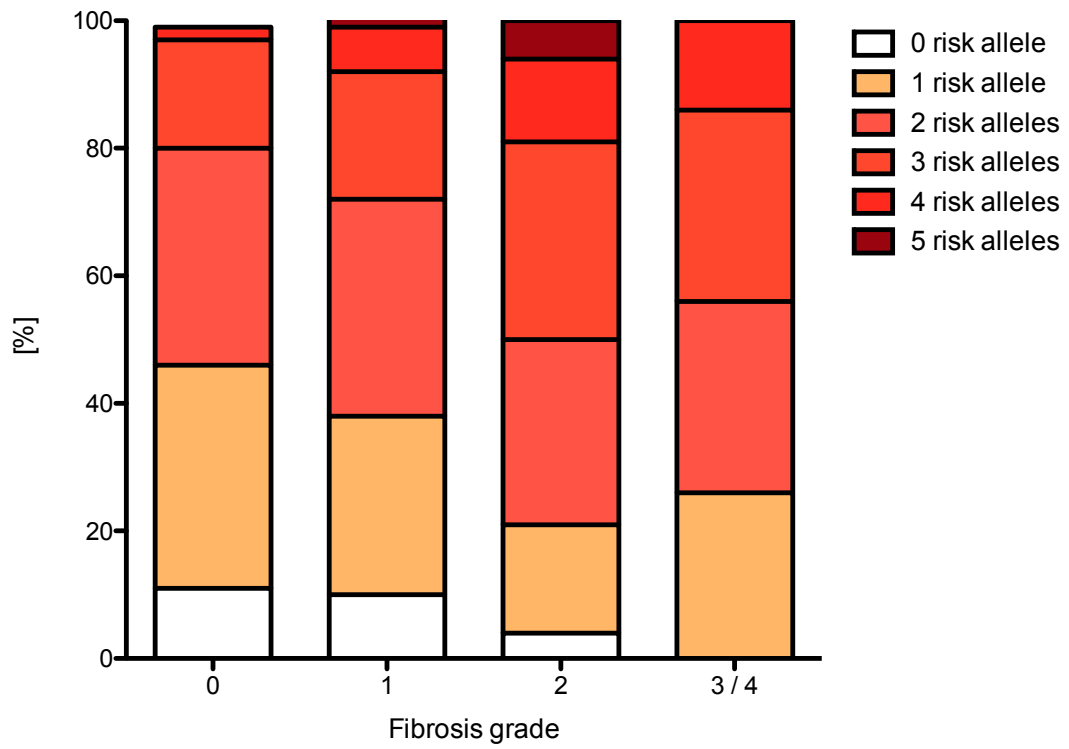


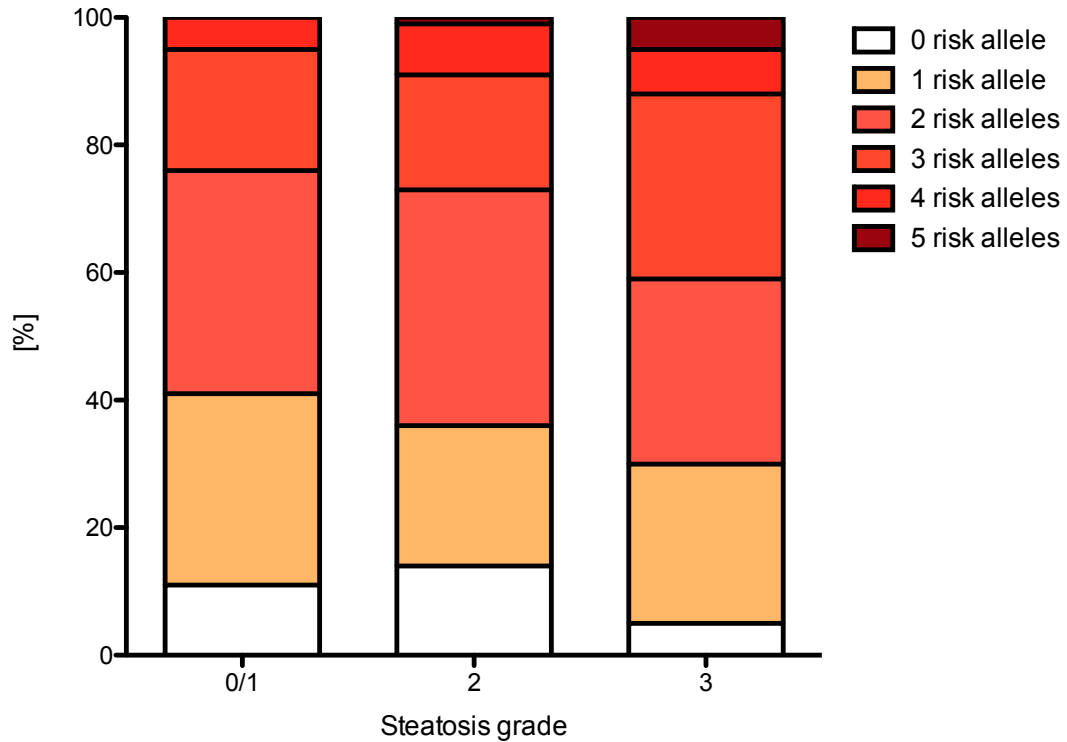
Supplementary Figure S1

Relation between the number of *PNPLA3*, *TM6SF2* and *MBOAT7* risk alleles and fibrosis



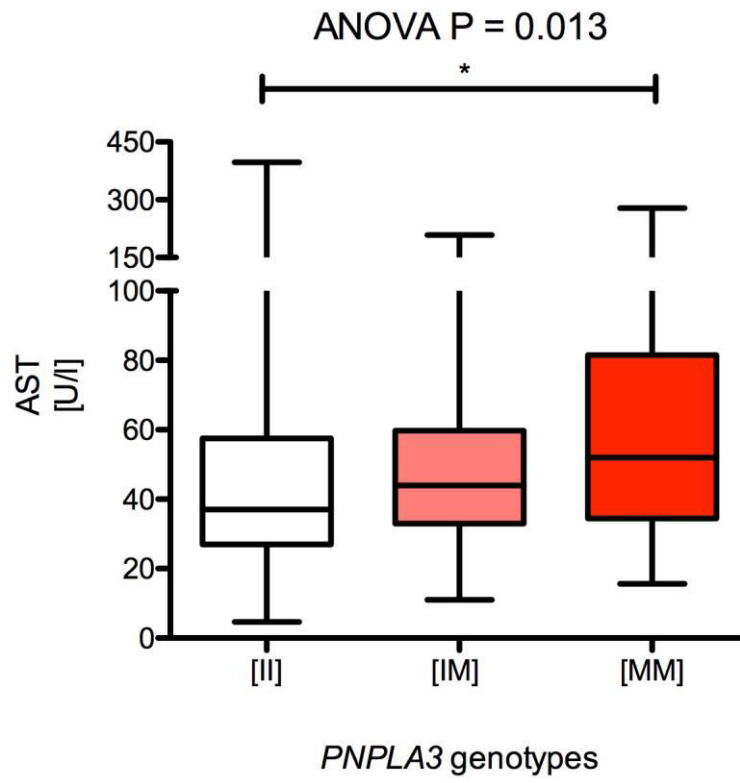
Supplementary Figure S2

Relation between the number of *PNPLA3*, *TM6SF2* and *MBOAT7* risk alleles and steatosis



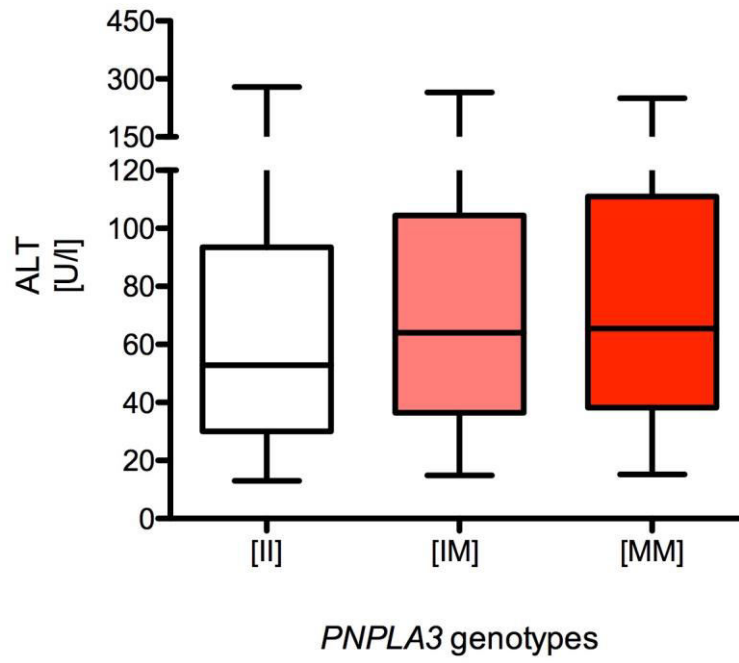
Supplementary Figures 1 and 2: Combined analysis of the *PNPLA3* p.I148M, *TM6SF2* p.E167K and *MBOAT7* rs641738 risk alleles on liver fibrosis and steatosis in biopsied patients. Following frequencies of carriers of risk alleles were detected: 0 risk allele n=33, 1 risk allele n = 86, 2 risk alleles n = 109, 3 risk alleles n = 69, 4 risk alleles n = 20, 5 risk alleles n = 3.

Supplementary Figure S3A



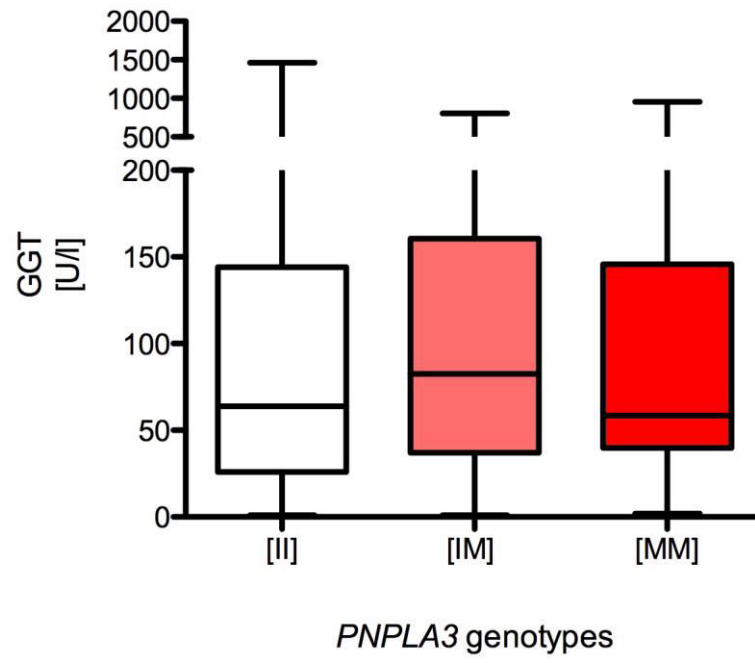
Supplementary Figure S3B

ANOVA P = 0.17



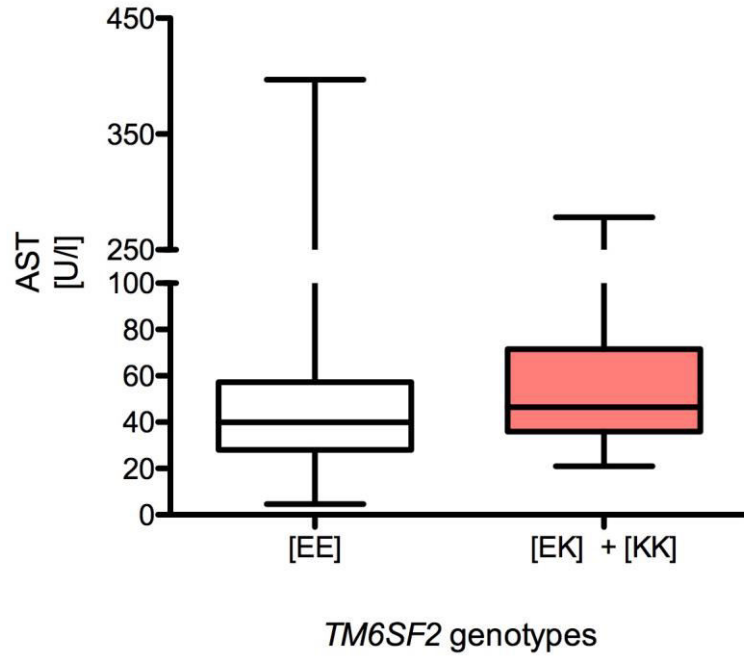
Supplementary Figure S3C

ANOVA P = 0.32

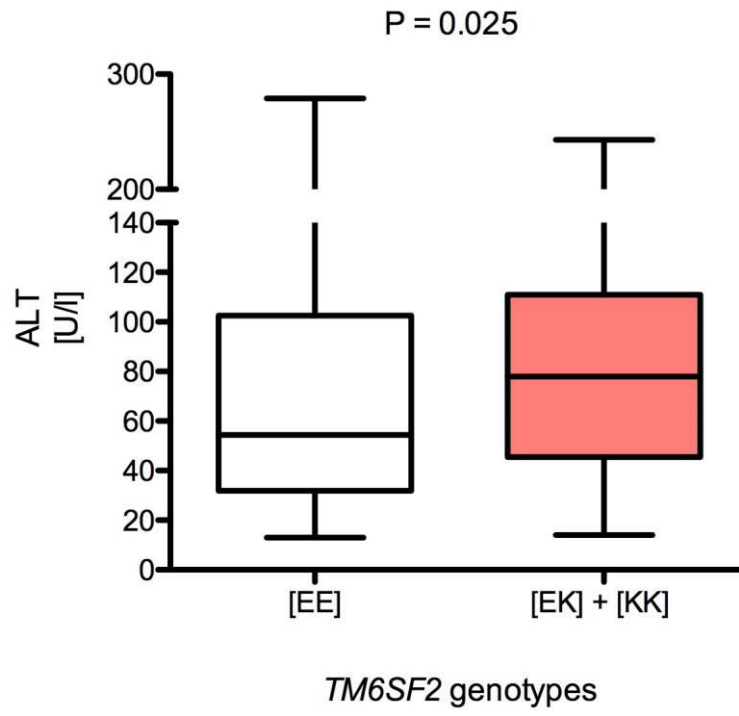


Supplementary Figure S3D

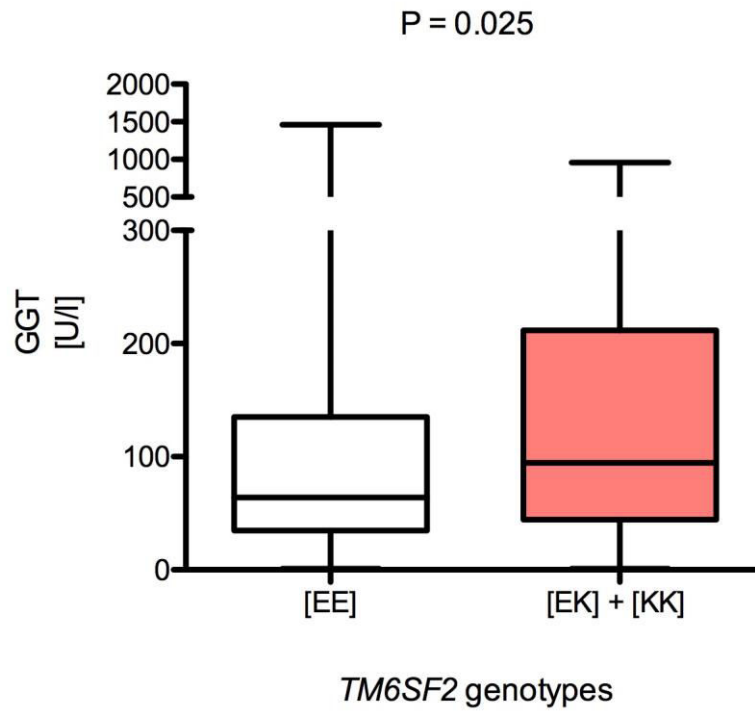
P = 0.005



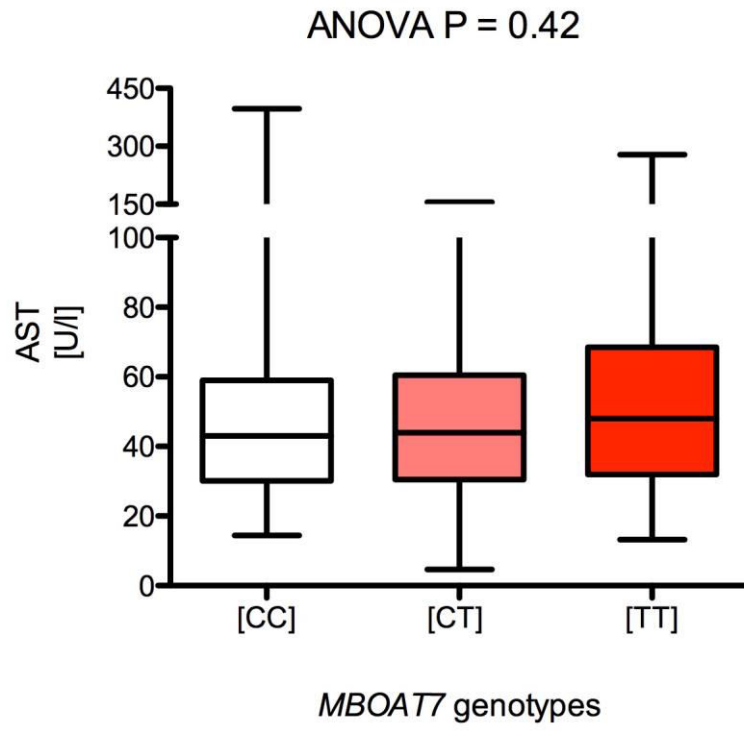
Supplementary Figure S3E



Supplementary Figure S3F

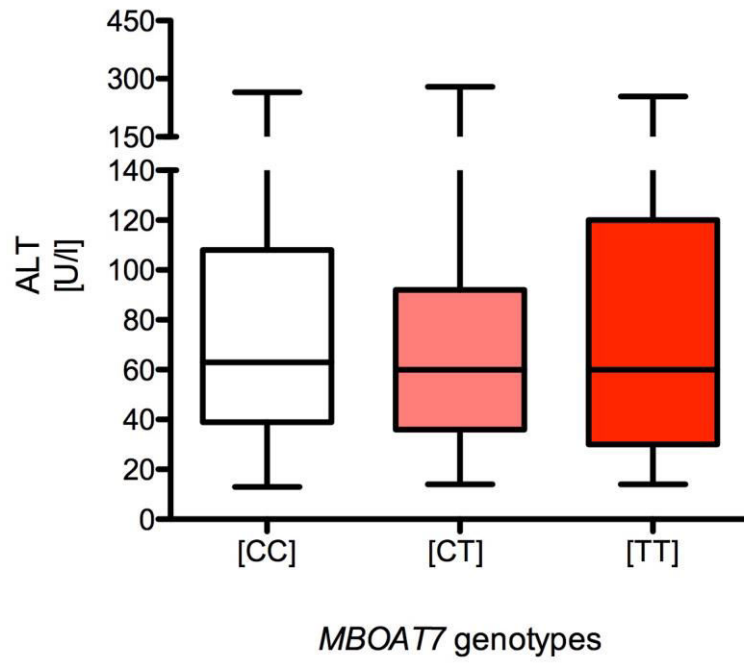


Supplementary Figure S3G

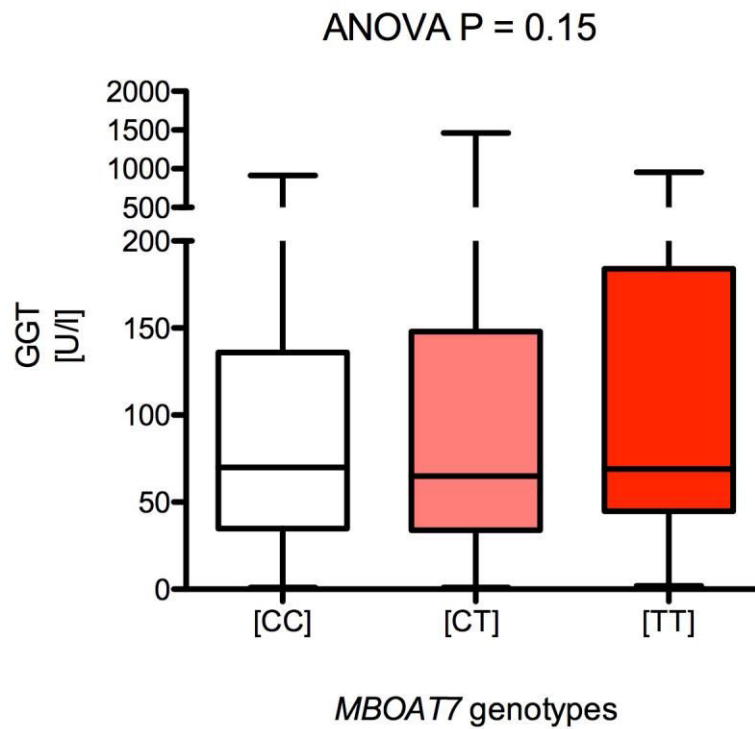


Supplementary Figure S3H

ANOVA P = 0.61



Supplementary Figure S3I



Supplementary Figures 3A-3I. Box-and-Whisker plots illustrating liver function tests in carriers of distinct *PNPLA3*, *TM6SF2* and *MBOAT7* variants – analysis restricted to patients scheduled for liver biopsy (n = 320). All tests were performed using ANOVA with post-hoc tests or with Mann-Whitney U, as appropriate.. *P<0.05 in post-hoc tests.

Supplementary Table S1

Patient baseline characteristics related to the *PNPLA3* p.I148M genotypes

Feature	<i>PNPLA3</i> p.I148M			P-value
	[II] (n = 215)	[IM] (n = 222)	[MM] (n = 78)	
Sex (% of females)	61%	49%	51%	0.04
Age (years)	50.0 (16.0 – 82.0)	50.0 (19.0 – 88.0)	48.0 (19.0 – 78.0)	0.58
BMI (kg/m ²)	36.0 (22.0 – 70.0)	32.0 (18.6 – 69.8)	30.0 (17.7 – 67.8)	<0.01
Glucose (mg/dl)	98.0 (70.0 – 286.0)	98.0 (55.0 – 367.0)	97.0 (63.0–340.0)	0.10
Total cholesterol (mg/dl)	2040 (107.0–379.0)	203.0 (72.0-356.0)	205.0 (116.0–306.0)	0.34
Triglycerides (mg/dl)	145.0 (78.0 – 429.0)	156.0 (60.0 – 531.0)	139.0 (58.0 – 770.0)	0.33

Abbreviations: BMI, body mass index; isoleucine; M, methionine; p, protein (amino acid number); *PNPLA3*, adiponutrin. Values are given as medians and ranges. Continuous variables were compared using linear regression, categorical variables were compared with logistic regression. Models were adjusted for gender, age, BMI and statin use, as appropriate. Genetic analyses were calculated by using an additive model.

Supplementary Table S2

Patient baseline characteristics related to the *TM6SF2* p.E167K genotypes

Feature	<i>TM6SF2</i> p.E167K genotype		P-value
	[EE] (n = 410)	[EK] + [KK] (n = 106)	
Sex (% of females)	54%	53%	0.82
Age (years)	49.0 (16.0 – 87.0)	51.0 (18.0 – 88.0)	0.57
BMI (kg/m ²)	34.1 (17.7 – 69.9)	29.9 (18.7 – 70.0)	0.01
Glucose (mg/dl)	105.0 (70.0 – 221.0)	103.0 (89.0–169.0)	0.55
Total cholesterol (mg/dl)	206.0 (72.0 – 379.0)	198.0 (87.0 – 360.0)	0.14
Triglycerides (mg/dl)	150.0 (45.0 – 752.0)	155.5 (49.0 – 770.0)	0.22

Abbreviations: BMI, body mass index; E, glutamic acid; K, lysine; p, protein (amino acid number); *TM6SF2*, transmembrane 6 superfamily member 2. Values are given as medians and ranges. Continuous variables were compared using linear regression, categorical variables were compared with logistic regression. Models were adjusted for gender, age, BMI and statin use, as appropriate. Genetic analyses were calculated by using an additive model.

Supplementary Table S3

Patient baseline characteristics related to the *MBOAT7* rs641738 genotypes

Feature	<i>MBOAT7</i> rs641738			P-value
	[CC] (n = 159)	[CT] (n = 242)	[TT] (n = 114)	
Sex (% of females)	54.7%	55.7%	50.8%	0.64
Age (years)	49.0 (20.0 – 88.0)	50.0 (16.0 – 87.0)	49.0 (18.0 – 82.0)	0.63
BMI (kg/m ²)	32.0 (22.0 – 69.0)	32.5 (22.0 – 69.0)	32.5 (17.0 – 70.0)	0.60
Glucose (mg/dl)	101.0 (71.0 – 228.0)	97.0 (55.0 – 367.0)	98.0 (70.0 – 286.0)	0.20
Total cholesterol (mg/dl)	203.0 (107.0–335.0)	205.0 (72.0 – 360.0)	205.0 (114.0 – 379.0)	0.89
Triglycerides (mg/dl)	154.0 (55.0 – 752.0)	144.0 (45.0 – 770.0)	160.0 (66.0 – 416.0)	0.36

Abbreviations: BMI, body mass index; *MBOAT7*, membrane bound O-acyltransferase domain containing 7. Values are given as medians and ranges. Continuous variables were compared using linear regression, categorical variables were compared with logistic regression. Models were adjusted for gender, age, BMI and statin use, as appropriate. Genetic analyses were calculated by using an additive model.