

SUPPLEMENTAL INFORMATION TO:

Hepatic molecular signatures of statin treatment are associated with impaired glucose homeostasis in severely obese patients

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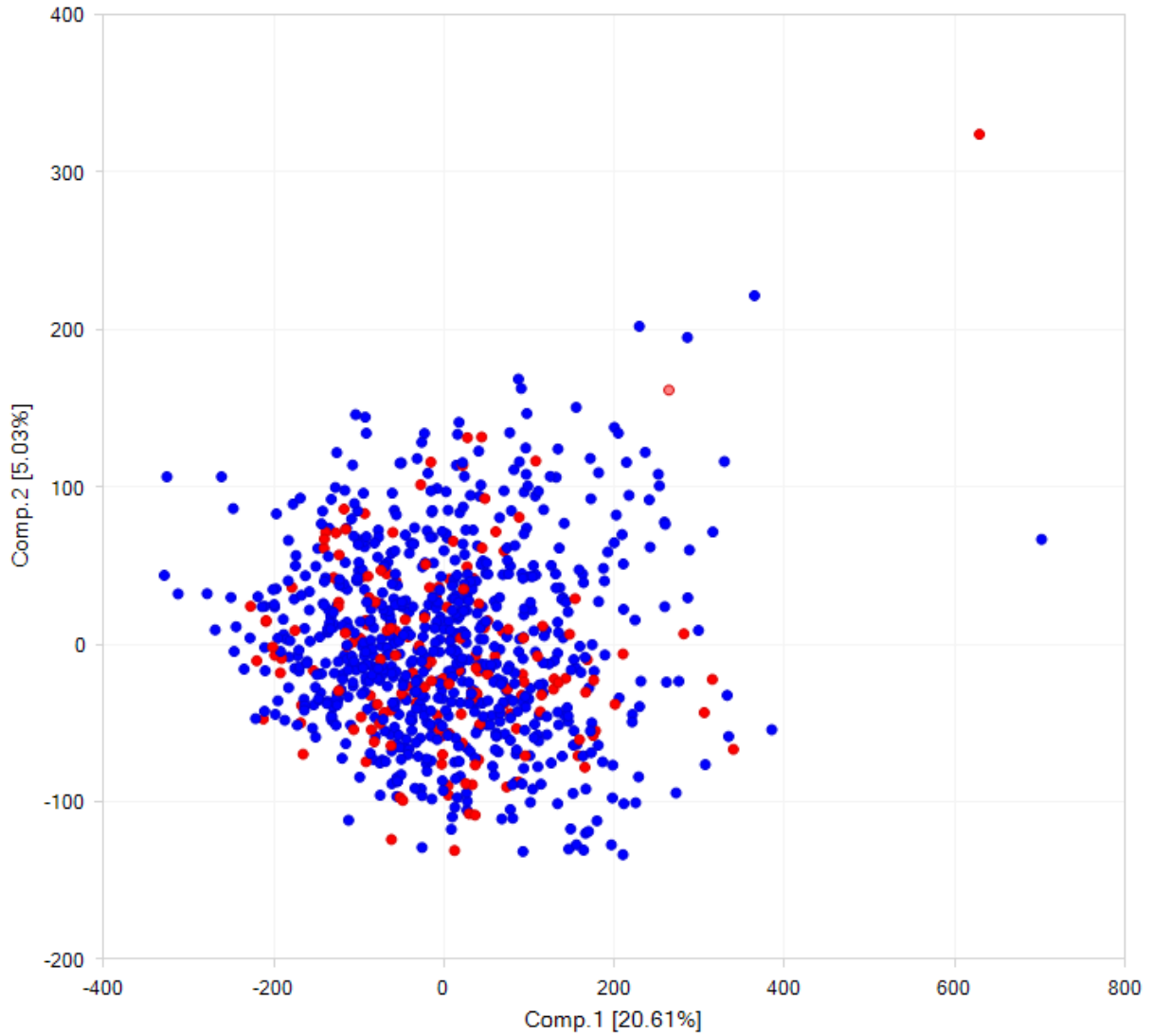
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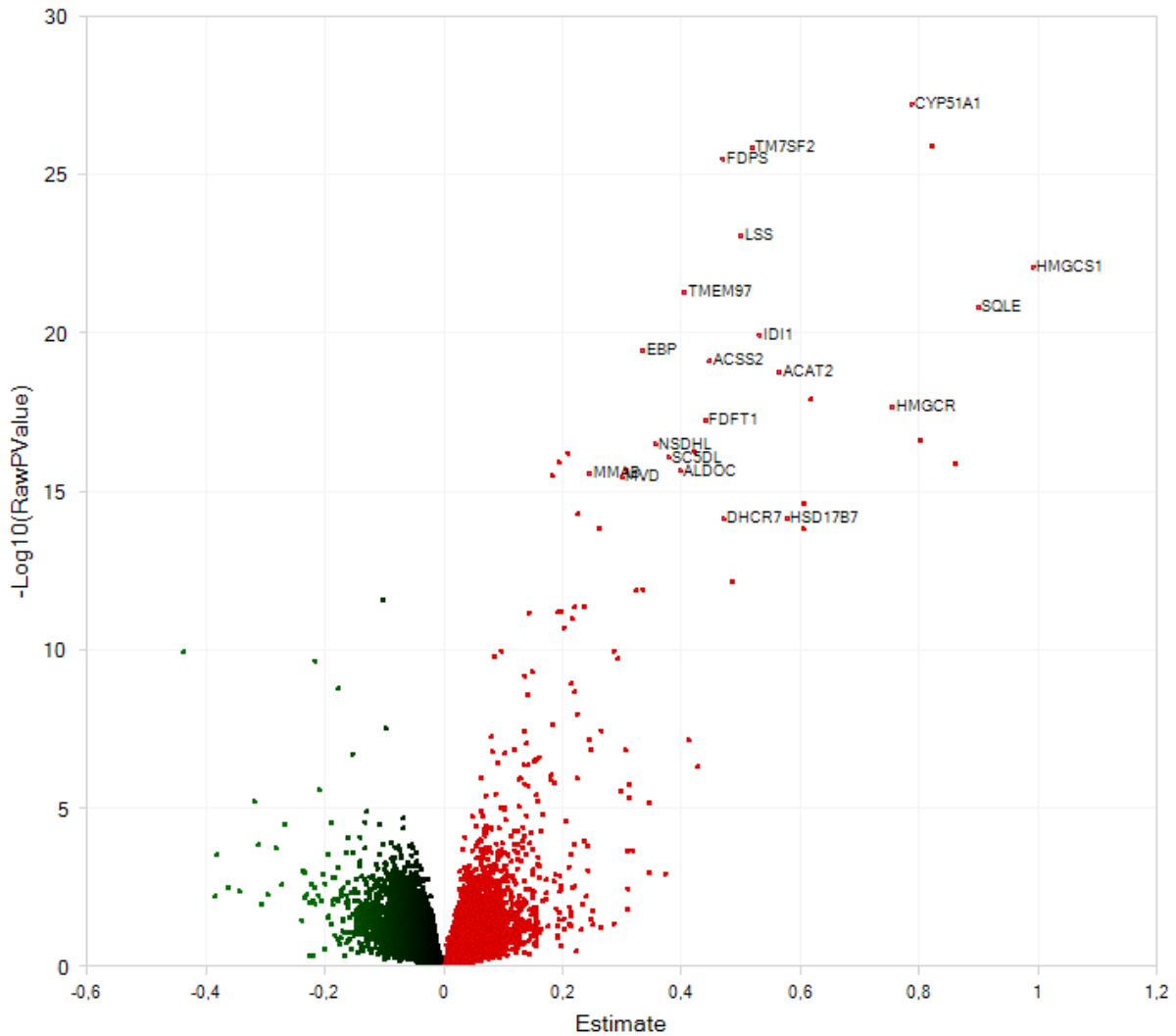
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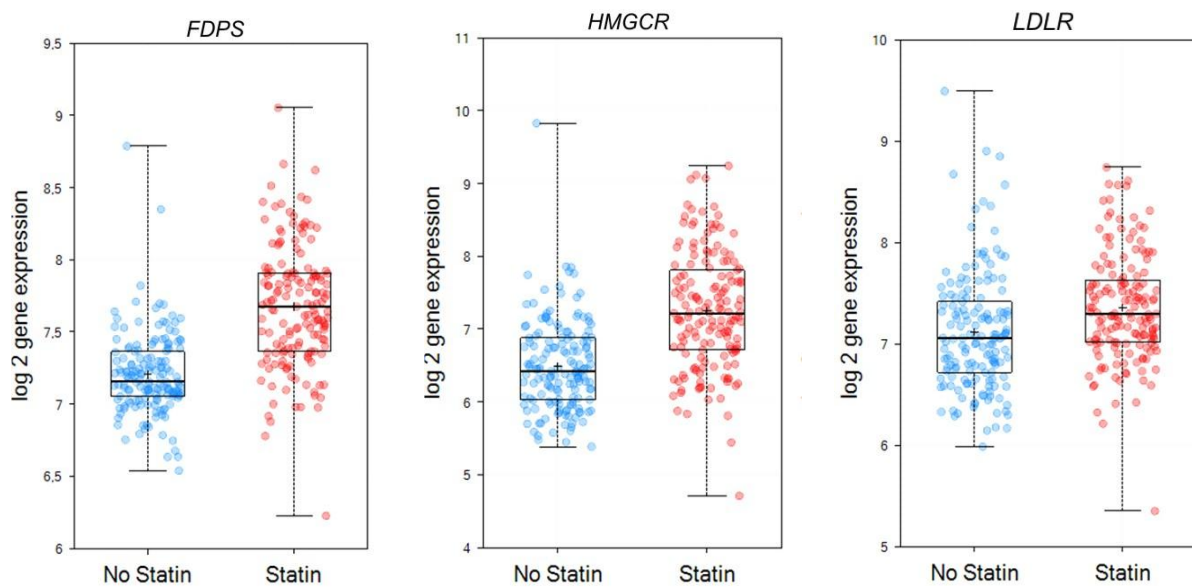
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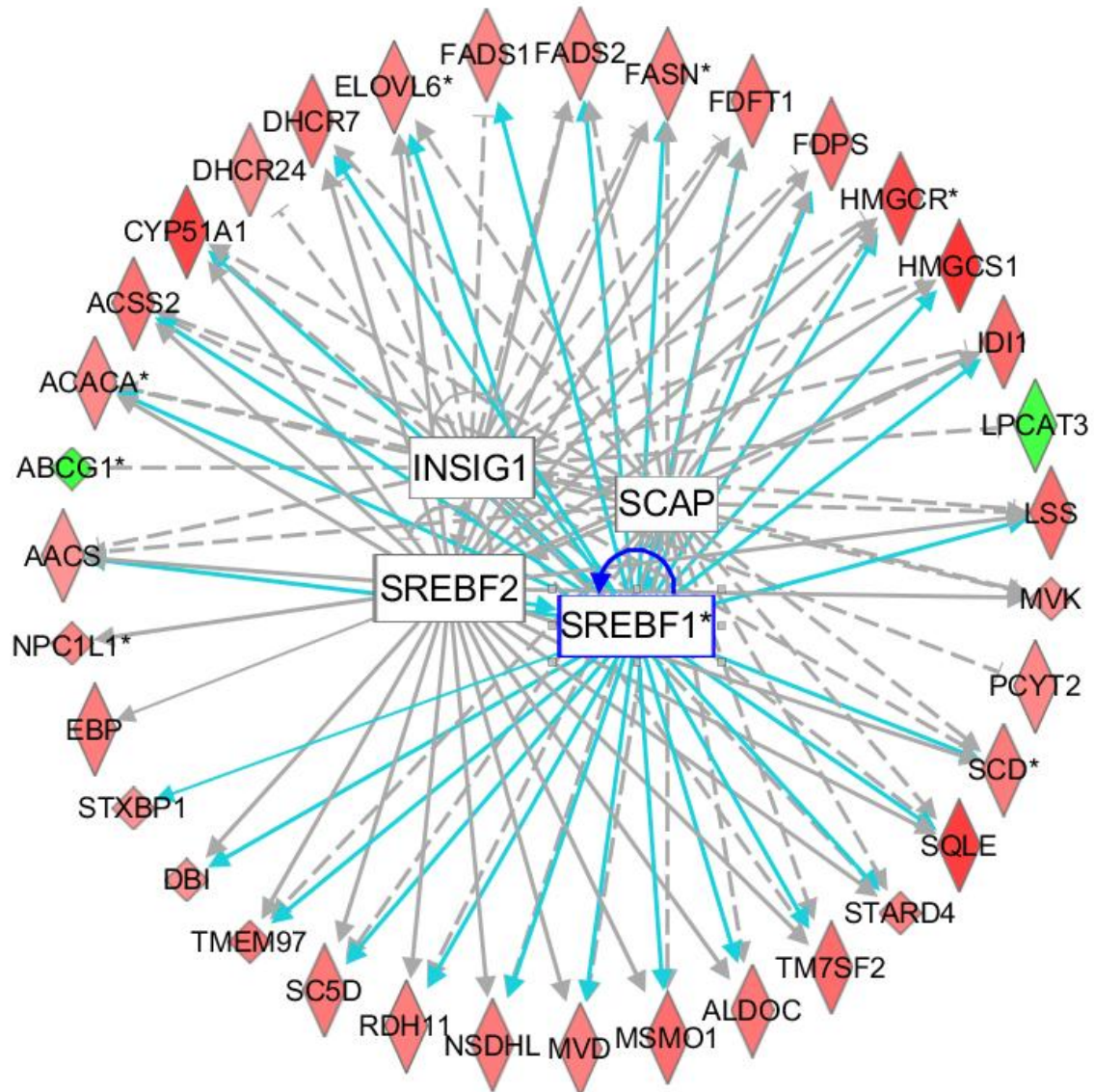
Supplemental Figure 1: *Principal component analysis (PCA) from 910 liver biopsies.* The PCA is based on all 70,523 transcript IDs from the Affymetrix Human Transcriptome Array (HTA) 2.0. Data points marked in red represent liver samples from statin-treated patients (n=173), data points marked in blue represent samples from non-statin treated patients (n=737).



Supplemental Figure 2: Differential gene expression in the propensity score-matched cohort. The volcano-plot is based on the pairwise comparison of statin-treated (n=157) vs non-statin-treated (n=157) patients of the matched patient cohort and shows the minus (-) \log_{10} adjusted P value on the Y-axis vs the fold-change estimate on the X-axis. The estimate is defined as the statistically adjusted difference between the means of the two compared groups (ANOVA). Top 20 differentially expressed genes with adjusted P values < 0.05 and \log_2 fold-changes (FC) ≥ 1.2 are indicated (more details about these genes are given in Supplemental Table 2). Differentially expressed genes in green: downregulated by statins, red: upregulated by statins.



Supplemental Figure 3: Gene expression values of representative genes. Boxplots with \log_2 gene expression values of key metabolic genes in liver samples from the matched patient cohort are shown according to statin treatment. Genes are farnesyl-diphosphate synthase (*FDPS*: $\log_2\text{FC}=1.7$, $P=4.3\times 10^{-23}$), 3-hydroxy-3-methylglutaryl-CoA reductase (*HMGCR*: $\log_2\text{FC}=1.7$, $P=1.1\times 10^{-14}$) and low density lipoprotein receptor (*LDLR*: $\log_2\text{FC}=1.2$, $P=2.0\times 10^{-04}$). Liver samples from statin-treated group are marked red ($n=157$) and liver samples from the non-statin treated group are marked blue ($n=157$). Abbreviations: FC:fold change.



Supplemental Figure 4: Gene network in statin-treated patients. The network illustrates statin-induced transcriptional upregulation (red) and downregulation (green) of 39 genes involved in cholesterol (e.g. *HMGCR*, *HMGCS1*, *SQLE*), fatty acid and triglyceride metabolism (e.g. *ACACA*, *FASN*, *SCD*) in the matched patient cohort, mediated by the predicted inhibition of *INSIG1*, activation of *SCAP* and subsequent activation of *SREBP1* and *SREBP2*, encoded by the *SREBF1* and *SREBF2* genes. Lipid genes activated by *SREBP1* are highlighted by interactions marked in blue. Genes marked with * are linked to hepatic steatosis according to literature findings reported by IPA.

Characteristics	Before Propensity Score-Matching*			After Propensity Score-Matching*		
	Statin group (n=173)	Non-statin group (n=737)	AS D, (%)	Statin group (n=157)	Non-statin group (n=157)	AS D, (%)
Age† [yr]	52.1 ± 7.4	39.2 ± 11.1	136.1	51.4 ± 7.3	51.2 ± 8.3	2.6
Females†	96 (55.5)	562 (76.3)	44.9	90 (57.5)	96 (61.6)	8.2
Diabetic father†	41 (23.4)	170 (23.1)	0.7	37 (23.4)	36 (23.1)	0.8
Diabetic mother†	67 (38.7)	223 (30.2)	18.0	57 (36.7)	62 (39.9)	6.6
Body mass index†* [kg/m ²]	46.1 ± 7.2	46.9 ± 9.0	9.7	46.2 ± 7.0	46.7 ± 9.2	6.3
Waist circumference† [cm]	134.8 ± 16.0	129.2 ± 18.3	32.2	134.3 ± 15.1	134.9 ± 20.2	4.3
Systolic BP† [mmHg]	137.4 ± 18.0	135.6 ± 18.8	10.0	138.0 ± 18.4	137.7 ± 22.6	2.2
Diastolic BP† [mmHg]	76.0 ± 12.9	76.4 ± 14.5	2.7	76.7 ± 13.1	76.1 ± 16.8	4.6
Fasting plasma insulin [mUI/L]	17.7 (11.0 to 31.6)	13.8 (9.0 to 19.8)	42.0	18.4 (11.1 to 31.5)	15.5 (10.0 to 24.9)	22.6
Fasting plasma C-peptide [ng/ml]	4.0 (3.0 to 5.3)	3.8 (3.0 to 4.8)	12.7	4.1 (3.1 to 5.4)	4.1 (3.2 to 5.4)	2.6
2 hour plasma insulin [mUI/L]	50.9 (28.4 to 103.2)	58.0 (29.9 to 99.9)	2.3	51.6 (27.9 to 99.4)	59.8 (33.1 to 104.7)	5.5
2 hour plasma C-peptide [ng/ml]	9.2 (6.3 to 12.7)	10.5 (7.6 to 13.0)	24.4	9.4 (6.4 to 12.9)	10.6 (7.6 to 13.0)	19.6
HOMA2-B	99.5(59.7 to 148.8)	120.2 (88.2 to 165.4)	27.0	101.8 (61.2 to 151.1)	108.4 (77.2 to 153.7)	9.0
HOMA2-IR	2.9 (1.8 to 4.9)	2.1 (1.4 to 3.0)	49.5	2.9 (1.8 to 4.8)	2.4 (1.6 to 4.0)	25.7
Hypertension	163 (94.2)	565 (76.7)	51.3	146 (93.6)	147 (94.0)	1.8
Patients on anti-hypertensive drugs†	142 (82.1)	244 (33.1)	114.1	125 (80.1)	127 (81.6)	4.0
Total cholesterol [mmol/L]	4.6 ± 1.1	5.0 ± 0.9	35.5	4.6 ± 1.1	5.1 ± 1.1	43.0
LDL cholesterol [mmol/L]	2.6 ± 0.9	3.1 ± 0.8	56.9	2.6 ± 1.0	3.1 ± 0.9	50.8
HDL cholesterol [mmol/L]	1.1 ± 0.3	1.2 ± 0.3	17.9	1.1 ± 0.3	1.2 ± 0.3	26.0
Triglycerides [mmol/L]	2.0 ± 1.1	1.6 ± 1.5	30.4	2.0 ± 1.2	1.9 ± 2.5	11.9

Supplemental Table 1: Patient characteristics in the statin and non-statin treatment groups before and after propensity score-matching. Values expressed as numbers (%), mean ± SD or median (IQR) as appropriate. * calculated after handling missing data using multiple imputation procedure. † factors included in the propensity score.

Abbreviations: ASD=absolute standardized difference, BP=blood pressure, HOMA2-B=homeostasis model assessment assessing β -cell function, HOMA2-IR=homeostasis model assessment assessing insulin resistance, HDL=high density lipoprotein, LDL=low density lipoprotein, IQR=interquartile range, SD=standard deviation.

Affymetrix Transcript ID	log ₂ FC	Adjusted P value	Gene Symbol	Pearson correlation HbA1c	P value	Pearson correlation HOMA2-IR	P value
TC01001299.hg.1	1.73	4.26E-23	<i>FDPS*</i>	2.50E-01	7.64E-06	8.00E-02	2.15E-01
TC07003361.hg.1	1.77	3.49E-22	<i>CYP51A1</i>	1.92E-01	6.00E-04	9.84E-02	1.27E-01
TC11003460.hg.1	1.39	5.92E-22	<i>TM7SF2*</i>	2.64E-01	2.09E-06	1.38E-01	3.20E-02
TC21000554.hg.1	1.41	1.25E-19	<i>LSS*</i>	2.30E-01	3.97E-05	1.58E-02	8.07E-01
TC05001316.hg.1	1.99	9.70E-19	<i>HMGCS1</i>	2.80E-01	4.58E-07	1.54E-01	1.64E-02
TC17000319.hg.1	1.32	5.43E-18	<i>TMEM97</i>	2.40E-01	1.83E-05	3.88E-02	5.48E-01
TC08000729.hg.1	1.87	1.34E-17	<i>SQLE*</i>	2.96E-01	9.93E-08	1.42E-01	2.69E-02
TC10000967.hg.1	1.45	9.22E-17	<i>IDI1</i>	2.50E-01	7.90E-06	8.25E-02	2.01E-01
TC0X000253.hg.1	1.26	2.61E-16	<i>EBP</i>	1.93E-01	6.00E-04	8.32E-02	1.97E-01
TC20000245.hg.1	1.36	5.06E-16	<i>ACSS2</i>	2.53E-01	5.77E-06	5.18E-02	4.22E-01
TC06003166.hg.1	1.54	6.95E-15	<i>ACAT2</i>	1.44E-01	1.06E-02	1.97E-02	7.61E-01
TC05000363.hg.1	1.69	1.11E-14	<i>HMGCR*</i>	2.51E-01	6.98E-06	7.56E-02	2.42E-01
TC08000093.hg.1	1.36	2.78E-14	<i>FDFT1</i>	2.65E-01	1.93E-06	7.45E-02	2.48E-01
TC0X000743.hg.1	1.28	1.39E-13	<i>NSDHL</i>	2.72E-01	1.00E-06	1.53E-01	1.73E-02
TC14001324.hg.1	1.34	2.16E-13	<i>ERG28</i>	2.08E-01	2.00E-04	3.14E-02	6.27E-01
TC17002830.hg.1	1.16	2.39E-13	<i>PCYT2</i>	2.20E-01	8.97E-05	-7.15E-02	2.68E-01
TC11001106.hg.1	1.30	3.13E-13	<i>SC5D</i>	1.74E-01	2.00E-03	2.70E-02	6.76E-01
TC07000627.hg.1	1.14	4.25E-13	<i>PCOLCE</i>	1.77E-01	1.70E-03	-4.40E-02	4.96E-01
TC17001301.hg.1	1.32	6.86E-13	<i>ALDOC</i>	2.26E-01	5.57E-05	-1.85E-02	7.74E-01
TC16001340.hg.1	1.23	9.62E-13	<i>MVD</i>	2.80E-01	4.95E-07	9.78E-02	1.29E-01
TC10000256.hg.1	1.52	6.40E-12	<i>HSD17B7P2</i>	3.04E-01	4.18E-08	9.72E-02	1.32E-01
TC22000347.hg.1	1.17	1.31E-11	<i>SREBF2</i>	2.44E-01	1.31E-05	4.22E-02	5.13E-01
TC11002038.hg.1	1.39	1.73E-11	<i>DHCR7</i>	2.09E-01	2.00E-04	1.24E-01	5.33E-02
TC01001426.hg.1	1.49	1.73E-11	<i>HSD17B7</i>	2.95E-01	1.10E-07	8.10E-02	2.09E-01
TC12003078.hg.1	1.20	3.31E-11	<i>MMAB</i>	2.41E-01	1.69E-05	-2.90E-02	6.53E-01
TC04000828.hg.1	1.40	1.53E-09	<i>MSMO1</i>	1.83E-01	1.10E-03	4.88E-02	4.50E-01
TC14002328.hg.1	1.25	2.70E-09	<i>RDH11</i>	1.36E-01	1.62E-02	1.42E-01	2.77E-02
TC11003438.hg.1	1.18	8.01E-09	<i>FADS1</i>	2.03E-01	3.00E-04	4.61E-02	4.76E-01
TC10000581.hg.1	1.15	1.07E-08	<i>FAM213A</i>	1.17E-01	3.90E-02	1.09E-01	9.18E-02
TC0X001506.hg.1	1.14	1.12E-08	<i>CETN2</i>	1.95E-01	5.00E-04	1.55E-01	1.58E-02
TC14000604.hg.1	1.10	1.16E-08	<i>AK7</i>	2.11E-01	2.00E-04	6.08E-02	3.46E-01
TC06004142.hg.1	1.16	1.76E-08	<i>SOD2</i>	9.06E-02	1.10E-01	7.40E-03	9.09E-01
TC16000523.hg.1	1.15	3.33E-08	<i>PDP2</i>	1.42E-01	1.20E-02	8.50E-03	8.96E-01
TC06000083.hg.1	1.07	1.72E-07	<i>TMEM170B</i>	5.35E-02	3.45E-01	-4.75E-02	4.62E-01
TC06001182.hg.1	-1.35	1.80E-07	<i>UNC93A</i>	-1.01E-01	7.44E-02	6.46E-02	3.17E-01
TC07001334.hg.1	1.06	2.55E-07	<i>POLD2</i>	1.78E-01	1.60E-03	-3.00E-02	6.43E-01
TC05001673.hg.1	1.23	2.77E-07	<i>STARD4</i>	1.75E-01	1.90E-03	6.55E-02	3.10E-01
TC21000200.hg.1	-1.16	3.26E-07	<i>ABCG1</i>	-1.81E-01	1.30E-03	-1.48E-01	2.09E-02
TC16001701.hg.1	1.11	7.13E-07	<i>SNAI3-AS1</i>	1.73E-01	2.10E-03	-4.60E-02	4.77E-01
TC12000849.hg.1	1.10	9.23E-07	<i>MVK</i>	3.55E-01	9.45E-11	1.29E-01	4.48E-02
TC11000367.hg.1	1.16	1.58E-06	<i>HSD17B12</i>	4.69E-02	4.08E-01	2.85E-02	6.59E-01
TC19001502.hg.1	1.17	2.82E-06	<i>CAPN12</i>	2.88E-01	2.07E-07	1.37E-01	3.29E-02
TC01000874.hg.1	1.17	1.36E-05	<i>LOC729970</i>	1.41E-01	1.23E-02	1.30E-01	4.29E-02
TC17001406.hg.1	1.13	2.85E-05	<i>ACACA*</i>	1.99E-01	4.00E-04	1.33E-01	3.87E-02
TC07001184.hg.1	-1.07	3.66E-05	<i>CDCA7L</i>	-2.13E-01	1.00E-04	-1.79E-01	5.20E-03
TC04001467.hg.1	1.20	4.25E-05	<i>ELOVL6*</i>	1.15E-01	4.26E-02	-1.45E-02	8.22E-01
TC04002196.hg.1	1.10	4.29E-05	<i>LOC100507487</i>	1.40E-01	1.30E-02	1.10E-01	8.82E-02
TC0X002327.hg.1	1.06	6.53E-05	<i>PIR</i>	2.25E-01	5.87E-05	8.71E-02	1.77E-01
TC11000542.hg.1	1.19	7.89E-05	<i>FADS2*</i>	1.85E-01	1.00E-03	6.64E-02	3.03E-01
TC06003966.hg.1	1.10	9.90E-05	<i>SOD2-OT1</i>	2.02E-02	7.22E-01	-8.80E-03	8.92E-01

TC17001192.hg.1	-1.11	2.00E-04	<i>SREBF1</i>	-9.50E-03	8.67E-01	-1.04E-01	1.05E-01
TC11003444.hg.1	1.06	2.00E-04	<i>DNHD1</i>	1.17E-01	3.87E-02	-6.87E-02	2.87E-01
TC01003229.hg.1	1.07	2.00E-04	<i>TDRKH</i>	1.89E-01	8.00E-04	1.27E-01	4.86E-02
TC11003443.hg.1	1.09	2.00E-04	<i>TIMM10B</i>	1.20E-01	3.43E-02	-7.60E-03	9.06E-01
TC07001342.hg.1	1.19	2.00E-04	<i>NPC1L1</i>	2.36E-01	2.55E-05	3.74E-02	5.63E-01
TC19000191.hg.1	1.18	2.00E-04	<i>LDLR</i>	2.50E-01	7.65E-06	2.80E-03	9.66E-01
TC01003314.hg.1	1.07	3.00E-04	<i>RUSC1-AS1</i>	1.84E-01	1.00E-03	6.04E-02	3.50E-01
TC06002088.hg.1	1.11	3.00E-04	<i>ECHDC1</i>	1.07E-01	5.98E-02	-7.40E-03	9.09E-01
TC16000569.hg.1	1.11	3.00E-04	<i>CYB5B</i>	1.02E-01	7.21E-02	4.68E-02	4.69E-01
TC01000129.hg.1	1.10	4.00E-04	<i>PGD</i>	1.62E-01	4.00E-03	1.26E-01	5.05E-02
TC21000940.hg.1	1.13	8.00E-04	<i>KCNE1</i>	1.10E-01	5.29E-02	-4.62E-02	4.75E-01
TC14000454.hg.1	1.05	1.00E-03	<i>BBOF1</i>	2.06E-01	2.00E-04	-4.49E-02	4.87E-01
TC16002069.hg.1	1.09	1.00E-03	<i>QPRT</i>	7.06E-02	2.13E-01	8.48E-02	1.88E-01
TC05001674.hg.1	1.10	1.40E-03	<i>NREP</i>	-5.48E-02	3.34E-01	-9.80E-02	1.29E-01
TC06001692.hg.1	1.10	1.60E-03	<i>GLO1</i>	-3.40E-03	9.53E-01	7.20E-03	9.12E-01
TC01003565.hg.1	-1.16	2.20E-03	<i>ANGPTL1</i>	-4.93E-02	3.85E-01	-2.73E-01	1.64E-05
TC17001973.hg.1	1.23	2.40E-03	<i>FASN*</i>	2.62E-01	2.55E-06	1.32E-01	4.00E-02
TC15000305.hg.1	1.06	2.80E-03	<i>OIP5-AS1</i>	-3.19E-02	5.74E-01	-7.20E-02	2.65E-01
TC02000751.hg.1	1.05	3.00E-03	<i>DBI</i>	-4.00E-02	4.81E-01	-4.73E-02	4.64E-01
TC19001505.hg.1	1.24	3.70E-03	<i>LGALS4</i>	3.06E-01	3.19E-08	2.93E-01	3.63E-06
TC08001556.hg.1	-1.25	4.70E-03	<i>ENPP2</i>	-7.49E-02	1.86E-01	-4.76E-02	4.61E-01
TC10000721.hg.1	1.27	4.80E-03	<i>SCD*</i>	2.26E-01	5.42E-05	4.90E-02	4.48E-01
TC01004184.hg.1	1.07	7.90E-03	<i>NPPA-AS1</i>	2.06E-01	2.00E-04	-1.54E-01	1.69E-02
TC08000169.hg.1	1.04	8.70E-03	<i>PIWIL2</i>	1.28E-01	2.33E-02	-5.84E-02	3.65E-01
TC0X001092.hg.1	1.05	1.19E-02	<i>ARHGEF9</i>	-5.53E-02	3.30E-01	-7.74E-02	2.31E-01
TC11003435.hg.1	1.03	1.21E-02	<i>SERGEF</i>	1.40E-01	1.29E-02	-6.73E-02	2.97E-01
TC05001996.hg.1	-1.05	1.38E-02	<i>RNF145</i>	-9.57E-02	9.08E-02	1.31E-01	4.23E-02
TC03002549.hg.1	1.07	1.50E-02	<i>NUDT16</i>	-1.05E-01	6.30E-02	-7.06E-02	2.74E-01
TC03003123.hg.1	1.15	1.72E-02	<i>PCOLCE2</i>	-1.38E-01	1.49E-02	-1.06E-01	1.01E-01
TC01003847.hg.1	-1.14	1.89E-02	<i>DUSP10</i>	-6.60E-03	9.07E-01	-3.04E-01	1.48E-06
TC02000280.hg.1	-1.08	2.03E-02	<i>PRKCE</i>	6.80E-03	9.04E-01	2.45E-01	1.00E-04
TC01002307.hg.1	-1.20	2.12E-02	<i>PLA2G2A</i>	-1.69E-02	7.66E-01	-8.70E-03	8.93E-01
TC03000773.hg.1	1.05	2.16E-02	<i>PAQR9-AS1</i>	-6.60E-03	9.07E-01	1.22E-02	8.50E-01
TC12001003.hg.1	1.04	2.30E-02	<i>AACS</i>	2.42E-01	1.49E-05	1.89E-01	3.20E-03
TC05002041.hg.1	1.10	2.47E-02	<i>PANK3</i>	1.05E-01	6.29E-02	-1.95E-02	7.63E-01
TC17002528.hg.1	1.06	2.49E-02	<i>SHMT1</i>	4.25E-02	4.54E-01	6.05E-02	3.48E-01
TC17002142.hg.1	-1.05	2.55E-02	<i>SLC13A2</i>	-5.20E-03	9.27E-01	-5.67E-02	3.80E-01
TC01001781.hg.1	1.07	2.59E-02	<i>FLVCR1</i>	2.58E-01	3.62E-06	9.61E-02	1.36E-01
TC21000257.hg.1	1.06	2.61E-02	<i>MCM3AP-AS1</i>	1.95E-01	5.00E-04	8.28E-02	1.99E-01
TC03001466.hg.1	1.05	2.68E-02	<i>TKT</i>	2.82E-01	3.93E-07	8.78E-02	1.73E-01
TC14000401.hg.1	1.09	2.88E-02	<i>GPHN</i>	-4.25E-02	4.53E-01	-1.16E-01	7.18E-02
TC11003343.hg.1	1.05	3.28E-02	<i>TIMM8B</i>	9.14E-02	1.07E-01	1.62E-01	1.16E-02
TC06001072.hg.1	1.11	3.43E-02	<i>SAMD5</i>	1.87E-02	7.42E-01	-1.16E-01	7.26E-02
TC09000668.hg.1	1.05	3.95E-02	<i>STXBP1</i>	3.02E-01	4.84E-08	1.03E-01	1.10E-01
TC01002694.hg.1	1.10	4.00E-02	<i>DHCR24</i>	5.00E-04	9.93E-01	-4.70E-03	9.42E-01
TC04000829.hg.1	-1.10	4.33E-02	<i>CPE</i>	7.90E-02	1.63E-01	9.38E-02	1.46E-01
TC10000010.hg.1	1.03	4.41E-02	<i>WDR37</i>	-1.10E-03	9.84E-01	-1.44E-01	2.52E-02
TC12001155.hg.1	-1.12	4.51E-02	<i>LPCAT3</i>	-3.54E-02	5.33E-01	-5.93E-02	3.59E-01

Supplemental Table 2A: Differentially expressed genes between statin and non-statin treated patient groups from the matched patient cohort with Pearson correlation parameters to HbA1c and HOMA2-IR. Genes were ranked according to the corrected p value. *selected genes for validation in quantitative polymerase chain reaction (qPCR) assays

(Supplemental Table 3). Abbreviations: FC=fold change. Red, bold characters: highest upregulated gene; green, bold characters: highest downregulated gene.

Affymetrix Transcript ID	Without adjustment for diabetes status		Gene Symbol	With adjustment for diabetes status	
	log ₂ FC	Adjusted P value		log ₂ FC	Adjusted P value
TC01001299.hg.1	1.73	4.26E-23	<i>FDPS</i>	1.70	7.77E-21
TC07003361.hg.1	1.77	3.49E-22	<i>CYP51A1</i>	1.38	8.93E-20
TC11003460.hg.1	1.39	5.92E-22	<i>TM7SF2</i>	1.41	1.42E-19
TC21000554.hg.1	1.41	1.25E-19	<i>LSS</i>	1.40	9.82E-18
TC05001316.hg.1	1.99	9.70E-19	<i>HMGCS1</i>	1.91	4.25E-16
TC17000319.hg.1	1.32	5.43E-18	<i>TMEM97</i>	1.31	9.45E-16
TC08000729.hg.1	1.87	1.34E-17	<i>SQLE</i>	1.79	6.77E-15
TC10000967.hg.1	1.45	9.22E-17	<i>IDI1</i>	1.41	1.63E-14
TC0X000253.hg.1	1.26	2.61E-16	<i>EBP</i>	1.26	1.15E-14
TC20000245.hg.1	1.36	5.06E-16	<i>ACSS2</i>	1.35	3.28E-14

Supplemental Table 2B: Top 10 differentially expressed genes between statin and non-statin treated patient groups from the matched patient cohort with and without adjustment for diabetes status. Genes were ranked according to the corrected p value. Abbreviations: FC=fold change. Red, bold characters: highest upregulated gene.

Affymetrix Transcript ID	Log ₂ FC (Affymetrix)	Adjusted P value (Affymetrix)	FC (qPCR)	P value (qPCR)	Gene Symbol
TC11003460.hg.1	1.4	5.94E-22	1.9	<0.0001	<i>TM7SF2</i> *
TC01001299.hg.1	1.7	4.26E-23	1.9	<0.0001	<i>FDPS</i> *
TC21000554.hg.1	1.4	1.25E-19	n.d.		<i>LSS</i> *
TC08000729.hg.1	1.9	1.34E-17	2.9	<0.0001	<i>SQLE</i> *
TC05000363.hg.1	1.7	1.11E-13	2.6	<0.0001	<i>HMGCR</i> *
TC04001467.hg.1	1.2	6.91E-09	1.6	<0.0001	<i>ELOVL6</i> **
TC11000542.hg.1	1.2	6.89E-05	1.0	n.s.	<i>FADS2</i> **
TC10000721.hg.1	1.3	4.80E-03	1.6	<0.0001	<i>SCD</i> **
TC17001406.hg.1	1.1	2.85E-05	1.1	n.s.	<i>ACACA</i> **
TC17001973.hg.1	1.2	2.40E-03	1.5	<0.05	<i>FASN</i> **

Supplemental Table 3: Q-PCR validation of 10 statin-regulated genes identified from the Affymetrix microarray analysis. Selected genes are part of cholesterologenic (SREBP2-regulated *) and lipogenic (SREBP1-regulated **) pathways and were measured in liver samples from statin-treated (n=40) and non-statin treated (n=40) patients. Abbreviations: FC=fold change, n.d.=not detectable, n.s.=not significant.

Pathway or Disease	# Genes	Statin-regulated genes (Gene Symbols)
Superpathway of cholesterol biosynthesis	19	ACAT2, CYP51A1, DHCR7, DHCR24, EBP, FDFT1, FDPS, HMGCR, HMGCS1, HSD17B7, IDI1, LSS, MSMO1, MVD, MVK, NSDHL, SC5D, SQLE, TM7SF2
Fatty acid metabolism	18	AACS, ABCG1, ACACA, ACSS2, DBI, ELOVL6, FADS1, FADS2, FASN, LSS, MSMO1, NPC1L1, PCOLCE2, PLA2G2A, SC5D, SCD, SREBF1, STARD4
LXR/RXR signaling	8	ABCG1, ACACA, CYP51A1, FASN, FDFT1, HMGCR, SCD, SREBF1
AMPK signaling	4	ACACA, AK7, FASN, HMGCR
Metabolic disease	31	AACS, ABCG1, ACACA, ACAT2, CPE, CYP51A1, DHCR7, DHCR24, EBP, FADS2, FASN, FDFT1, FDPS, GPHN, HMGCR, KCNE1, LSS, MMAB, MSMO1, MVK, NPC1L1, PLA2G2A, PRKCE, QPRT, SC5D, SCD, SLC13A2, SOD2, SREBF1, SREBF2, STXBP1
Type 2 diabetes mellitus	15	AACS, ABCG1, ACACA, FADS2, FASN, FDFT1, HMGCR, KCNE1, NPC1L1, PRKCE, QPRT, SCD, SOD2, SREBF1, SREBF2
Insulin resistance	10	ACACA, ACAT2, CPE, FASN, HMGCR, NPC1L1, PRKCE, QPRT, SCD, SREBF1

Supplemental Table 4: Pathway assignment to statin-dysregulated genes. The list of genes from Supplemental Table 2 were assigned to main metabolic and signaling pathways or disease processes using the Ingenuity Pathway Analysis (IPA). Abbreviations: LXR/RXR=liver X receptor/retinoid X receptor, AMPK=AMP-activated protein kinase.