

Supplementary Table 1. Multiple regression analysis for the association between the SLCO1B1 388A>G polymorphism and the lipid-lowering effects from 4 weeks of simvastatin treatment

Variable	388A>G	N	Change(%)		Unadjusted			Adjusted		
			Mean±SD		β	SE	P Value	β	SE	P Value
TC	GG	283	-31.1±8.8							
	AG	212	-31.7±9.5	-0.006	0.008	0.475		-0.006	0.008	0.444
	AA	47	-31.6±7.5	-0.003	0.007	0.712		-0.003	0.007	0.662
	GG+AG	495	-31.4±9.1							
LDL-C	AA	47	-31.6±7.5	-0.002	0.014	0.855		-0.003	0.014	0.804
	GG	283	-40.7±12.6							
	AG	212	-40.5±12.0	0.003	0.011	0.817		0.002	0.011	0.838
	AA	47	-39.5±14.3	0.006	0.01	0.546		0.007	0.01	0.52
TG	GG+AG	495	-40.6±12.3							
	AA	47	-39.5±14.3	0.011	0.019	0.561		0.011	0.019	0.564
	GG	283	-22.0±33.0							
	AG	212	-23.0±34.4	-0.011	0.031	0.723		-0.012	0.03	0.704
HDL-C	AA	47	-24.7±36.2	-0.014	0.026	0.608		-0.017	0.026	0.522
	GG+AG	495	-22.4±33.6							
	AA	47	-24.7±36.2	-0.022	0.052	0.665		-0.029	0.051	0.568
	GG	283	-8.9±16.9							
	AG	212	-11.3±15.8	-0.024	0.015	0.106		-0.023	0.015	0.123
	AA	47	-10.2±14.4	-0.007	0.013	0.617		-0.006	0.013	0.643
	GG+AG	495	-9.9±16.5							
	AA	47	-10.2±14.4	-0.003	0.025	0.913		-0.001	0.025	0.965

Adjusted for BMI, age, alcohol consumption and smoking.

Supplementary Table 2. Multiple regression analysis for the association between the SLCO1B1 521T>C polymorphism and the lipid-lowering effects from four weeks of simvastatin treatment

Variable	521T>C	N	Change(%)		Unadjusted			Adjusted		
			Mean±SD		β	SE	P Value	β	SE	P Value
TC	TT	425	-31.9±8.7							
	TC	113	-29.9±9.6	0.02	0.009	0.037		0.02	0.009	0.037
	CC	4	-21.6±12.2	0.051	0.022	0.019		0.052	0.022	0.018
	CC+TC	117	-29.6±9.7							
LDL-C	TT	425	-31.9±8.7	-0.022	0.009	0.016		-0.023	0.009	0.016
	TT	425	-41.2±12.4							
	TC	113	-38.3±12.7	0.029	0.013	0.03		0.029	0.013	0.026
	CC	4	-29.6±16.3	0.058	0.031	0.062		0.059	0.031	0.06
TG	CC+TC	117	-38.0±12.8							
	TT	425	-41.2±12.4	-0.032	0.013	0.015		-0.033	0.013	0.013
	TT	425	-22.8±33.9							
	TC	113	-22.2±33.4	0.006	0.036	0.864		0.004	0.036	0.907
HDL-C	CC	4	-9.7±40.0	0.066	0.085	0.442		0.056	0.085	0.507
	CC+TC	117	-21.8±33.5							
	TT	425	-22.8±33.9	-0.01	0.035	0.768		-0.008	0.035	0.828
	TT	425	-10.1±16.3							
	TC	113	-8.9±16.3	0.012	0.017	0.501		0.009	0.017	0.594
	CC	4	-19.2±13.9	-0.045	0.041	0.268		-0.054	0.04	0.181
	CC+TC	117	-9.3±16.3							
	TT	425	-10.1±16.3	-0.008	0.017	0.634		-0.005	0.017	0.752

Adjusted for BMI, age, alcohol consumption and smoking.

Supplementary Table 3. Multiple Regression analysis to analyze gene-gene joint associations with the lipid-lowering effects from four weeks of simvastatin treatment.

388A>G	521T>C	N	Change(%)		Unadjusted			Adjusted		
			Mean±SD	β	SE	P Value	β	SE	P Value	
TC										
GG+AG	CC+TC	116	-29.5±9.8	-	-	-	-	-	-	-
GG+AG	TT	379	-31.9±8.8	-0.024	0.01	0.013	-0.024	0.01	0.014	
AA	CC+TC	1	-	-	-	-	-	-	-	-
AA	TT	46	-31.4±7.5	-0.006	0.005	0.236	-0.007	0.005	0.178	
LDL-C										
GG+AG	CC+TC	116	-37.9±12.8	-	-	-	-	-	-	-
GG+AG	TT	379	-41.4±12.1	-0.035	0.013	0.007	-0.036	0.013	0.006	
AA	CC+TC	1	-	-	-	-	-	-	-	-
AA	TT	46	-39.2±14.3	-0.004	0.008	0.574	-0.005	0.008	0.492	
TG										
GG+AG	CC+TC	116	-21.7±33.6	-	-	-	-	-	-	-
GG+AG	TT	379	-22.6±33.6	-0.009	0.036	0.798	-0.004	0.036	0.909	
AA	CC+TC	1	-	-	-	-	-	-	-	-
AA	TT	46	-24.5±36.6	-0.009	0.02	0.641	-0.01	0.02	0.635	
HDL-C										
GG+AG	CC+TC	116	-9.2±16.3	-	-	-	-	-	-	-
GG+AG	TT	379	-10.1±16.6	-0.01	0.018	0.585	-0.008	0.017	0.665	
AA	CC+TC	1	-	-	-	-	-	-	-	-
AA	TT	46	-9.9±14.4	-0.002	0.009	0.794	-0.002	0.009	0.815	

Adjusted for BMI, age, alcohol consumption and smoking.

Supplementary Table 4. Multiple regression analysis for the association between the SLCO1B1 388A>G polymorphism and the lipid-lowering effects from eight weeks of simvastatin treatment

Variable	388A>G	N	Change(%)		Unadjusted			Adjusted		
			Mean±SD		β	SE	P Value	β	SE	P Value
TC	GG	283	-29.4±9.7							
	AG	212	-30.5±10.4	-0.011	0.009	0.241	0.05	-0.012	0.009	0.181
	AA	47	-32.4±8.5	-0.015	0.008			-0.015	0.008	0.048
	GG+AG	495	-29.9±10.0							
TG	AA	47	-32.4±8.5	-0.025	0.015	0.099		-0.026	0.015	0.088
	GG	283	-19.7±31.7							
	AG	212	-18.7±44.8	0.01	0.034	0.771		0.009	0.035	0.804
	AA	47	-25.9±27.5	-0.031	0.025	0.21		-0.032	0.025	0.193
HDL-C	GG+AG	495	-19.3±37.8							
	AA	47	-25.9±27.5	-0.066	0.057	0.244		-0.068	0.057	0.233
	GG	283	-13.0±17.6							
	AG	212	-13.4±18.3	-0.004	0.016	0.802		-0.003	0.016	0.869
LDL-C	AA	47	-18.1±18.6	-0.026	0.014	0.068		-0.024	0.014	0.079
	GG+AG	495	-13.2±17.9							
	AA	47	-18.1±18.6	-0.049	0.027	0.072		-0.048	0.027	0.074
	GG	283	-35.6±15.5							
LDL-C	AG	212	-36.2±14.9	-0.006	0.014	0.649		-0.009	0.014	0.535
	AA	47	-36.4±12.7	-0.004	0.012	0.729		-0.004	0.012	0.711
	GG+AG	495	-35.8±15.2							
	AA	47	-36.4±12.7	-0.006	0.023	0.808		-0.006	0.023	0.779

Change(%) = (serum lipid levels after 8 weeks' treatment – serum lipid levels at baseline)/serum lipid levels at baseline

Supplementary Table 5. Multiple regression analysis for the association between the SLCO1B1 521T>C polymorphism and the lipid-lowering effects from eight weeks of simvastatin treatment

Variable	521T>C	N	Change(%)		Unadjusted			Adjusted		
			Mean±SD	β	SE	P Value	β	SE	P Value	
TC	TT	425	-30.2±10.0							
	TC	113	-29.7±10.4	0.006	0.011	0.598	0.005	0.011	0.621	
	CC	4	-28.3±2.2	0.01	0.025	0.694	0.012	0.025	0.618	
	CC+TC	117	-29.6±10.2							
TG	TT	425	-30.2±10.0	-0.006	0.01	0.561	-0.006	0.01	0.572	
	TT	425	-20.7±36.1							
	TC	113	-17.1±40.8	0.035	0.039	0.372	0.032	0.04	0.413	
	CC	4	-11.4±27.5	0.046	0.091	0.609	0.044	0.091	0.626	
HDL-C	CC+TC	117	-16.9±40.4							
	TT	425	-20.7±36.1	-0.037	0.039	0.338	-0.034	0.039	0.382	
	TT	425	-13.8±18.3							
	TC	113	-12.9±17.1	0.01	0.019	0.22	0.008	0.019	0.673	
LDL-C	CC	4	-16.0±7.9	-0.011	0.046	0.812	-0.017	0.045	0.701	
	CC+TC	117	-13.0±16.8							
	TT	425	-13.8±18.3	-0.009	0.019	0.648	-0.007	0.019	0.724	
	TT	425	-35.9±15.3							
LDL-C	TC	113	-36.0±14.5	-0.001	0.016	0.93	-0.001	0.016	0.973	
	CC	4	-34.0±6.0	0.009	0.038	0.806	0.017	0.038	0.65	
	CC+TC	117	-36.0±14.3							
	TT	425	-35.9±15.3	0.001	0.016	0.964	-0.001	0.016	0.969	

Change(%) = (serum lipid levels after 8 weeks treatment – serum lipid levels at baseline)/serum lipid levels at baseline

Supplementary Table 6. Multiple Regression analysis to analyze gene-gene joint associations with the lipid-lowering effects from eight weeks of simvastatin treatment.

388A>G	521T>C	N	Change(%)		Unadjusted			Adjusted		
			Mean±SD	β	SE	P Value	β	SE	P Value	
TC										
GG+AG	CC+TC	116	-29.6±10.2							
GG+AG	TT	379	-30.0±10.0	-0.004	0.011	0.74	-0.003	0.011	0.758	
AA	CC±TC	1								
AA	TT	46	-32.4±8.6	-0.009	0.006	0.104	-0.009	0.006	0.101	
TG										
GG+AG	CC+TC	116	-16.8±40.5	-	-	-	-	-	-	-
GG+AG	TT	379	-20.0±37.0	-0.032	0.04	0.429	-0.028	0.041	0.497	
AA	CC+TC	1	-	-	-	-	-	-	-	
AA	TT	46	-25.8±27.8	-0.03	0.022	0.17	-0.025	0.022	0.255	
HDL-C										
GG+AG	CC+TC	116	-12.9±16.9	-	-	-	-	-	-	-
GG+AG	TT	379	-13.3±18.2	-0.004	0.019	0.833	-0.003	0.019	0.881	
AA	CC+TC	1	-	-	-	-	-	-	-	
AA	TT	46	-18.1±18.8	-0.017	0.01	0.088	-0.015	0.01	0.132	
LDL-C										
GG+AG	CC+TC	116	-35.9±14.3	-	-	-	-	-	-	-
GG+AG	TT	379	-35.8±15.5	0.001	0.016	0.069	-	0.016	0.998	
AA	CC+TC	1	-	-	-	-	-	-	-	
AA	TT	46	-36.4±12.9	-0.001	0.008	0.859	-0.003	0.008	0.702	

Change(%) = (serum lipid levels after 8 weeks' treatment – serum lipid levels at baseline)/serum lipid levels at baseline

Supplementary Table 7. Association between the 388A>G and 521T>C polymorphisms and the elevation of CK levels after four and eight weeks of simvastatin treatment

CK levels	N	Baseline	4 weeks of treatment	Change ^A	P1	8 weeks of treatment	Change ^B	P2
388A>G								
AA	47	119.83±51.79	136.81±76.16	16.98±49.88	0.024	197.05±132.78	77.22±116.81	p<0.001
AG	212	108.35±49.71	140.90±111.44	32.55±87.00	p<0.001	173.70±137.16	65.34±113.49	p<0.001
GG	283	102.16±43.50	127.80±68.51	25.64±57.19	p<0.001	157.85±110.30	55.69±96.13	p<0.001
521T>C								
TT	425	107.83±47.81	134.60±89.39	26.77±70.90	p<0.001	170.68±128.96	62.85±110.66	p<0.001
TC	113	99.47±43.12	128.80±83.38	29.33±65.63	p<0.001	152.72±101.27	53.25±81.23	p<0.001
CC	4	111.50±54.02	176.75±135.84	65.25±91.90	0.251	240.00±123.76	128.50±77.61	0.045

P1:paired student *t* test was used to compare CK levels before and after four weeks of simvastatin treatment.

P2:paired student *t* test was used to compare CK levels before and after eight weeks of simvastatin treatment.

^Achange = CK levels after 4 weeks treatment – serum CK levels at baseline

^Bchange = CK levels after 8 weeks treatment – serum CK levels at baseline

Supplementary Table 8. Association between the SLCO1B1 388A>G polymorphism and CK response after four and eight consecutive weeks of treatment with simvastatin.

Variable	388A>G	N	Change(%) Mean±SD	Unadjusted			adjusted		
				β	SE	P Value	β	SE	P Value
CK elevation at 4 weeks	GG	283	25.6±57.2						
	AG	212	32.5±87.0	6.907	6.493	0.288	6.477	6.44	0.315
	AA	47	17.0±49.9	-4.33	4.428	0.329	-4.35	4.486	0.333
CK elevation at 8 weeks	GG	283	55.7±96.1						
	AG	212	65.3±113.5	9.655	9.439	0.307	9.817	9.417	0.298
	AA	47	77.2±116.8	10.766	7.819	0.169	11.048	8.027	0.17

Adjusted for: age, sex, BMI, smoking, and alcohol consumption.

Change(%) = (serum CK levels after 4 or 8 weeks' treatment - serum CK levels at baseline)/serum CK levels at baseline

Supplementary Table 9. Association between the SLCO1B1 521T>C polymorphism and CK response after four and eight consecutive weeks of treatment with simvastatin.

Variable	521T>C	N	Change(%)		Unadjusted			adjusted		
			Mean±SD	β	SE	P Value	β	SE	P Value	
CK elevation at 4 weeks	TT	425	26.8±70.9							
	TC	113	29.3±65.6	2.552	7.391	0.73	2.745	7.391	0.711	
	CC	4	65.3±91.9	19.238	17.851	0.282	22.058	17.676	0.213	
CK elevation at 8 weeks	TT	425	62.8±110.7							
	TC	113	53.3±81.2	-9.593	11.134	0.389	-8.469	11.231	0.451	
	CC	4	128.5±77.6	32.827	27.744	0.234	35.142	27.83	0.207	

Adjusted for: age, sex, BMI, smoking, and alcohol consumption.

Change (%) = (serum CK levels after 4 or 8 weeks' treatment – serum CK levels at baseline)/serum CK levels at baseline