

## **ONLINE SUPPORTING MATERIAL**

### **Genome-Wide Association Study (GWAS) on Bilirubin Concentrations in Subjects with Metabolic Syndrome: Sex-Specific GWAS Analysis and Gene-Diet Interactions in a Mediterranean Population**

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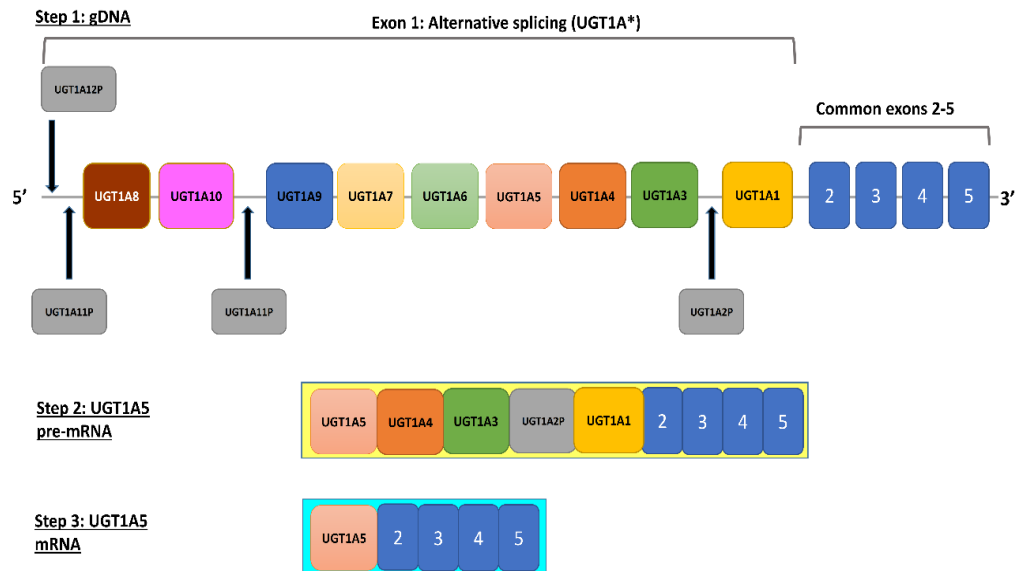
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**Supplemental Table 1.** Quantitative 17-item questionnaire for Adherence to Mediterranean diet.

Food items and frequency of consumption	Criteria for 1 point <sup>1</sup>
1. Do you use olive oil as main culinary fat?	Yes
2. How many vegetable servings do you consume per day? (1 serving = 200g [consider side dish as half serving])	≥2 (≥1 portion raw or as salad)
3. How many fruit units (including natural fruit juices) do you consume per day?	≥3
4. How many servings of red meat, hamburger or meat products (ham, sausage, etc.) do you consume per week? (1 serving = 100–150g)	<1
5. How many servings of butter, margarine, or cream do you consume per week? (1 serving = 12g)	<1
6. How many sweetened beverages (soft drinks, cola, bitter, juices without added sugars) do you drink per week?	<1
7. How many servings of legumes do you consume per week? (1 serving = 150g)	≥3
8. How many servings of fish or shellfish do you consume per week? (1 serving = 100-150g of fish or 4-5 units or 200g of shellfish)	≥3
9. How many times per week do you consume pastries, such as cookies, custard, sweets or cakes?	<3
10. How many servings of nuts (including peanuts) do you consume per week? (1 serving = 30g)	≥1
11. Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, hamburger, or sausage?	Yes
12. How many times per week do you consume vegetables, pasta, rice, or other dishes seasoned with <i>sofrito</i> (sauce made with tomato and onion, leek, or garlic and simmered with olive oil)?	≥2
13. Do you add sugar to the coffee or tea?	No/use artificial sweeteners
14. How many servings of white bread do you consume per day? (1 serving = 75g)	<1
15. How many servings of cereals and whole grains (bread, rice, pasta) do you consume per week?	≥5
16. How many servings of white bread, rice and/or pasta do you consume per week?	<3
17. How much wine do you drink per week?	2-3 glasses/day for men and 1-2 glasses/day for women

<sup>1</sup> '0' points if these criteria are not met.

**Supplemental Figure 1.** Graphic representation of the human UGT1A cluster, indicating the 9 protein-coding (UGT1A1, UGT1A3, UGT1A4, UGT1A5, UGT1A6, UGT1A7, UGT1A8, UGT1A9 and UGT1A10) genes and the 4 non-coding genes (pseudogenes), as well as the process of alternative splicing with a first exon followed by a set of common exons 2–5.



**Supplemental Table 2.** Linkage disequilibrium parameters between the lead SNP (rs4148325) and the other top-ranked SNPs in chromosome 2 at the GWAS significance level for total bilirubin concentrations in the whole population.

GWAS SNPs	Lead SNP	D'	r <sup>2</sup>	Distance
rs6742078	rs4148325	1.000	1.000	670
rs887829	rs4148325	1.000	1.000	4739
rs4148324	rs4148325	0.995	0.985	587
rs3771341	rs4148325	1.000	0.899	70
rs17862875	rs4148325	0.989	0.870	24007
rs17863787	rs4148325	0.928	0.839	62215
rs6744284	rs4148325	0.923	0.786	48012
rs2070959	rs4148325	0.884	0.757	71118
rs2018985	rs4148325	0.994	0.724	24449
rs2741045	rs4148325	0.917	0.707	93169
rs1105879	rs4148325	0.867	0.668	71107
rs1105880	rs4148325	0.867	0.668	71344
rs7604115	rs4148325	0.885	0.644	15193
rs6725478	rs4148325	0.920	0.627	57909
rs7583278	rs4148325	0.918	0.612	55902
rs10179091	rs4148325	0.993	0.566	15326
rs4124874	rs4148325	1.000	0.565	7650
rs4399719	rs4148325	1.000	0.564	6848
rs3755319	rs4148325	0.993	0.562	5727
rs871514	rs4148325	0.993	0.562	44780
rs2602374	rs4148325	0.878	0.562	104345
rs6431628	rs4148325	0.993	0.560	25831
rs2008595	rs4148325	0.993	0.560	36117
rs4663333	rs4148325	0.993	0.559	18006
rs4663963	rs4148325	0.993	0.559	23116
rs10179094	rs4148325	0.859	0.558	75484
rs1875263	rs4148325	0.833	0.556	47687
rs4663965	rs4148325	0.985	0.553	22705
rs10197460	rs4148325	0.857	0.550	84119
rs4294999	rs4148325	0.985	0.549	37842
rs2602373	rs4148325	0.781	0.500	111356
rs7563561	rs4148325	0.872	0.497	74318
rs6736743	rs4148325	0.872	0.497	77359
rs6753320	rs4148325	0.872	0.497	77694
rs6736508	rs4148325	0.871	0.496	77562
rs4261716	rs4148325	0.871	0.496	80192
rs4347832	rs4148325	0.871	0.495	80268
rs10168155	rs4148325	0.871	0.494	76473
rs2741029	rs4148325	0.775	0.494	143149
rs13015720	rs4148325	0.870	0.492	72310

rs4553819	rs4148325	0.869	0.492	79226
rs12623271	rs4148325	0.865	0.491	73368
rs11680450	rs4148325	0.865	0.491	75826
rs6753569	rs4148325	0.865	0.491	77492
rs2741027	rs4148325	0.771	0.491	155298
rs6724485	rs4148325	0.870	0.489	80493
rs7556676	rs4148325	0.868	0.479	15059
rs2741012	rs4148325	0.754	0.477	164346
rs7572563	rs4148325	0.942	0.448	56073
rs17862866	rs4148325	0.934	0.441	62397
rs12988520	rs4148325	0.847	0.279	65915

GWAS SNPs: top-ranked SNPs for the whole population.

Lead SNP: the first SNP in the top-ranked SNP list.

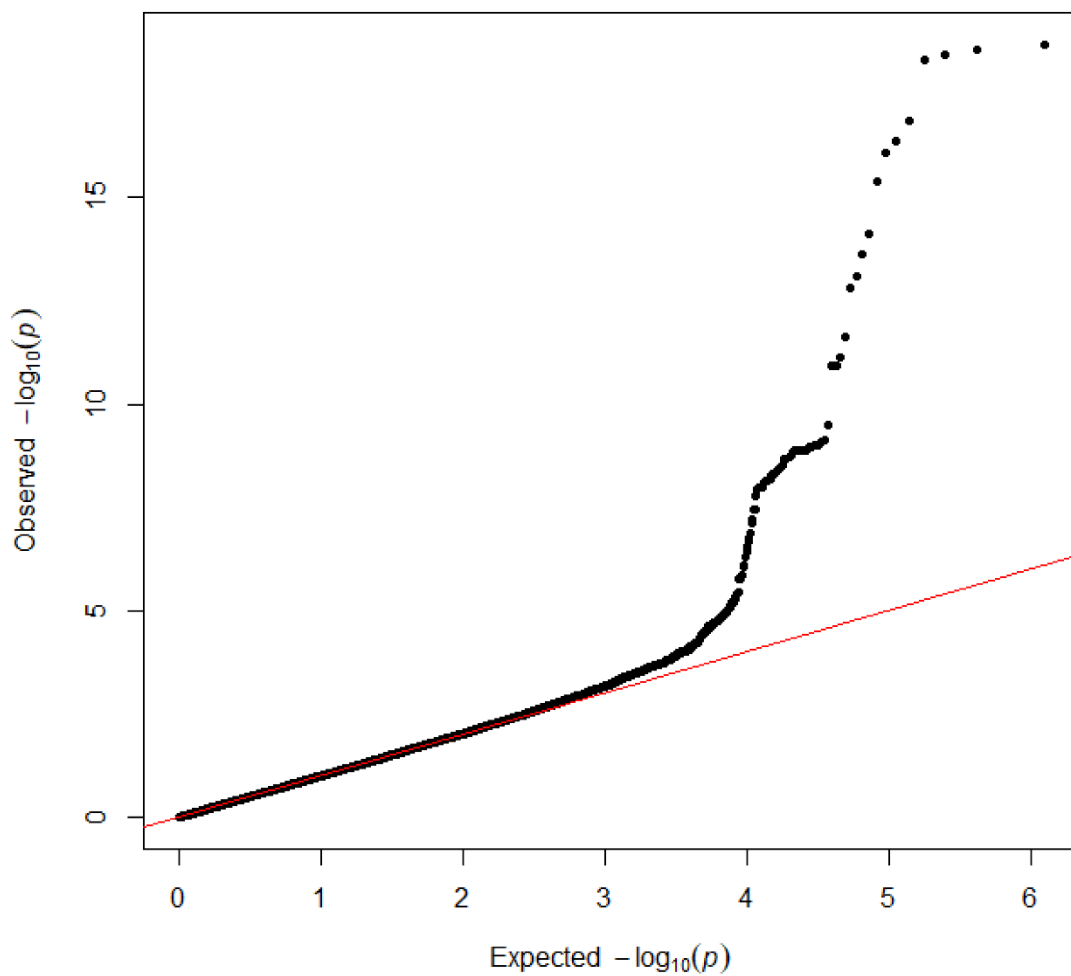
D': value of D prime between the lead SNP and GWAS SNPs.

r<sup>2</sup>: correlation (linkage disequilibrium) between the lead SNP and the GWAS SNPs.

Distance: distance (in base-pairs) between the loci.

n = 430 subjects analyzed.

**Supplemental Figure 2.** Q-Q plot for the GWAS on total serum bilirubin concentrations in the whole population (n=430).



**Supplemental Table 3.** GWAS results (at  $P < 1 \times 10^{-5}$ ) for the association between bilirubin concentrations and the top-ranked SNPs in men.

CHR	SNP	BP	BETA	SE	R2	P <sup>1</sup>	P <sup>2</sup>	MA	MAF	SO	Gene
2	rs4148324	234672722	0.177	0.027	0.189	4.44E-10	4.77E-11	G	0.353	+	UGT1A1
2	rs887829	234668570	0.176	0.027	0.188	5.89E-10	7.04E-11	T	0.354	-	UGT1A1
2	rs3771341	234673239	0.174	0.028	0.166	6.20E-09	1.20E-09	A	0.330	-	UGT1A1
2	rs17862875	234649302	0.173	0.029	0.161	1.00E-08	2.40E-09	A	0.295	+	UGT1A6
2	rs929596	234674476	0.171	0.029	0.154	2.29E-08	3.75E-09	G	0.324	-	UGT1A1
2	rs17863787	234611094	0.159	0.028	0.149	4.37E-08	1.04E-08	G	0.263	+	UGT1A6 <sup>3</sup>
2	rs1105879	234602202	0.150	0.027	0.144	8.14E-08	1.07E-08	C	0.325	-	UGT1A6
2	rs2070959	234602191	0.155	0.028	0.143	8.44E-08	2.15E-08	G	0.278	+	UGT1A6
2	rs1105880	234601965	0.148	0.027	0.139	1.35E-07	1.81E-08	G	0.343	-	UGT1A6
2	rs6744284	234625297	0.157	0.029	0.140	1.50E-07	2.97E-08	T	0.390	+	UGT1A6
18	rs9957684	72866863	0.427	0.079	0.136	2.13E-07	1.40E-07	T	0.073	+	—
17	rs9903658	32056226	0.218	0.043	0.120	1.14E-06	1.36E-06	G	0.141	+	ASIC2
18	rs658995	70207340	0.307	0.062	0.118	1.42E-06	1.40E-06	A	0.282	+	CBLN2
2	rs2741045	234580140	0.142	0.029	0.114	2.06E-06	2.38E-07	T	0.159	+	UGT1A10
4	rs11942650	166854139	0.263	0.055	0.111	2.93E-06	4.27E-06	G	0.077	+	TLL1
4	rs17035736	106472904	0.484	0.102	0.108	4.32E-06	5.08E-06	G	0.058	+	ARHGEF38
2	rs7583278	234617407	0.123	0.026	0.107	4.79E-06	1.59E-06	T	0.391	+	UGT1A6
17	rs4796796	76614120	0.244	0.052	0.105	5.42E-06	3.51E-06	T	0.159	+	LOC101928710
2	rs2602374	234568964	0.138	0.030	0.104	5.76E-06	1.95E-06	T	0.173	+	UGT1A10
2	rs6725478	234615400	0.122	0.026	0.104	6.31E-06	2.71E-06	T	0.388	+	UGT1A6
2	rs2018985	234648860	0.123	0.026	0.105	6.49E-06	2.52E-06	G	0.441	+	UGT1A6
1	rs11206328	54776175	0.181	0.039	0.103	7.24E-06	6.53E-06	G	0.035	+	SSBP3
8	rs10090456	89664364	0.434	0.095	0.100	9.15E-06	8.91E-06	C	0.050	+	—
2	rs2741029	234530160	0.127	0.028	0.100	1.02E-05	3.56E-06	G	0.177	+	UGT1A8

CHR: Chromosome.

SNP: Single Nucleotide Polymorphism.

BP: Base pair indicating the SNP location in the chromosome according to the GRCh37 genome assembly.

Beta: indicates the regression coefficients showing the increase or decrease in the bilirubin concentrations (mg/dL) per minor allele.

SE: Standard error of Beta.

R<sup>2</sup>: Indicates the determination coefficient (variability explained).

MA: Minor allele.

MAF: minor allele (MA) frequency.

SO: strand orientation.

n = 188 subjects analyzed.

<sup>1</sup>: Unadjusted P-value in the additive model.

<sup>2</sup>: Adjusted P-value for age (additive model).

<sup>3</sup>: SNP scored as 3a in the RegulomeDB with the meaning of less likely to affect binding.

**Supplemental Table 4.** GWAS results (at  $P < 1 \times 10^{-5}$ ) for the association between bilirubin concentrations and the top-ranked SNPs in women.

CHR	SNP	BP	BETA	SE	R <sup>2</sup>	P <sup>1</sup>	P <sup>2</sup>	MA	MAF	SO	Gene
2	rs4148324	234672722	0.142	0.017	0.218	1.99E-14	2.15E-14	G	0.353	+	UGT1A1
2	rs6742078	234672639	0.142	0.018	0.217	2.69E-14	2.97E-14	T	0.348	+	UGT1A1
2	rs17863787	234611094	0.135	0.017	0.202	2.14E-13	2.40E-13	G	0.263	+	UGT1A6 <sup>4</sup>
2	rs17862875	234649302	0.141	0.018	0.199	3.61E-13	4.03E-13	A	0.295	+	UGT1A6
2	rs3771341	234673239	0.136	0.018	0.189	1.52E-12	1.67E-12	A	0.330	-	UGT1A1
2	rs6744284	234625297	0.134	0.018	0.182	5.16E-12	5.70E-12	T	0.390	+	UGT1A6
2	rs929596	234674476	0.128	0.019	0.166	4.48E-11	4.65E-11	G	0.324	-	UGT1A1
2	rs2018985	234648860	0.115	0.018	0.147	9.23E-10	1.00E-09	G	0.441	+	UGT1A6
2	rs2070959	234602191	0.111	0.018	0.139	2.40E-09	2.57E-09	G	0.278	+	UGT1A6
2	rs2741045	234580140	0.108	0.018	0.128	1.08E-08	1.07E-08	T	0.159	+	UGT1A10
1	rs359935	89983184	0.353	0.061	0.126	1.99E-08	2.17E-08	A	0.053	-	—
2	rs6725478	234615400	0.104	0.018	0.123	2.13E-08	2.28E-08	T	0.388	+	UGT1A6
2	rs1105880	234601965	0.103	0.018	0.123	2.30E-08	2.40E-08	G	0.343	-	UGT1A6
2	rs1105879	234602202	0.103	0.018	0.123	2.30E-08	2.40E-08	C	0.325	-	UGT1A6
2	rs7583278	234617407	0.105	0.018	0.124	2.57E-08	2.75E-08	T	0.391	+	UGT1A6
2	rs7604115	234658116	0.107	0.019	0.122	2.57E-08	2.76E-08	T	0.350	+	UGT1A6
2	rs10179091	234657983	-0.102	0.019	0.112	1.06E-07	1.13E-07	T	0.482	+	UGT1A6
2	rs3755319	234667582	-0.102	0.019	0.112	1.29E-07	1.36E-07	A	0.450	-	UGT1A1
2	rs4294999	234635467	-0.101	0.019	0.109	1.56E-07	1.67E-07	A	0.426	+	UGT1A6
2	rs2008595	234637192	-0.101	0.019	0.109	1.57E-07	1.67E-07	C	0.412	-	UGT1A6
2	rs871514	234628529	-0.101	0.019	0.109	1.64E-07	1.76E-07	T	0.428	-	UGT1A6
2	rs4124874	234665659	-0.100	0.019	0.107	2.10E-07	2.23E-07	T	0.412	-	UGT1A6 <sup>3</sup>
2	rs4399719	234666461	-0.100	0.019	0.107	2.10E-07	2.23E-07	T	0.415	+	UGT1A6
2	rs6431628	234647478	-0.099	0.019	0.107	2.14E-07	2.28E-07	A	0.410	+	UGT1A6
2	rs4663965	234650604	-0.099	0.019	0.107	2.14E-07	2.28E-07	T	0.415	+	UGT1A6
2	rs4663333	234655303	-0.099	0.019	0.107	2.14E-07	2.28E-07	G	0.411	+	UGT1A6
2	rs4663963	234650193	-0.099	0.019	0.107	2.27E-07	2.42E-07	T	0.420	+	UGT1A6
2	rs4148326	234673462	-0.099	0.019	0.107	2.29E-07	2.43E-07	T	0.480	+	UGT1A1
2	rs1875263	234625622	0.097	0.019	0.103	3.71E-07	3.86E-07	T	0.417	+	UGT1A6 <sup>3</sup>
5	rs2963791	3844541	0.152	0.030	0.098	7.05E-07	6.85E-07	C	0.232	-	—
2	rs2741027	234518011	0.095	0.019	0.097	8.15E-07	7.89E-07	A	0.177	+	—
2	rs2741029	234530160	0.095	0.019	0.097	8.15E-07	7.89E-07	G	0.177	+	UGT1A8
2	rs2602373	234561953	0.095	0.019	0.094	1.16E-06	1.10E-06	C	0.177	+	UGT1A10
11	rs4387351	62380732	0.326	0.065	0.095	1.21E-06	1.27E-06	T	0.063	+	ROM1 <sup>4</sup>
2	rs2741012	234508963	0.090	0.019	0.090	2.09E-06	2.02E-06	T	0.191	+	—
2	rs2602374	234568964	0.092	0.019	0.088	2.93E-06	2.79E-06	T	0.173	+	UGT1A10
3	rs6439106	127718954	0.383	0.081	0.086	3.75E-06	3.92E-06	T	0.221	+	—
2	rs7556676	234658250	0.090	0.019	0.086	3.84E-06	4.04E-06	G	0.497	+	UGT1A6
9	rs11145243	79669154	0.204	0.043	0.085	4.36E-06	4.57E-06	G	0.043	+	LOC105376096
2	rs10197460	234589190	0.086	0.018	0.083	5.81E-06	6.05E-06	T	0.298	+	UGT1A10
2	rs10179094	234597825	0.084	0.018	0.082	6.53E-06	6.81E-06	A	0.297	+	UGT1A10 <sup>3</sup>
9	rs11145236	79663576	0.197	0.043	0.082	6.73E-06	7.00E-06	C	0.045	+	LOC105376096

9	rs10974637	468705	0.189	0.042	0.080	8.12E-06	7.31E-06	C	0.105	+	KANK1
5	rs11948295	3800097	0.153	0.034	0.078	1.13E-05	1.07E-05	T	0.132	+	—

CHR: Chromosome.

SNP: Single Nucleotide Polymorphism.

BP: Base pair indicating the SNP location in the chromosome according to the GRCh37 genome assembly.

Beta: indicates the regression coefficients showing the increase or decrease in the bilirubin concentrations (mg/dL) per minor allele.

SE: Standard error of Beta.

R<sup>2</sup>: Indicates the determination coefficient (variability explained).

MA: Minor allele.

MAF: minor allele (MA) frequency.

SO: strand orientation.

n = 242 subjects analyzed.

<sup>1</sup>: Unadjusted P-value in the additive model.

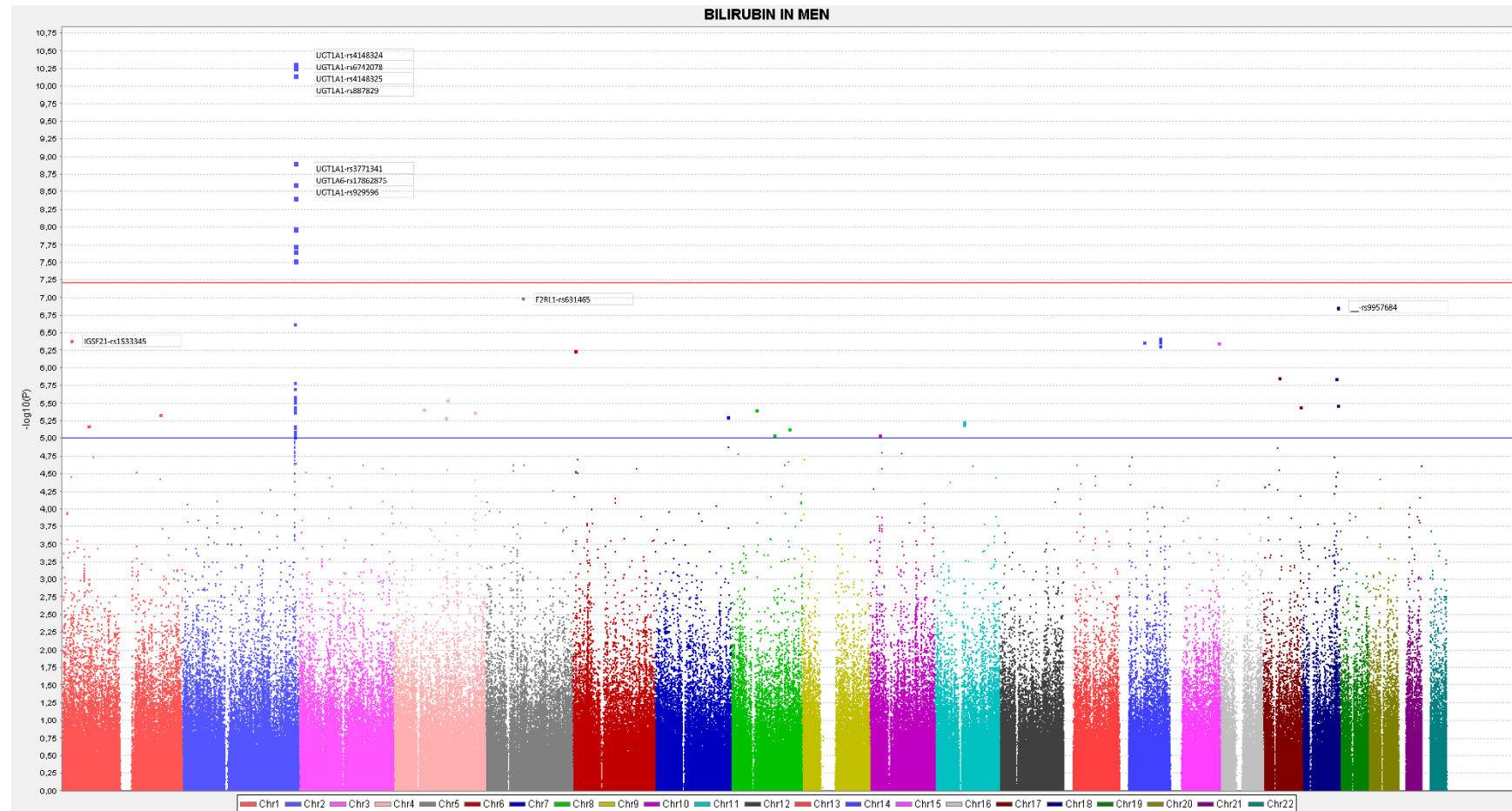
<sup>2</sup>: Adjusted P-value for age (additive model).

<sup>3</sup>: SNP scored as 2b in the RegulomeDB with the meaning of likely to affect binding.

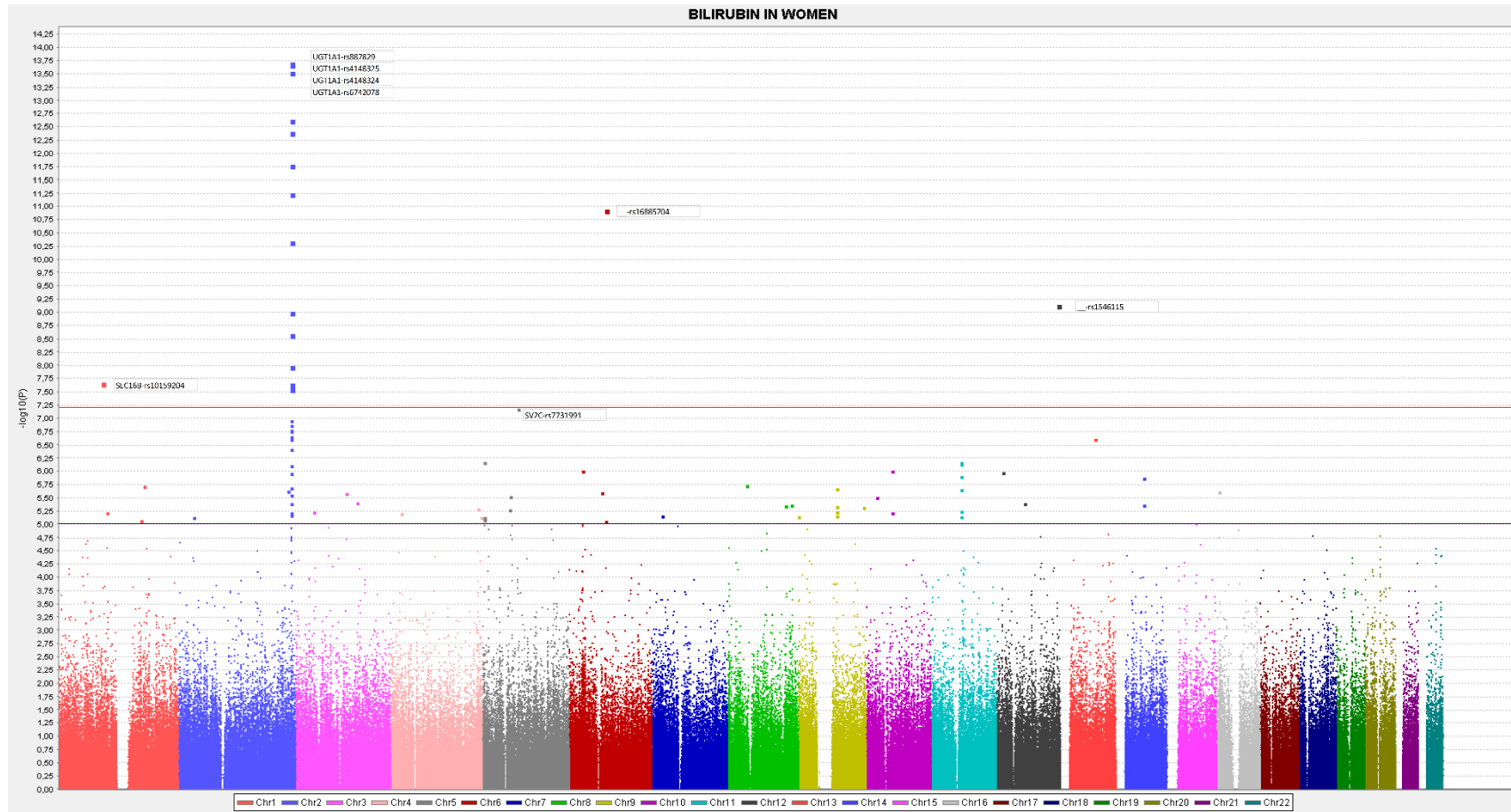
<sup>4</sup>: SNP scored as 3a in the RegulomeDB with the meaning of less likely to affect binding.

**Supplemental Figure 3.** Manhattan plot for the GWAS analysis on total serum bilirubin concentrations in men (A) (n=188 participants), and women (B) (n=242 participants) obtained in the genetic additive model adjusted for age, expressed in  $-\log_{10}(P\text{-value})$ . Blue line represents the threshold 1 [ $-\log_{10}(5 \times 10^{-8})$ ] for the GWAS statistical significance. Red Line represents the threshold 2 [ $-\log_{10}(1 \times 10^{-5})$ ].

A



B



**Supplemental Table 5.** GWAS results for the interaction term between sex and the top-ranked SNPs (at  $P < 1 \times 10^{-5}$ ) for bilirubin concentrations in the whole sample.

CHR	SNP	MEN		WOMEN		P <sup>3</sup> interaction sex-SNP	MAF	Gene
		BETA <sup>1</sup>	SE <sup>1</sup>	BETA <sup>2</sup>	SE <sup>2</sup>			
6	rs16885704	0.044	0.083	0.770	0.109	1.14E-07	0.119	—
14	rs10484092	1.279	0.242	0.012	0.070	4.80E-07	0.074	FRMD6-AS2
7	rs3937443	0.110	0.029	-0.060	0.019	1.03E-06	0.174	LOC105375238
7	rs1558162	0.109	0.029	-0.060	0.019	1.07E-06	0.228	LOC105375238
5	rs13189262	-0.127	0.053	0.189	0.038	1.26E-06	0.199	—
4	rs17046724	1.279	0.242	0.066	0.074	1.59E-06	0.055	—
4	rs28823272	0.594	0.123	-0.131	0.093	2.50E-06	0.061	—
5	rs631465	0.326	0.058	-0.034	0.050	2.68E-06	0.118	F2RL1
8	rs9325854	0.307	0.068	-0.068	0.044	3.75E-06	0.085	—
4	rs884711	0.377	0.079	-0.064	0.057	5.25E-06	0.160	—
10	rs10786848	0.078	0.027	-0.072	0.019	7.02E-06	0.460	LOC105378465/SORCS3
4	rs10470807	0.100	0.028	-0.051	0.019	7.36E-06	0.254	LOC105374525
13	rs2274545	-0.084	0.028	0.067	0.020	8.17E-06	0.171	COL4A2
1	rs1533345	0.189	0.036	-0.011	0.027	8.55E-06	0.168	IGSF21
11	rs2779154	0.087	0.029	-0.064	0.018	8.92E-06	0.436	LOC105376605
11	rs2793472	0.100	0.031	-0.066	0.021	8.93E-06	0.186	LOC105376605

CHR: Chromosome.

SNP: Single Nucleotide Polymorphism.

BP: Base pair indicating the SNP location in the chromosome according to the GRCh37 genome assembly.

Beta<sup>1</sup>: indicates the regression coefficients showing the increase or decrease in the bilirubin concentrations (mg/dL) per minor allele in men.

SE<sup>1</sup>: Standard error of Beta in men.

Beta<sup>2</sup>: indicates the regression coefficients showing the increase or decrease in the bilirubin concentrations (mg/dL) per minor allele in women.

SE<sup>2</sup>: Standard error of Beta in women.

<sup>3</sup>: P-value for interaction term between the corresponding SPN and sex.

MAF: minor allele (MA) frequency.

n = 430 subjects analyzed.

**Supplemental Table 6.** GWAS results for the interaction term between Mediterranean diet adherence and the corresponding SNPs (at  $P < 1 \times 10^{-5}$ ) for bilirubin concentrations in men.

CHR	SNP	Low Adherence Mediterranean Diet <sup>1</sup>		High Adherence Mediterranean Diet <sup>2</sup>		P <sup>3</sup> gene-diet interaction	MA	MAF	Gene
		Beta <sup>1</sup>	SE <sup>1</sup>	Beta <sup>2</sup>	SE <sup>2</sup>				
4	rs11935905	0.074	0.023	-0.099	0.028	2.06E-06	C	0.295	—
11	rs4936822	0.069	0.028	-0.123	0.033	8.12E-06	A	0.155	GRAMD1B
1	rs12404348	0.066	0.025	-0.100	0.028	9.71E-06	C	0.425	LOC105373215

CHR: Chromosome.

SNP: Single Nucleotide Polymorphism.

<sup>1</sup>: Low Adherence to the Mediterranean Diet: from 0 to 8 points in the 17-item score.

Beta<sup>1</sup>: indicates the regression coefficients showing the increase or decrease in the bilirubin concentrations (mg/dL) per minor allele in the low adherence stratum.

SE<sup>1</sup>: Standard error of Beta in the low adherence stratum.

Beta<sup>2</sup>: indicates the regression coefficients showing the increase or decrease in the bilirubin concentrations (mg/dL) per minor allele in the high adherence stratum.

SE<sup>2</sup>: Standard error of Beta in the high adherence stratum.

<sup>2</sup>: High Adherence to the Mediterranean Diet: from 9 to 17 points in the 17-item score.

<sup>3</sup>: P-value for interaction term between Mediterranean diet adherence and the corresponding SNP.

n=181 subjects analyzed.

MAF: minor allele (MA) frequency.

**Supplemental Table 7.** GWAS results for the interaction term between Mediterranean diet adherence and the corresponding SNPs (at  $P < 1 \times 10^{-5}$ ) for bilirubin concentrations in women.

CHR	SNP	Low Adherence Mediterranean Diet <sup>1</sup>		High Adherence Mediterranean Diet <sup>2</sup>		P <sup>3</sup> gene-diet interaction	MA	MAF	GENE
		BETA1	SE1	BETA2	SE2				
10	rs10886342	0.079	0.022	-0.078	0.024	1.15E-06	A	0.277	___
19	rs892051	-0.071	0.023	0.095	0.026	1.31E-06	T	0.149	LOC105376917
8	rs2157651	-0.085	0.021	0.071	0.025	1.77E-06	T	0.248	NAT1
7	rs2677071	-0.052	0.027	0.133	0.028	2.62E-06	T	0.214	___
10	rs1071895	-0.064	0.018	0.065	0.020	2.69E-06	A	0.447	___
20	rs2425479	-0.084	0.032	0.151	0.038	2.86E-06	T	0.035	PTPRT
10	rs4752217	-0.068	0.018	0.058	0.020	2.89E-06	T	0.479	___
10	rs6585514	-0.068	0.021	0.072	0.022	3.84E-06	A	0.395	___
1	rs3010872	-0.117	0.030	0.105	0.038	3.94E-06	C	0.295	___
10	rs4752219	0.072	0.019	-0.062	0.022	4.12E-06	T	0.386	___
10	rs4751680	0.069	0.019	-0.061	0.022	5.47E-06	G	0.352	___
10	rs7908018	-0.062	0.019	0.063	0.021	7.48E-06	A	0.420	___
10	rs10510050	-0.062	0.018	0.059	0.020	9.45E-06	A	0.482	___
10	rs11198670	0.065	0.019	-0.061	0.021	9.76E-06	C	0.316	___
10	rs10749275	0.065	0.019	-0.061	0.021	9.76E-06	T	0.317	___

CHR: Chromosome.

SNP: Single Nucleotide Polymorphism.

<sup>1</sup>: Low Adherence to the Mediterranean Diet: from 0 to 8 points in the 17-item score.

Beta<sup>1</sup>: indicates the regression coefficients showing the increase or decrease in the bilirubin concentrations (mg/dL) per minor allele in the low adherence stratum.

SE<sup>1</sup>: Standard error of Beta in the low adherence stratum.

Beta<sup>2</sup>: indicates the regression coefficients showing the increase or decrease in the bilirubin concentrations (mg/dL) per minor allele in the high adherence stratum.

SE<sup>2</sup>: Standard error of Beta in the high adherence stratum.

<sup>2</sup>: High Adherence to the Mediterranean Diet: from 9 to 17 points in the 17-item score.

<sup>3</sup>: P-value for interaction term between Mediterranean diet adherence and the corresponding SNP.

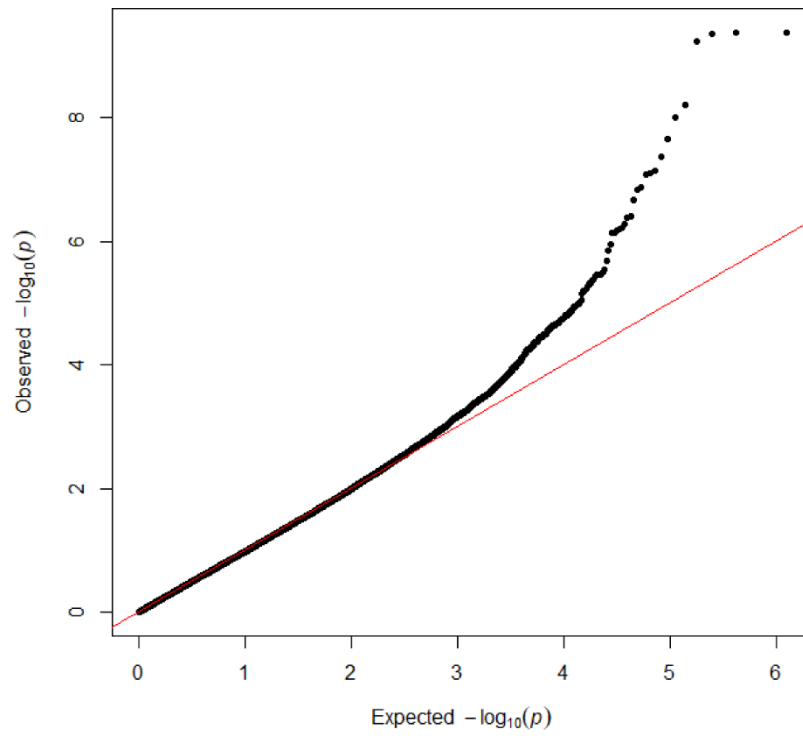
<sup>1</sup>: Low Adherence to the Mediterranean Diet: from 0 to 8 points in the 17-item score.

n=237 subjects analyzed.

MAF: minor allele (MA) frequency.

**Supplemental Figure 4.** Q-Q plot for the GWAS on total serum bilirubin concentrations in the men (**A**) (n=188) and women (**B**) (n=242).

**A**



**B**

