

A targeted analysis reveals relevant shifts in the methylation and transcription of genes responsible for bile acid homeostasis and drug metabolism in non-alcoholic fatty liver disease

Supplement

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Additional file 5: Table S5. NAFLD dependent associations between the methylation of CpG sites belonging to genes listed in table 5 and 6 and transcripts of a maximum of 10 neighboring genes

Table S5 NAFLD dependent associations between the methylation of CpG sites belonging to genes listed in table 5 and 6 and transcripts of a maximum of 10 neighboring genes

No.*	Gene	Neighboring Genes	Up/Downstream	Affymetrix ID	Robust Linear Regression Model** (n=50)				Pearson Correlation***			
					p (Expr.)	Coef. (Expr.)	p (Expr.*Fib)	Coef. (Expr.*Fib)	NAFLD & NASH (n=20)		Controls (n=30)	
									p (Expr.)	Coef. (Expr.)	p (Expr.)	Coef. (Expr.)
1.1	CYP1A2	CYP1A1	Downstream	7990391	1.20E-03	-0.18	ns	-	ns	-	ns	-
1.2	CYP1A2	EDC3	Downstream	7990379	ns	-	ns	-	ns	-	3.94E-02	0.38
1.3	CYP1A2	CLK3	Downstream	7984846	ns	-	ns	-	ns	-	ns	-
1.4	CYP1A2	ARID3B	Downstream	7902592	ns	-	ns	-	ns	-	ns	-
1.5	CYP1A2	UBL7	Downstream	7990361	1.16E-02	-0.67	ns	-	ns	-	ns	-
1.6	CYP1A2	CSK	Upstream	7984871	1.96E-03	-0.83	ns	-	ns	-	ns	-
1.7	CYP1A2	LMAN1L	Upstream	7984892	ns	-	ns	-	ns	-	ns	-
1.8	CYP1A2	CPLX3	Upstream	7984908	ns	-	ns	-	ns	-	ns	-
1.9	CYP1A2	ULK3	Upstream	7990400	ns	-	ns	-	ns	-	ns	-
1.10	CYP1A2	SCAMP2	Upstream	7990417	4.78E-02	-0.48	ns	-	ns	-	ns	-
2.1	CYP27A1	TTL4	Downstream	8048411	ns	-	ns	-	ns	-	ns	-
2.2	CYP27A1	STK36	Downstream	8048381	ns	-	ns	-	ns	-	ns	-
2.3	CYP27A1	BCS1L	Downstream	8048370	ns	-	ns	-	ns	-	7.04E-03	-0.48
2.4	CYP27A1	PLCD4	Downstream	8048350	ns	-	ns	-	ns	-	ns	-
2.5	CYP27A1	PRKAG3	Upstream	8058997	ns	-	ns	-	ns	-	ns	-
2.6	CYP27A1	WNT6	Upstream	8048445	ns	-	ns	-	ns	-	ns	-
2.7	CYP27A1	CDK5R2	Upstream	8048460	2.03E-02	-0.41	ns	-	ns	-	ns	-
2.8	CYP27A1	WNT10A	Upstream	8048452	ns	-	ns	-	ns	-	ns	-
3.1	CYP2B6	CYP2A7	Downstream	8036981	ns	-	ns	-	ns	-	ns	-
3.2	CYP2B6	CYP2A6	Downstream	8028973	ns	-	ns	-	ns	-	ns	-
3.3	CYP2B6	EGLN2	Downstream	8028940	ns	-	ns	-	ns	-	ns	-
3.4	CYP2B6	RAB4B	Downstream	8028930	ns	-	ns	-	2.69E-02	-0.49	ns	-
3.5	CYP2B6	C19orf54	Downstream	8036956	ns	-	ns	-	ns	-	ns	-
3.6	CYP2B6	CYP2A13	Upstream	8028973	ns	-	ns	-	ns	-	ns	-
3.7	CYP2B6	CYP2F1	Upstream	8028984	ns	-	5.92E-03	-2.45	ns	-	ns	-
3.8	CYP2B6	CYP2S1	Upstream	8028991	ns	-	ns	-	ns	-	ns	-
3.9	CYP2B6	AXL	Upstream	8029006	ns	-	ns	-	ns	-	ns	-
3.10	CYP2B6	HNRNPUL1	Upstream	8029029	ns	-	ns	-	ns	-	ns	-
4.1	CYP2C19	CYP2C18	Downstream	7929466	ns	-	ns	-	ns	-	ns	-
4.2	CYP2C19	HELLS	Downstream	7929438	ns	-	ns	-	ns	-	ns	-
4.3	CYP2C19	TBC1D12	Downstream	7929424	ns	-	ns	-	ns	-	ns	-
4.4	CYP2C19	NOC3L	Downstream	7935146	ns	-	ns	-	ns	-	ns	-
4.5	CYP2C19	PLCE1	Downstream	7929388	ns	-	ns	-	ns	-	ns	-
4.6	CYP2C19	CYP2C8	Upstream	7935169	ns	-	ns	-	ns	-	ns	-
4.7	CYP2C19	CYP2C9	Upstream	7929487	ns	-	ns	-	ns	-	ns	-
4.8	CYP2C19	PDLIM1	Upstream	7935180	ns	-	ns	-	ns	-	ns	-
4.9	CYP2C19	SORBS1	Upstream	7935188	ns	-	ns	-	1.74E-03	0.65	ns	-
4.10	CYP2C19	ENTPD1	Upstream	7929511	ns	-	ns	-	2.96E-02	0.49	ns	-
5.1	EPHX1	LBR	Downstream	7910096	ns	-	2.34E-02	-2.39	ns	-	ns	-
5.2	EPHX1	DNAH14	Downstream	7910030	ns	-	8.15E-03	13.12	ns	-	ns	-
5.3	EPHX1	WDR26	Downstream	7924582	3.46E-02	0.42	ns	-	ns	-	2.61E-02	0.41
5.4	EPHX1	PYCR2	Upstream	7924669	ns	-	ns	-	ns	-	ns	-
5.5	EPHX1	TMEM63A	Upstream	7924636	ns	-	ns	-	ns	-	ns	-
5.6	EPHX1	LEFTY1	Upstream	7924663	2.83E-02	-0.35	ns	-	ns	-	ns	-
5.7	EPHX1	LEFTY2	Upstream	7924682	ns	-	ns	-	ns	-	ns	-
6.1	FGFR4	ZNF346	Downstream	8110253	ns	-	ns	-	ns	-	ns	-
6.2	FGFR4	UIMC1	Downstream	8115978	3.96E-03	0.57	ns	-	ns	-	ns	-
6.3	FGFR4	UNC5A	Downstream	8110237	ns	-	ns	-	ns	-	ns	-
6.4	FGFR4	TSPAN17	Downstream	8110224	ns	-	ns	-	ns	-	ns	-
6.5	FGFR4	EIF4E1B	Downstream	8110218	ns	-	ns	-	ns	-	ns	-
6.6	FGFR4	NSD1	Upstream	8110289	ns	-	ns	-	ns	-	ns	-
6.7	FGFR4	RAB24	Upstream	8115997	ns	-	ns	-	2.29E-03	0.64	ns	-

6.8	FGFR4	PRELID1	Upstream	8110318	6.97E-03	-0.28	ns	-	ns	-	ns	-
6.9	FGFR4	MXD3	Upstream	8116012	ns	-	ns	-	ns	-	ns	-
6.10	FGFR4	LMAN2	Upstream	8116020	ns	-	ns	-	2.50E-02	0.50	ns	-
7.1	GSTP1	CABP2	Downstream	7949843	ns	-	ns	-	ns	-	ns	-
7.2	GSTP1	CDK2AP2	Downstream	7949836	ns	-	ns	-	ns	-	ns	-
7.3	GSTP1	PITPNM1	Downstream	7949808	ns	-	ns	-	ns	-	ns	-
7.4	GSTP1	AIP	Downstream	7949863	ns	-	ns	-	ns	-	ns	-
7.5	GSTP1	NDUFV1	Upstream	7941946	ns	-	ns	-	ns	-	ns	-
7.6	GSTP1	NUDT8	Upstream	7949857	1.20E-04	0.42	ns	-	ns	-	2.60E-02	0.41
7.7	GSTP1	TBX10	Upstream	7949863	ns	-	ns	-	ns	-	ns	-
9.1	SLC10A1	SLC39A9	Downstream	7975344	ns	-	ns	-	ns	-	ns	-
9.2	SLC10A1	ERH	Downstream	7979864	ns	-	ns	-	ns	-	ns	-
9.3	SLC10A1	SMOC1	Upstream	7975390	ns	-	ns	-	ns	-	ns	-
9.4	SLC10A1	SLC8A3	Upstream	7979888	ns	-	ns	-	ns	-	ns	-
9.5	SLC10A1	COX16	Upstream	7979906	ns	-	ns	-	ns	-	ns	-
9.6	SLC10A1	ADAM21P1	Upstream	7975406	ns	-	ns	-	ns	-	ns	-
9.7	SLC10A1	SYNJ2BP	Upstream	7979916	ns	-	ns	-	ns	-	ns	-
10.1	SLC27A5	ZNF446	Downstream	8031962	ns	-	ns	-	ns	-	ns	-
10.2	SLC27A5	ZNF324	Downstream	8031956	ns	-	ns	-	ns	-	ns	-
10.3	SLC27A5	ZNF324B	Downstream	8031949	1.54E-02	-0.38	ns	-	ns	-	ns	-
10.4	SLC27A5	ZNF132	Downstream	8039771	ns	-	ns	-	ns	-	ns	-
10.5	SLC27A5	ZNF584	Downstream	8031939	ns	-	ns	-	ns	-	ns	-
10.6	SLC27A5	ZBTB45	Upstream	8039791	ns	-	ns	-	ns	-	ns	-
10.7	SLC27A5	TRIM28	Upstream	8031913	ns	-	ns	-	ns	-	ns	-
10.8	SLC27A5	CHMP2A	Upstream	8039796	ns	-	ns	-	ns	-	ns	-
10.9	SLC27A5	UBE2M	Upstream	8001111	ns	-	1.21E-04	-4.44	ns	-	ns	-
11.1	SLC47A1	RNF112	Downstream	8005586	ns	-	ns	-	ns	-	ns	-
11.2	SLC47A1	B9D1	Downstream	8013331	ns	-	ns	-	ns	-	ns	-
11.3	SLC47A1	MFAP4	Downstream	8013341	ns	-	ns	-	ns	-	ns	-
11.4	SLC47A1	MAPK7	Downstream	8005576	ns	-	ns	-	ns	-	8.21E-03	-0.47
11.5	SLC47A1	MFAP4	Downstream	8013341	ns	-	ns	-	ns	-	ns	-
11.6	SLC47A1	ALDH3A2	Upstream	8005638	5.81E-04	-0.74	ns	-	ns	-	2.43E-03	-0.53
11.7	SLC47A1	SLC47A2	Upstream	8013364	ns	-	ns	-	ns	-	ns	-
11.8	SLC47A1	ALDH3A1	Upstream	8013384	ns	-	ns	-	ns	-	ns	-
11.9	SLC47A1	ULK2	Upstream	8013399	ns	-	ns	-	ns	-	ns	-
11.10	SLC47A1	AKAP10	Upstream	8013431	1.05E-04	1.08	ns	-	ns	-	ns	-
12.1	SLC51A	TFRC	Downstream	8093053	ns	-	ns	-	3.68E-02	0.47	1.04E-02	0.46
12.2	SLC51A	TNK2	Downstream	8093013	ns	-	ns	-	ns	-	ns	-
12.3	SLC51A	MUC4	Downstream	8092978	ns	-	ns	-	ns	-	ns	-
12.4	SLC51A	MUC20	Downstream	8084895	ns	-	ns	-	ns	-	ns	-
12.5	SLC51A	PCYT1A	Upstream	8093086	ns	-	ns	-	ns	-	ns	-
12.6	SLC51A	CTEX1D2	Upstream	8093096	ns	-	ns	-	ns	-	ns	-
12.7	SLC51A	TM4SF19	Upstream	8093104	ns	-	ns	-	ns	-	ns	-
12.8	SLC51A	RNF168	Upstream	8093130	ns	-	ns	-	ns	-	ns	-
13.1	SLCO2B1	NEU3	Downstream	7942562	ns	-	ns	-	ns	-	ns	-
13.2	SLCO2B1	SPCS2	Downstream	7914180	ns	-	ns	-	ns	-	ns	-
13.3	SLCO2B1	XRRA1	Downstream	7942544	ns	-	ns	-	ns	-	ns	-
13.4	SLCO2B1	RNF169	Downstream	7942544	ns	-	ns	-	ns	-	ns	-
13.5	SLCO2B1	CHRDL2	Downstream	7950425	ns	-	3.35E-06	7.11	ns	-	ns	-
13.6	SLCO2B1	RPS3	Upstream	7896740	ns	-	ns	-	ns	-	ns	-
13.7	SLCO2B1	KLHL35	Upstream	7950492	ns	-	ns	-	ns	-	ns	-
13.8	SLCO2B1	GDPD5	Upstream	7950501	ns	-	6.13E-06	-3.79	ns	-	ns	-
13.9	SLCO2B1	SERPINH1	Upstream	7942596	ns	-	ns	-	ns	-	ns	-
14.1	SULT1A1	SULT1A2	Downstream	8000582	1.80E-06	-0.30	3.67E-04	-1.39	ns	-	7.02E-04	-0.58
14.2	SULT1A1	NUPR1	Downstream	8000574	ns	-	ns	-	ns	-	3.24E-03	-0.52
14.3	SULT1A1	IL27	Downstream	8000567	ns	-	ns	-	ns	-	4.98E-02	-0.36
14.4	SULT1A1	CLN3	Downstream	8000543	1.46E-02	-0.83	ns	-	ns	-	3.56E-04	-0.61
14.5	SULT1A1	EIF3C	Upstream	7994415	ns	-	ns	-	ns	-	ns	-
14.6	SULT1A1	ATXN2L	Upstream	7994386	ns	-	ns	-	ns	-	ns	-
14.7	SULT1A1	TUFM	Upstream	8000603	ns	-	ns	-	ns	-	ns	-

Shown are genes that showed NAFLD dependent methylation transcription associations as listed in table 5 and 6 (alphabetical order). The expression of up to five upstream and 5 downstream located genes (if available and measured by the affymetrix array) was linearly regressed to the average methylation changes of the CpG sites associated to the key genes listed in column 2.

* The number allocates a running number to the key gene investigated and listed in table 5 followed by a running number for the neighbouring gene investigated here with regard to associations between methylation and transcriptional expression.

**Regression analyses studying the association between average methylation in the TSS1500 interval of the gene listed in column 2 and transcription of the neighbouring genes listed in column 3 in the EC cohort. Analyses are taking the strength of fibrosis into account either as independent covariate (column 6 and 7) or as interaction term that combines fibrosis and expression (column 8 and 9).

***Pearson`s correlation analyses correlating average methylation state in the TSS1500 interval and strength of transcription in NAFLD and non-NAFLD patients of the EC cohort

-, no coefficient given for non significant results;No, number; ns, not significant; coef, coefficient; ID, identification number