

**Additional file 1: Supplementary Table S1** Clinicopathological characteristics of patients in the initial and validation cohorts.

(A) Initial cohort

Parameters	Patient groups		
	Patients with colorectal cancer (CRC) (n=36)	Patients with morbid obesity (n=91)	Patients with hepatocellular carcinoma (HCC) (n=22)
Subjected tissue samples	Normal liver tissue (NLT) (n=36)	Non-cancerous liver tissue (N) showing non-alcoholic steatohepatitis (NASH) (NASH-O) (n=91)	N showing NASH (NASH-W) (n=22) and HCC (T) (n=22)
Clinicopathological features			
Age (years)	61.50 ± 8.05	42.49 ± 10.17	71.23 ± 7.65
Sex			
Male	27	41	20
Female	9	50	2
Histological findings in N			
Steatosis <sup>a</sup>			
<5%	N/A	3	0
5-33%	N/A	55	15
33-66%	N/A	21	6
>66%	N/A	11	1
Lobular inflammation <sup>a</sup>			
None	N/A	1	0
<2 foci per 200 x field	N/A	74	17
2-4 foci per 200 x field	N/A	16	5
>4 foci per 200 x field	N/A	0	0
Ballooning <sup>a</sup>			
None	N/A	1	0
Few	N/A	88	19
Many	N/A	2	3
Fibrosis <sup>b</sup>			
0	N/A	3	0
1a	N/A	43	5
1b	N/A	6	0
1c	N/A	0	0
2	N/A	22	10
3	N/A	13	5
4	N/A	4	2
NASH stage <sup>b</sup>			
Grade 1	N/A	69	17
Grade 2	N/A	18	4
Grade 3	N/A	1	1
Burned-out NASH	N/A	3	0
HCCs			
Tumor diameter (cm)	N/A	N/A	5.46 ± 2.66
Histological grade <sup>c</sup>			
Well differentiated	N/A	N/A	3
Moderately differentiated	N/A	N/A	14
Poorly differentiated	N/A	N/A	5
TNM stage			
I	N/A	N/A	7
II	N/A	N/A	11
IIIA	N/A	N/A	2
IIIB	N/A	N/A	2
IVA	N/A	N/A	0
IVB	N/A	N/A	0

(B) Validation cohort

Parameters	Patient groups				
	Patients with CRC (n=34)			Patients with HCC (n=21)	
Subjected tissue samples	NLT (n=22)	N showing non-alcoholic fatty liver (NAFL) (NAFL-O) (n=9)	NASH-O (n=3)	N showing NAFL (NAFL-W) (n=10)	NASH-W (n=11) and T (n=11)
Clinicopathological features					
Age (years)	58.77 ± 12.23	63.78 ± 11.72	60.33 ± 11.72	69.00 ± 10.66	70.36 ± 8.78
Sex					
Male	13	7	2	8	8
Female	9	2	1	2	3
Histological findings in N					
Steatosis <sup>a</sup>					
<5%	N/A	0	0	0	0
5-33%	N/A	9	2	10	6
33-66%	N/A	0	1	0	4
>66%	N/A	0	0	0	1
Lobular inflammation <sup>a</sup>					
None	N/A	7	0	8	0
<2 foci per 200 x field	N/A	2	0	0	4
2-4 foci per 200 x field	N/A	0	3	2	7
>4 foci per 200 x field	N/A	0	0	0	0
Ballooning <sup>a</sup>					
None	N/A	9	0	10	0
Few	N/A	0	3	0	11
Many	N/A	0	0	0	0
Fibrosis <sup>b</sup>					
0	N/A	6	0	1	0
1a	N/A	2	1	0	3
1b	N/A	0	1	0	1
1c	N/A	1	0	5	0
2	N/A	0	1	2	0
3	N/A	0	0	2	7
4	N/A	0	0	0	0
NASH stage <sup>b</sup>					
Grade 1	N/A	N/A	1	NA	4
Grade 2	N/A	N/A	2	NA	7
Grade 3	N/A	N/A	0	NA	0
Burned-out NASH	N/A	N/A	0	NA	0
HCCs					
Tumor diameter (cm)	N/A	N/A	N/A	7.14 ± 4.64	5.76 ± 2.95
Histological grade <sup>c</sup>					
Well differentiated	N/A	N/A	N/A	2	3
Moderately differentiated	N/A	N/A	N/A	7	7
Poorly differentiated	N/A	N/A	N/A	1	1
TNM stage					
I	N/A	N/A	N/A	0	0
II	N/A	N/A	N/A	8	4
IIIA	N/A	N/A	N/A	2	6
IIIB	N/A	N/A	N/A	0	0
IVA	N/A	N/A	N/A	0	1
IVB	N/A	N/A	N/A	0	0

<sup>a</sup>Microscopic features (steatosis, lobular inflammation, ballooning and fibrosis) were evaluated according to the non-alcoholic fatty disease (NAFLD) activity score (Ref. 26). <sup>b</sup>NASH stage was defined according to the Brunt classification (Ref. 27). <sup>c</sup>Histological grade of HCCs was in accordance with the World Health Organization classification (Ref. 28). <sup>d</sup>TNM stage was defined according to the Union for International Cancer Control Tumor-Node-Metastasis classification (Ref. 29). N/A, not applicable.

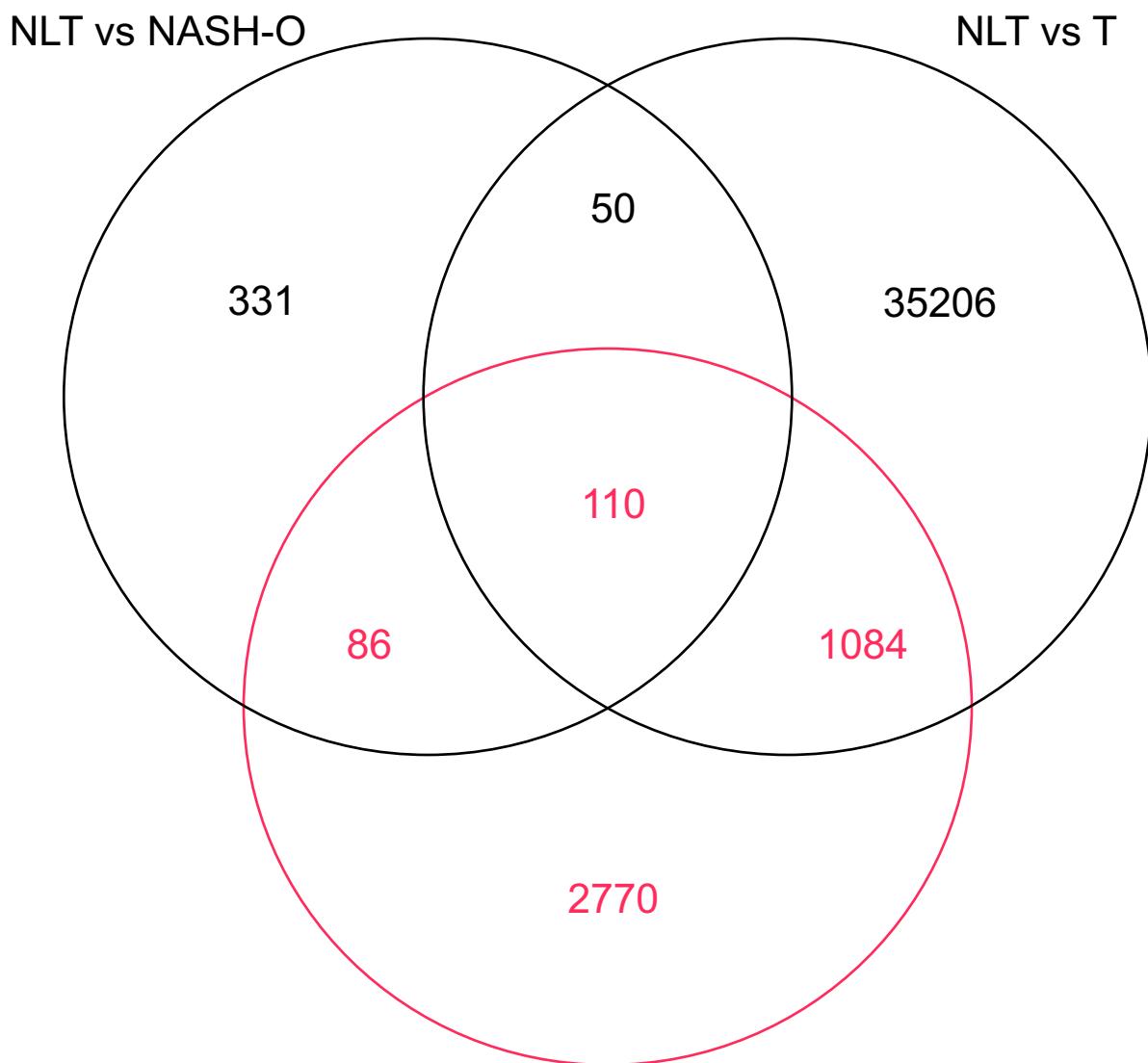
**Additional file 2: Supplementary Table S2** Primer sequences and PCR products for high-performance liquid chromatography.

PCR product ID	Probe ID <sup>a</sup>	Gene symbol	PCR primers (5'-3')		Target sequence (5'-3') <sup>b</sup>
			Forward	Reverse	
1	cg09580822	N/A	GGAAGTTGATTTGATGGGTAGTA	TCCAAAATAACTAATAAAAAACATCC	GGAAGTTGATTTGATGGGCAGCACCGACCAAACCA <b>C</b> GACTTATGAGGCTTGAGATGCATGTGAGAATTAGGC TGCTATGAAAT <b>ACGGCG</b> TGATCTGTTCCACCTTCTGTAAGTTTCTCAGAAGTGAGGACTCTACTCTCAGAAACA <b>GCG</b> TCCCTCCCTGCCACAGCCATCAATGTGCATGTGGT <b>CGACACACCG</b> CATTACACACACT <b>CAGCG</b> GCTCATTAAA ATG <b>CG</b> TTGTGAACTTGG <b>CG</b> TAATCCCCAGGATGTTTCTTCATTAGCTATTTTGG
2	cg15050398	LOC401242	AAGTGTTTTTTTGTAGGAGGG	TAAACTCCAAACTAAAACCTCTACC	AAGTGTTCCTTCGTAGGAGGG <b>CG</b> TAGGCAGCCATGG <b>CG</b> CCCAGCAGGAATGGCATGATGTTGAAGCCCCA CTTCCACAAGGACTGGCAGCAG <b>CG</b> TGTGGCC <b>CG</b> TGGTTCAACCAGAAGAT <b>CG</b> CAGAATCAAGGCC <b>CG</b> GCA AGCCAAAGGG <b>CG</b> TGCAT <b>CG</b> CCC <b>CGCG</b> CC <b>CG</b> GAGAGT <b>CG</b> GGACCCATCTGGCCATTGTGCTGTGCCCTGCT GT <b>CG</b> TTATCACATCAAGGTG <b>CGCG</b> CC <b>CG</b> CAGAGGCTTACGCTGGAGCTCA
3	cg18210511	ZC3H3	GGTAGGTAGGATTTGATTAGTGTTT	CTAAAATCTAATCAAACCTATTATCCCCA	GGCAGGCAGGATCTGACCAGTGTTC <b>CG</b> TGTGCTCACACTGGCACCC <b>CG</b> TGGGAAGGACAGG <b>CGAGCG</b> TGCC <b>CG</b> TGCTGTG <b>CG</b> TGCACATG <b>CG</b> CCACAG <b>CG</b> GCCCACACAGCAGC <b>CG</b> GGGCAAG <b>CG</b> GCC <b>CG</b> CCTCACCTTT CACAG <b>CG</b> CAGGCCCC <b>CG</b> TTTTCAGGCCACTGGGACAACAGCCTGACCAGACCCAG
4	cg09580859	ZC3H3	GGTAAGATGAGTTTATGTGTTTTGA	TAAAATCTAATCAAACCTATTATCCCCA	GGTAAGATGAGCTCATGTGTCTTAAAG <b>CG</b> CAAAGGTTAAAAATGAGTAAGCCTTGATTCTCT <b>CG</b> TTACCCAG GCCTGAGCACCCACATCACAG <b>CG</b> CAGAAA <b>CG</b> GAGGCTCAGGCTGCC <b>CG</b> GAGGCAAGCCCCAAG <b>CG</b> GCAG GCAGGATCTGACCAGTGTTC <b>CG</b> TGTGCTCACACTGGCACCC <b>CG</b> TGGGAAGGACAGG <b>CGAGCG</b> TG <b>CG</b> TGCT GTGTG <b>CG</b> TGCACATG <b>CG</b> CCACAG <b>CG</b> GCCCACACAGCAGC <b>CG</b> GGGCAAG <b>CG</b> GCC <b>CG</b> CCTCACCTTTACAG <b>CG</b> CAGGCCCC <b>CG</b> TTTTCAGGCCACTGGGACAACAGCCTGACCAGACCCCA
5	cg13719443	LOC285847	GTTTAGGGTAGGGTAATTTTTTTTTAG	CCAAACAATACTATTAATAAATCCTCTAC	GTTTAGGGTAGGGTAATTTCCCTTAGCTTCTATG <b>CG</b> CACAAGTGCTGGCC <b>CG</b> CTGCAG <b>CG</b> TCAACCT <b>CG</b> GG AATGG <b>CG</b> GTGCTTTT <b>CG</b> TAGAGGACCCCAACAGTATCTGTCTGG

<sup>a</sup>Probe ID of the Infinium HumanMethylation450 BeadChip.

<sup>b</sup>Infinium probe CpG sites are shown in bold and all CpG sites in target sequences are underlined.

N/A, not annotated (designed in the intergenic regions).



NLT vs NASH-W → 4050 probes in total were subjected to the Jonckheere-Terpstra trend test (Figure 1).

**Additional file 3: Supplementary Figure S1** Venn diagram showing the numbers of common and individual differentially methylated probes ( $P < 0.05$  after Bonferroni correction and  $|\Delta\beta| \geq 0.1$ ) based on the Infinium assay among samples of normal liver tissue (NLT), non-cancerous liver tissue showing non-alcoholic steatohepatitis (NASH) from partial hepatectomy specimens from patients without hepatocellular carcinoma (HCC) (NASH-O), non-cancerous liver tissue showing NASH from partial hepatectomy specimens from patients with HCC (NASH-W) and cancerous tissue (T).

**Additional file 4: Supplementary Table S3** The 415 CpG sites for which receiver operating characteristic curve analysis showed area under the curve (AUC) values larger than 0.95 for discrimination of non-cancerous liver tissue showing non-alcoholic steatohepatitis (NASH) derived from partial hepatectomy specimens from patients with hepatocellular carcinoma (NASH-W) from normal liver tissue (NLT) samples.

Probe ID <sup>a</sup>	Gene symbol <sup>b</sup>	AUC	Cutoff value <sup>c</sup>	<i>P</i> value	Sensitivity <sup>d</sup>	Specificity <sup>e</sup>	DNA methylation status <sup>f</sup>
cg18457818	<i>RAN</i>	0.994	0.597	3.27x10 <sup>-7</sup>	0.972	0.955	NLT < NASH-W
cg19349861	<i>OPCML</i>	0.992	0.157	2.57x10 <sup>-12</sup>	1	0.909	NLT < NASH-W
cg07724654	<i>N/A</i>	0.99	0.841	1.26x10 <sup>-7</sup>	0.944	0.955	NLT < NASH-W
cg14427382	<i>PPP1R2P1</i>	0.99	0.654	8.75x10 <sup>-10</sup>	0.917	1	NLT > NASH-W
cg21980338	<i>ZNF141</i>	0.99	0.3	1.44x10 <sup>-9</sup>	0.944	1	NLT < NASH-W
cg24147392	<i>LOC440461</i>	0.99	0.306	4.11x10 <sup>-4</sup>	0.944	0.955	NLT < NASH-W
cg03505117	<i>N/A</i>	0.987	0.128	3.61x10 <sup>-2</sup>	0.944	0.955	NLT < NASH-W
cg15606745	<i>CACNG2</i>	0.987	0.609	1.17x10 <sup>-8</sup>	0.944	0.955	NLT > NASH-W
cg16319310	<i>N/A</i>	0.987	0.606	8.55x10 <sup>-11</sup>	1	0.909	NLT > NASH-W
cg03571507	<i>ZNF611</i>	0.986	0.719	2.56x10 <sup>-6</sup>	0.944	0.955	NLT > NASH-W
cg12424965	<i>EXOC2</i>	0.986	0.857	4.43x10 <sup>-4</sup>	0.972	0.955	NLT < NASH-W
cg14381908	<i>RASGEF1A</i>	0.986	0.296	2.21x10 <sup>-7</sup>	0.889	1	NLT < NASH-W
cg25824760	<i>ANKRD30B</i>	0.986	0.264	5.18x10 <sup>-14</sup>	0.889	1	NLT < NASH-W
cg20426671	<i>PITPNA</i>	0.985	0.496	8.97x10 <sup>-11</sup>	0.944	1	NLT < NASH-W
cg14299696	<i>N/A</i>	0.984	0.799	3.43x10 <sup>-9</sup>	0.914	1	NLT < NASH-W
cg12074375	<i>N/A</i>	0.984	0.806	1.09x10 <sup>-6</sup>	0.972	0.909	NLT > NASH-W
cg21152376	<i>N/A</i>	0.984	0.313	1.00x10 <sup>-2</sup>	0.917	1	NLT < NASH-W
cg25987208	<i>N/A</i>	0.983	0.271	7.30x10 <sup>-5</sup>	0.972	0.905	NLT < NASH-W
cg07076175	<i>FAM150A</i>	0.982	0.263	1.94x10 <sup>-2</sup>	0.944	1	NLT < NASH-W
cg07738077	<i>ZNF28</i>	0.982	0.601	6.17x10 <sup>-11</sup>	0.917	1	NLT > NASH-W
cg07886142	<i>MEGF10</i>	0.982	0.694	7.85x10 <sup>-8</sup>	0.917	0.955	NLT > NASH-W
cg11070069	<i>N/A</i>	0.982	0.183	1.14x10 <sup>-2</sup>	0.917	1	NLT < NASH-W
cg11213199	<i>MRPS24</i>	0.982	0.426	6.98x10 <sup>-13</sup>	0.861	1	NLT < NASH-W
cg12809925	<i>PARK7</i>	0.982	0.31	3.06x10 <sup>-5</sup>	1	0.909	NLT < NASH-W
cg22083325	<i>LOC440461</i>	0.982	0.245	2.61x10 <sup>-4</sup>	1	0.864	NLT < NASH-W
cg07138452	<i>FLCN</i>	0.981	0.203	2.65x10 <sup>-9</sup>	0.944	0.909	NLT < NASH-W
cg07956857	<i>N/A</i>	0.981	0.673	1.03x10 <sup>-10</sup>	0.972	0.909	NLT > NASH-W
cg07959490	<i>CCDC57</i>	0.981	0.532	1.67x10 <sup>-9</sup>	0.917	0.955	NLT < NASH-W
cg13161852	<i>N/A</i>	0.981	0.761	2.39x10 <sup>-10</sup>	0.972	0.909	NLT > NASH-W
cg13468249	<i>DULLARD</i>	0.981	0.265	6.04x10 <sup>-10</sup>	0.917	0.955	NLT < NASH-W
cg20251199	<i>SNORA14B</i>	0.981	0.264	1.41x10 <sup>-11</sup>	1	0.909	NLT < NASH-W
cg03666506	<i>TBC1D26</i>	0.98	0.654	1.71x10 <sup>-3</sup>	0.972	0.909	NLT > NASH-W
cg08081407	<i>ARF4</i>	0.98	0.213	2.22x10 <sup>-11</sup>	0.889	0.955	NLT < NASH-W
cg11036936	<i>RAD51L1</i>	0.98	0.646	3.21x10 <sup>-9</sup>	0.917	0.955	NLT > NASH-W
cg18855143	<i>LCE2B</i>	0.98	0.681	4.09x10 <sup>-2</sup>	0.972	0.909	NLT > NASH-W
cg21407906	<i>C20orf20</i>	0.98	0.256	1.46x10 <sup>-10</sup>	0.944	1	NLT < NASH-W
cg25512188	<i>RPS6KA2</i>	0.98	0.83	2.29x10 <sup>-5</sup>	0.972	0.909	NLT > NASH-W
cg01160882	<i>DKK1</i>	0.979	0.153	6.65x10 <sup>-6</sup>	0.861	1	NLT < NASH-W
cg16282892	<i>N/A</i>	0.979	0.625	7.62x10 <sup>-7</sup>	0.889	0.955	NLT > NASH-W
cg19003337	<i>KRT17</i>	0.979	0.714	7.75x10 <sup>-8</sup>	0.944	0.955	NLT > NASH-W
cg20592700	<i>WIPI2</i>	0.979	0.327	7.16x10 <sup>-10</sup>	0.889	0.955	NLT < NASH-W
cg23481024	<i>N/A</i>	0.979	0.61	1.39x10 <sup>-19</sup>	0.889	0.955	NLT > NASH-W
cg14100946	<i>CDK6</i>	0.978	0.457	2.03x10 <sup>-5</sup>	0.971	0.909	NLT < NASH-W
cg10328259	<i>TSSC1</i>	0.977	0.738	6.60x10 <sup>-11</sup>	0.944	0.909	NLT > NASH-W
cg14648311	<i>N/A</i>	0.977	0.769	4.43x10 <sup>-10</sup>	0.889	0.955	NLT > NASH-W
cg20464143	<i>MYO10</i>	0.977	0.494	4.09x10 <sup>-8</sup>	1	0.864	NLT > NASH-W
cg02051077	<i>PODXL</i>	0.976	0.315	3.35x10 <sup>-3</sup>	1	0.864	NLT < NASH-W
cg05478392	<i>N/A</i>	0.976	0.426	1.38x10 <sup>-6</sup>	0.861	1	NLT < NASH-W
cg06361278	<i>N/A</i>	0.976	0.265	3.40x10 <sup>-9</sup>	1	0.818	NLT < NASH-W
cg10162914	<i>MFAP3L</i>	0.976	0.661	4.75x10 <sup>-8</sup>	0.944	0.909	NLT < NASH-W
cg15064753	<i>ZNF662</i>	0.976	0.664	7.04x10 <sup>-8</sup>	0.833	1	NLT > NASH-W
cg15284457	<i>N/A</i>	0.976	0.782	1.79x10 <sup>-5</sup>	0.972	0.955	NLT < NASH-W
cg15646741	<i>N/A</i>	0.976	0.457	2.31x10 <sup>-7</sup>	0.972	0.909	NLT > NASH-W

cg15920791	N/A	0.976	0.313	1.11x10 <sup>-6</sup>	0.972	0.909	NLT < NASH-W
cg18159180	CUL7	0.976	0.434	3.38x10 <sup>-8</sup>	0.861	1	NLT < NASH-W
cg20326359	SNORD114-23	0.976	0.823	3.38x10 <sup>-4</sup>	0.944	0.909	NLT > NASH-W
cg22216431	NRIP2	0.976	0.505	1.31x10 <sup>-8</sup>	0.944	0.955	NLT > NASH-W
cg22793065	PCDHB4	0.976	0.325	2.60x10 <sup>-5</sup>	0.944	0.909	NLT < NASH-W
cg02073839	KIF25	0.975	0.749	1.74x10 <sup>-4</sup>	0.972	0.909	NLT > NASH-W
cg03468541	ZC3H14	0.975	0.164	3.29x10 <sup>-7</sup>	0.972	0.864	NLT < NASH-W
cg04449562	MYT1L	0.975	0.73	2.35x10 <sup>-2</sup>	0.889	1	NLT > NASH-W
cg04867257	N/A	0.975	0.493	1.48x10 <sup>-6</sup>	0.972	0.909	NLT > NASH-W
cg05707844	EIF2AK2	0.975	0.25	4.80x10 <sup>-9</sup>	0.972	0.864	NLT < NASH-W
cg08941173	PKNOX2	0.975	0.356	2.25x10 <sup>-10</sup>	0.889	1	NLT < NASH-W
cg15936935	PACS2	0.975	0.611	5.70x10 <sup>-7</sup>	0.889	1	NLT > NASH-W
cg19105961	CYB5D2	0.975	0.332	9.24x10 <sup>-10</sup>	0.889	0.955	NLT < NASH-W
cg15470736	UBE3C	0.974	0.788	6.74x10 <sup>-9</sup>	1	0.905	NLT > NASH-W
cg00112042	N/A	0.973	0.192	1.22x10 <sup>-7</sup>	0.889	0.955	NLT < NASH-W
cg01593421	N/A	0.973	0.574	5.08x10 <sup>-10</sup>	0.833	1	NLT > NASH-W
cg03000596	LAT2	0.973	0.63	4.18x10 <sup>-8</sup>	0.917	0.955	NLT > NASH-W
cg03022552	ZNF431	0.973	0.781	2.60x10 <sup>-7</sup>	0.861	1	NLT > NASH-W
cg08912801	N/A	0.973	0.603	2.44x10 <sup>-5</sup>	0.972	0.909	NLT > NASH-W
cg09580822	N/A	0.973	0.682	2.01x10 <sup>-3</sup>	0.944	0.909	NLT > NASH-W
cg10526795	H6PD	0.973	0.68	4.39x10 <sup>-10</sup>	0.861	1	NLT > NASH-W
cg10824722	N/A	0.973	0.661	2.36x10 <sup>-8</sup>	0.889	0.955	NLT > NASH-W
cg12227411	SNORD115-15	0.973	0.682	9.36x10 <sup>-7</sup>	0.889	0.955	NLT > NASH-W
cg13178295	N/A	0.973	0.309	3.67x10 <sup>-3</sup>	0.889	0.955	NLT < NASH-W
cg13195185	TNFRSF13B	0.973	0.638	1.53x10 <sup>-10</sup>	0.917	0.955	NLT > NASH-W
cg18185028	DHX36	0.973	0.311	1.43x10 <sup>-8</sup>	0.889	0.955	NLT < NASH-W
cg24469923	ZNF440	0.973	0.094	1.07x10 <sup>-6</sup>	0.889	1	NLT < NASH-W
cg27248073	FAM64A	0.973	0.361	1.41x10 <sup>-9</sup>	0.917	0.909	NLT < NASH-W
cg00254681	PRRT1	0.972	0.205	1.39x10 <sup>-7</sup>	0.889	0.955	NLT < NASH-W
cg01073178	TESC	0.972	0.172	4.20x10 <sup>-11</sup>	0.889	1	NLT < NASH-W
cg01684248	N/A	0.972	0.414	1.59x10 <sup>-10</sup>	0.944	0.909	NLT < NASH-W
cg04294971	RFNG	0.972	0.299	1.57x10 <sup>-3</sup>	0.833	1	NLT < NASH-W
cg12313158	GRM4	0.972	0.574	4.83x10 <sup>-8</sup>	0.917	0.955	NLT > NASH-W
cg14497545	MAML3	0.972	0.604	9.04x10 <sup>-11</sup>	0.889	0.955	NLT > NASH-W
cg14977069	LIME1	0.972	0.439	1.07x10 <sup>-9</sup>	0.861	1	NLT < NASH-W
cg15473066	ZNF727	0.972	0.302	4.18x10 <sup>-8</sup>	0.889	1	NLT < NASH-W
cg16692538	N/A	0.972	0.568	3.85x10 <sup>-2</sup>	1	0.909	NLT > NASH-W
cg17810609	N/A	0.972	0.132	4.00x10 <sup>-4</sup>	0.944	0.909	NLT < NASH-W
cg19007908	TRPM4	0.972	0.628	2.13x10 <sup>-7</sup>	0.972	0.864	NLT < NASH-W
cg20673919	PATE4	0.972	0.469	3.64x10 <sup>-10</sup>	0.889	1	NLT > NASH-W
cg25220428	N/A	0.972	0.67	4.38x10 <sup>-4</sup>	0.833	1	NLT > NASH-W
cg03150409	WHSC1	0.971	0.717	2.62x10 <sup>-11</sup>	0.861	1	NLT > NASH-W
cg04176488	MGC23284	0.971	0.693	1.62x10 <sup>-8</sup>	0.833	1	NLT > NASH-W
cg04536393	C16orf91	0.971	0.486	2.25x10 <sup>-7</sup>	0.833	1	NLT > NASH-W
cg07576222	SMAD3	0.971	0.283	2.14x10 <sup>-8</sup>	0.889	1	NLT < NASH-W
cg08213792	N/A	0.971	0.648	3.59x10 <sup>-9</sup>	0.833	1	NLT > NASH-W
cg08524474	ARHGAP22	0.971	0.279	2.12x10 <sup>-9</sup>	0.917	0.955	NLT < NASH-W
cg13810766	PRKAG2	0.971	0.527	1.60x10 <sup>-11</sup>	0.861	0.955	NLT > NASH-W
cg14067770	IRF7	0.971	0.249	2.28x10 <sup>-8</sup>	0.833	1	NLT < NASH-W
cg14631053	SSTR4	0.971	0.288	5.06x10 <sup>-3</sup>	0.889	0.955	NLT < NASH-W
cg16357719	RNPS1	0.971	0.145	3.17x10 <sup>-5</sup>	0.917	0.955	NLT < NASH-W
cg18462141	N/A	0.971	0.672	1.59x10 <sup>-9</sup>	0.889	0.955	NLT > NASH-W
cg20615655	FAM21B	0.971	0.846	1.41x10 <sup>-5</sup>	0.861	1	NLT < NASH-W
cg24032568	PPP2R2D	0.971	0.874	8.33x10 <sup>-4</sup>	0.972	0.909	NLT < NASH-W
cg24153714	C10orf11	0.971	0.782	7.46x10 <sup>-3</sup>	0.861	0.955	NLT > NASH-W
cg27435660	FBXO18	0.971	0.714	8.83x10 <sup>-10</sup>	0.944	0.955	NLT > NASH-W
cg13551841	EHMT1	0.97	0.745	1.33x10 <sup>-6</sup>	1	0.909	NLT < NASH-W
cg00336022	N/A	0.97	0.735	1.42x10 <sup>-5</sup>	0.972	0.909	NLT < NASH-W

cg03973663	LYN	0.97	0.401	4.36x10 <sup>-8</sup>	0.889	1	NLT > NASH-W
cg04101934	N/A	0.97	0.488	9.49x10 <sup>-7</sup>	0.861	0.955	NLT < NASH-W
cg05211868	N/A	0.97	0.497	1.43x10 <sup>-8</sup>	0.833	1	NLT > NASH-W
cg06808467	LOC339290	0.97	0.181	4.02x10 <sup>-10</sup>	0.889	1	NLT < NASH-W
cg06959657	N/A	0.97	0.695	6.20x10 <sup>-9</sup>	0.972	0.909	NLT > NASH-W
cg08679807	ACOT7	0.97	0.709	1.54x10 <sup>-8</sup>	1	0.818	NLT > NASH-W
cg16678686	N/A	0.97	0.706	2.57x10 <sup>-6</sup>	0.917	0.909	NLT > NASH-W
cg22958118	N/A	0.97	0.653	2.53x10 <sup>-6</sup>	0.861	1	NLT > NASH-W
cg23770142	APOM	0.97	0.791	1.78x10 <sup>-7</sup>	0.917	0.909	NLT < NASH-W
cg24893198	N/A	0.97	0.865	1.05x10 <sup>-8</sup>	0.944	0.955	NLT < NASH-W
cg26272214	FAM5B	0.97	0.652	4.01x10 <sup>-3</sup>	0.889	1	NLT > NASH-W
cg27654966	CUX1	0.97	0.558	4.29x10 <sup>-8</sup>	0.944	0.909	NLT < NASH-W
cg01775802	RGS6	0.968	0.608	1.53x10 <sup>-9</sup>	0.917	0.909	NLT > NASH-W
cg01870519	EXOC2	0.968	0.634	1.91x10 <sup>-7</sup>	0.917	0.909	NLT > NASH-W
cg02173067	N/A	0.968	0.419	1.14x10 <sup>-3</sup>	0.833	1	NLT < NASH-W
cg02642298	PRDXDD1P	0.968	0.382	1.75x10 <sup>-7</sup>	0.889	1	NLT < NASH-W
cg03473408	MRPS18B	0.968	0.644	1.06x10 <sup>-5</sup>	0.972	0.909	NLT < NASH-W
cg04473235	N/A	0.968	0.617	8.13x10 <sup>-10</sup>	0.861	0.955	NLT > NASH-W
cg07737810	N/A	0.968	0.596	1.08x10 <sup>-7</sup>	0.944	0.864	NLT > NASH-W
cg09352908	N/A	0.968	0.835	1.66x10 <sup>-9</sup>	0.889	0.955	NLT > NASH-W
cg11964099	N/A	0.968	0.407	6.59x10 <sup>-7</sup>	0.861	1	NLT < NASH-W
cg23084309	MLLT1	0.968	0.238	1.69x10 <sup>-9</sup>	0.917	0.955	NLT < NASH-W
cg26330063	FAM105A	0.968	0.629	3.28x10 <sup>-8</sup>	0.806	1	NLT > NASH-W
cg26894854	SLC45A3	0.968	0.493	5.46x10 <sup>-4</sup>	0.972	0.864	NLT < NASH-W
cg00287477	ACSL1	0.967	0.27	4.26x10 <sup>-2</sup>	0.917	0.955	NLT < NASH-W
cg02524863	N/A	0.967	0.445	1.82x10 <sup>-5</sup>	0.889	0.955	NLT > NASH-W
cg06046629	CACNA1D	0.967	0.619	4.39x10 <sup>-10</sup>	0.833	1	NLT > NASH-W
cg06366345	SNORD114-31	0.967	0.755	9.16x10 <sup>-9</sup>	0.861	1	NLT > NASH-W
cg09741240	NQO2	0.967	0.167	1.03x10 <sup>-7</sup>	0.889	0.909	NLT < NASH-W
cg11311843	PHOSPHO1	0.967	0.308	1.91x10 <sup>-2</sup>	0.889	1	NLT < NASH-W
cg11677260	N/A	0.967	0.176	2.29x10 <sup>-4</sup>	0.833	1	NLT < NASH-W
cg12417549	N/A	0.967	0.634	1.15x10 <sup>-8</sup>	0.917	0.955	NLT > NASH-W
cg14094333	KLF3	0.967	0.264	3.79x10 <sup>-8</sup>	0.861	1	NLT < NASH-W
cg15465107	N/A	0.967	0.62	7.48x10 <sup>-11</sup>	0.917	0.955	NLT > NASH-W
cg19456996	GABBR1	0.967	0.208	6.42x10 <sup>-7</sup>	0.861	0.955	NLT < NASH-W
cg00593414	N/A	0.966	0.639	1.02x10 <sup>-6</sup>	1	0.818	NLT > NASH-W
cg01026613	TMEM214	0.966	0.521	1.08x10 <sup>-5</sup>	0.889	0.909	NLT < NASH-W
cg01400712	EFR3B	0.966	0.418	1.17x10 <sup>-7</sup>	0.889	1	NLT < NASH-W
cg06203912	N/A	0.966	0.745	1.53x10 <sup>-10</sup>	0.944	0.909	NLT > NASH-W
cg10420223	UBD	0.966	0.584	2.78x10 <sup>-9</sup>	0.972	0.955	NLT > NASH-W
cg12387604	ANKRD17	0.966	0.31	1.91x10 <sup>-9</sup>	0.861	0.955	NLT < NASH-W
cg14317230	MTDH	0.966	0.884	5.23x10 <sup>-5</sup>	0.972	0.818	NLT < NASH-W
cg16636571	GYPB	0.966	0.604	1.85x10 <sup>-6</sup>	0.861	1	NLT > NASH-W
cg17218154	KIAA0907	0.966	0.612	1.36x10 <sup>-7</sup>	0.944	0.864	NLT < NASH-W
cg17476752	N/A	0.966	0.563	1.01x10 <sup>-8</sup>	0.806	1	NLT > NASH-W
cg17499729	N/A	0.966	0.588	4.74x10 <sup>-8</sup>	0.861	0.955	NLT > NASH-W
cg17847344	EBF1	0.966	0.387	9.05x10 <sup>-5</sup>	0.972	0.864	NLT < NASH-W
cg20390253	C18orf22	0.966	0.308	4.05x10 <sup>-7</sup>	0.917	1	NLT < NASH-W
cg25738236	BRCA1	0.966	0.698	1.26x10 <sup>-7</sup>	0.861	0.955	NLT > NASH-W
cg00987699	WIPI2	0.965	0.199	2.14x10 <sup>-11</sup>	0.944	0.955	NLT < NASH-W
cg02531277	CUX1	0.965	0.613	2.96x10 <sup>-6</sup>	0.917	0.909	NLT < NASH-W
cg04396850	N/A	0.965	0.691	5.30x10 <sup>-6</sup>	0.944	0.909	NLT > NASH-W
cg05231098	SMARCA4	0.965	0.489	4.90x10 <sup>-8</sup>	0.861	1	NLT < NASH-W
cg08707819	RCOR1	0.965	0.363	1.30x10 <sup>-8</sup>	0.917	0.909	NLT < NASH-W
cg11397033	N/A	0.965	0.769	5.57x10 <sup>-5</sup>	0.917	0.909	NLT > NASH-W
cg12659254	FBRSL1	0.965	0.606	2.55x10 <sup>-9</sup>	0.944	0.864	NLT > NASH-W
cg13260314	N/A	0.965	0.651	1.09x10 <sup>-7</sup>	0.806	1	NLT > NASH-W
cg13896783	CCDC148	0.965	0.337	1.53x10 <sup>-9</sup>	0.861	1	NLT < NASH-W

cg14880282	LOC284232	0.965	0.624	5.69x10 <sup>-5</sup>	0.889	0.909	NLT > NASH-W
cg19933985	N/A	0.965	0.788	4.85x10 <sup>-8</sup>	0.889	0.909	NLT > NASH-W
cg20769334	SBF1	0.965	0.202	2.78x10 <sup>-8</sup>	0.889	0.955	NLT < NASH-W
cg20809690	TNIP2	0.965	0.369	6.58x10 <sup>-9</sup>	0.861	0.955	NLT < NASH-W
cg23129217	N/A	0.965	0.735	1.51x10 <sup>-5</sup>	0.889	0.955	NLT > NASH-W
cg23601374	HDAC4	0.965	0.55	4.16x10 <sup>-5</sup>	0.944	0.909	NLT < NASH-W
cg26112390	GOLGA2L1	0.965	0.721	1.17x10 <sup>-6</sup>	1	0.818	NLT > NASH-W
cg05310990	ZNF85	0.964	0.16	2.23x10 <sup>-6</sup>	0.806	1	NLT < NASH-W
cg04584009	REXO1	0.963	0.441	5.13x10 <sup>-7</sup>	0.917	0.909	NLT < NASH-W
cg04662828	N/A	0.963	0.525	1.86x10 <sup>-6</sup>	1	0.818	NLT > NASH-W
cg05703502	KIAA2018	0.963	0.506	8.60x10 <sup>-3</sup>	0.806	1	NLT < NASH-W
cg05909891	N/A	0.963	0.642	9.87x10 <sup>-9</sup>	0.861	0.955	NLT > NASH-W
cg08579753	N/A	0.963	0.534	6.88x10 <sup>-9</sup>	0.861	0.955	NLT > NASH-W
cg09570855	N/A	0.963	0.535	1.11x10 <sup>-6</sup>	0.778	1	NLT > NASH-W
cg10875261	N/A	0.963	0.811	3.36x10 <sup>-7</sup>	0.917	0.864	NLT > NASH-W
cg15617548	GORASP2	0.963	0.169	2.67x10 <sup>-8</sup>	0.806	1	NLT < NASH-W
cg15888301	NEO1	0.963	0.145	1.57x10 <sup>-5</sup>	0.917	0.955	NLT < NASH-W
cg16157055	N/A	0.963	0.578	1.64x10 <sup>-8</sup>	0.861	0.955	NLT > NASH-W
cg19861632	GPR125	0.963	0.545	3.86x10 <sup>-3</sup>	0.944	0.909	NLT < NASH-W
cg20943076	SDK1	0.963	0.757	4.85x10 <sup>-6</sup>	0.889	0.955	NLT > NASH-W
cg21530210	N/A	0.963	0.638	1.11x10 <sup>-6</sup>	0.972	0.909	NLT > NASH-W
cg23108607	KIAA0754	0.963	0.751	4.54x10 <sup>-7</sup>	0.861	0.955	NLT > NASH-W
cg25444615	N/A	0.963	0.374	3.74x10 <sup>-9</sup>	0.889	0.909	NLT > NASH-W
cg10187692	VPS13B	0.963	0.246	4.18x10 <sup>-3</sup>	0.861	1	NLT < NASH-W
cg00470768	INO80	0.962	0.583	3.48x10 <sup>-5</sup>	0.972	0.818	NLT > NASH-W
cg00731201	N/A	0.962	0.583	4.03x10 <sup>-4</sup>	0.917	0.955	NLT > NASH-W
cg01601050	STXBP6	0.962	0.233	1.35x10 <sup>-8</sup>	0.917	0.909	NLT > NASH-W
cg03196364	BEST3	0.962	0.538	1.77x10 <sup>-5</sup>	0.972	0.864	NLT > NASH-W
cg03321231	RPH3AL	0.962	0.711	1.31x10 <sup>-7</sup>	0.889	0.909	NLT > NASH-W
cg05526438	N/A	0.962	0.703	8.17x10 <sup>-9</sup>	0.917	0.955	NLT > NASH-W
cg07661849	ZNF827	0.962	0.643	4.77x10 <sup>-4</sup>	0.806	1	NLT > NASH-W
cg07867325	N/A	0.962	0.671	2.42x10 <sup>-8</sup>	0.889	0.955	NLT > NASH-W
cg08365438	N/A	0.962	0.654	1.04x10 <sup>-8</sup>	0.778	1	NLT > NASH-W
cg09622330	GRIN2A	0.962	0.77	3.15x10 <sup>-7</sup>	0.861	0.955	NLT > NASH-W
cg11855759	USP43	0.962	0.191	1.00x10 <sup>-8</sup>	0.889	0.955	NLT < NASH-W
cg12887985	N/A	0.962	0.187	3.01x10 <sup>-7</sup>	0.917	0.909	NLT < NASH-W
cg13435243	LRRC8A	0.962	0.858	1.04x10 <sup>-3</sup>	0.889	0.909	NLT < NASH-W
cg23322242	N/A	0.962	0.491	4.23x10 <sup>-11</sup>	0.806	1	NLT > NASH-W
cg23785719	STK17A	0.962	0.268	8.84x10 <sup>-8</sup>	0.944	0.909	NLT < NASH-W
cg24016617	N/A	0.962	0.625	1.00x10 <sup>-5</sup>	0.833	0.952	NLT > NASH-W
cg10475689	RUNDC2A	0.961	0.6	1.45x10 <sup>-8</sup>	0.829	1	NLT > NASH-W
cg01228685	PLEC1	0.961	0.659	3.90x10 <sup>-5</sup>	0.972	0.818	NLT > NASH-W
cg03916189	N/A	0.961	0.417	1.99x10 <sup>-4</sup>	0.972	0.909	NLT > NASH-W
cg04800503	HOXB3	0.961	0.409	1.90x10 <sup>-6</sup>	0.861	0.955	NLT < NASH-W
cg07797518	LRRFIP1	0.961	0.334	5.53x10 <sup>-6</sup>	0.944	0.864	NLT < NASH-W
cg09789536	KLHL17	0.961	0.308	3.90x10 <sup>-8</sup>	0.889	0.955	NLT < NASH-W
cg13041389	N/A	0.961	0.532	2.40x10 <sup>-5</sup>	0.972	0.909	NLT > NASH-W
cg13231117	N/A	0.961	0.757	1.28x10 <sup>-7</sup>	0.861	0.955	NLT > NASH-W
cg15615645	C10orf26	0.961	0.413	1.28x10 <sup>-3</sup>	0.917	0.909	NLT < NASH-W
cg15828524	CACNB3	0.961	0.738	1.61x10 <sup>-7</sup>	0.889	0.909	NLT < NASH-W
cg19569340	RNF216	0.961	0.427	1.15x10 <sup>-7</sup>	0.917	0.955	NLT < NASH-W
cg23113715	N/A	0.961	0.288	1.52x10 <sup>-9</sup>	0.861	1	NLT < NASH-W
cg23713156	WDR45L	0.961	0.193	6.56x10 <sup>-8</sup>	0.806	1	NLT < NASH-W
cg25548582	UTP14C	0.961	0.767	2.19x10 <sup>-4</sup>	0.917	1	NLT > NASH-W
cg00431813	C7orf50	0.96	0.542	1.38x10 <sup>-6</sup>	0.944	0.909	NLT < NASH-W
cg01779076	CFLAR	0.96	0.332	4.44x10 <sup>-7</sup>	0.889	0.909	NLT < NASH-W
cg02510736	ZCCHC24	0.96	0.186	1.38x10 <sup>-9</sup>	0.833	1	NLT < NASH-W
cg02792602	TNS1	0.96	0.214	7.17x10 <sup>-8</sup>	0.833	1	NLT < NASH-W

cg04607442	N/A	0.96	0.179	3.33x10 <sup>-8</sup>	0.889	0.955	NLT < NASH-W
cg04680436	N/A	0.96	0.548	4.32x10 <sup>-4</sup>	0.944	0.909	NLT < NASH-W
cg04762129	N/A	0.96	0.552	1.58x10 <sup>-7</sup>	0.806	1	NLT > NASH-W
cg04786142	N/A	0.96	0.698	7.34x10 <sup>-4</sup>	0.917	0.909	NLT > NASH-W
cg05393736	NRBF2	0.96	0.701	1.43x10 <sup>-6</sup>	0.972	0.818	NLT < NASH-W
cg06356708	RCC2	0.96	0.822	6.33x10 <sup>-6</sup>	0.806	1	NLT < NASH-W
cg06606511	N/A	0.96	0.617	7.12x10 <sup>-10</sup>	0.806	1	NLT > NASH-W
cg08648997	LRP5	0.96	0.683	3.15x10 <sup>-6</sup>	0.972	0.909	NLT < NASH-W
cg10199913	HIST1H3C	0.96	0.164	9.70x10 <sup>-5</sup>	0.778	1	NLT < NASH-W
cg14520079	N/A	0.96	0.524	4.10x10 <sup>-6</sup>	0.917	0.864	NLT > NASH-W
cg14564724	ABCA1	0.96	0.446	7.75x10 <sup>-5</sup>	0.889	0.955	NLT < NASH-W
cg15574461	SRC	0.96	0.822	3.56x10 <sup>-3</sup>	0.944	0.864	NLT < NASH-W
cg16136385	CKAP5	0.96	0.284	8.63x10 <sup>-9</sup>	0.889	1	NLT < NASH-W
cg16920238	CCDC57	0.96	0.547	2.31x10 <sup>-3</sup>	0.889	0.955	NLT < NASH-W
cg17030628	IL20	0.96	0.461	4.00x10 <sup>-4</sup>	0.889	0.955	NLT < NASH-W
cg17030981	ZNF876P	0.96	0.715	5.54x10 <sup>-9</sup>	0.833	0.955	NLT > NASH-W
cg18371636	POM121C	0.96	0.716	7.48x10 <sup>-8</sup>	0.861	0.955	NLT > NASH-W
cg19513374	ZNF311	0.96	0.714	1.59x10 <sup>-5</sup>	0.778	1	NLT > NASH-W
cg21610999	SPDYE4	0.96	0.609	6.56x10 <sup>-10</sup>	0.889	1	NLT > NASH-W
cg21685006	PPP1R2P1	0.96	0.578	3.87x10 <sup>-4</sup>	0.917	0.909	NLT < NASH-W
cg22900519	N/A	0.96	0.778	1.46x10 <sup>-8</sup>	0.889	1	NLT > NASH-W
cg27056425	HIST1H2AI	0.96	0.147	3.50x10 <sup>-4</sup>	0.889	0.955	NLT < NASH-W
cg01864791	BHLHE40	0.958	0.571	2.15x10 <sup>-2</sup>	0.917	0.955	NLT < NASH-W
cg05596328	N/A	0.958	0.241	3.87x10 <sup>-4</sup>	0.944	0.909	NLT < NASH-W
cg05997362	LYN	0.958	0.428	5.05x10 <sup>-7</sup>	0.833	1	NLT > NASH-W
cg06375525	ESPNL	0.958	0.796	8.04x10 <sup>-4</sup>	0.861	1	NLT < NASH-W
cg10827434	RPF1	0.958	0.108	2.41x10 <sup>-6</sup>	0.833	1	NLT < NASH-W
cg11223184	ANKRD44	0.958	0.837	4.70x10 <sup>-7</sup>	0.778	1	NLT < NASH-W
cg14325661	TRPM4	0.958	0.646	7.36x10 <sup>-7</sup>	0.972	0.909	NLT < NASH-W
cg15050398	N/A	0.958	0.473	1.68x10 <sup>-7</sup>	1	0.773	NLT > NASH-W
cg15610437	AZU1	0.958	0.7	6.70x10 <sup>-5</sup>	0.944	0.909	NLT > NASH-W
cg16015499	TAGLN2	0.958	0.821	2.79x10 <sup>-7</sup>	0.889	0.955	NLT > NASH-W
cg16674116	TOLLIP	0.958	0.531	1.98x10 <sup>-5</sup>	0.917	0.909	NLT < NASH-W
cg17095167	N/A	0.958	0.795	6.14x10 <sup>-8</sup>	0.806	1	NLT > NASH-W
cg21285133	ANP32E	0.958	0.364	3.99x10 <sup>-7</sup>	0.972	0.818	NLT > NASH-W
cg21397124	N/A	0.958	0.562	2.54x10 <sup>-5</sup>	0.889	0.909	NLT > NASH-W
cg26528255	TMEM222	0.958	0.713	7.40x10 <sup>-8</sup>	0.861	0.955	NLT > NASH-W
cg14950303	FOXD4L1	0.957	0.519	2.88x10 <sup>-6</sup>	0.914	0.909	NLT < NASH-W
cg00109302	N/A	0.957	0.167	5.88x10 <sup>-4</sup>	0.917	0.955	NLT < NASH-W
cg01236961	N/A	0.957	0.615	1.08x10 <sup>-6</sup>	0.861	0.955	NLT > NASH-W
cg01346915	UBE2I	0.957	0.877	3.44x10 <sup>-5</sup>	0.889	0.909	NLT < NASH-W
cg02095553	N/A	0.957	0.62	1.50x10 <sup>-6</sup>	0.889	0.909	NLT > NASH-W
cg02536431	TUBB	0.957	0.606	7.59x10 <sup>-6</sup>	0.75	1	NLT > NASH-W
cg03734864	PRR5L	0.957	0.505	3.67x10 <sup>-5</sup>	0.889	0.909	NLT < NASH-W
cg04680494	KIF25	0.957	0.733	2.12x10 <sup>-5</sup>	0.861	0.955	NLT > NASH-W
cg05357347	N/A	0.957	0.785	4.90x10 <sup>-5</sup>	0.778	1	NLT > NASH-W
cg10530613	TRIT1	0.957	0.83	1.16x10 <sup>-4</sup>	0.917	0.955	NLT < NASH-W
cg10558740	FLJ22536	0.957	0.688	2.51x10 <sup>-3</sup>	0.944	0.864	NLT > NASH-W
cg10632328	FLJ35220	0.957	0.183	2.97x10 <sup>-4</sup>	0.972	0.818	NLT < NASH-W
cg11152384	N/A	0.957	0.429	1.38x10 <sup>-6</sup>	0.972	0.909	NLT > NASH-W
cg11218561	N/A	0.957	0.756	6.05x10 <sup>-7</sup>	0.833	1	NLT > NASH-W
cg13048147	ATP5H	0.957	0.594	1.76x10 <sup>-5</sup>	0.861	0.955	NLT < NASH-W
cg17341174	BAIAP2L1	0.957	0.504	1.92x10 <sup>-5</sup>	0.944	0.909	NLT < NASH-W
cg18545992	NCRNA00164	0.957	0.498	9.86x10 <sup>-7</sup>	1	0.818	NLT > NASH-W
cg20407713	DLG2	0.957	0.791	2.18x10 <sup>-8</sup>	0.917	0.909	NLT > NASH-W
cg21290290	C1orf93	0.957	0.165	3.46x10 <sup>-6</sup>	0.889	0.909	NLT < NASH-W
cg25187967	N/A	0.957	0.804	1.73x10 <sup>-8</sup>	0.833	1	NLT > NASH-W
cg26015681	N/A	0.957	0.481	1.64x10 <sup>-3</sup>	0.944	0.864	NLT > NASH-W



cg25367568	GNAS	0.956	0.671	1.62x10 <sup>-2</sup>	0.914	0.955	NLT > NASH-W
cg01079950	N/A	0.956	0.651	3.13x10 <sup>-2</sup>	0.944	0.864	NLT > NASH-W
cg01730258	SNX32	0.956	0.528	9.00x10 <sup>-5</sup>	0.917	0.909	NLT < NASH-W
cg01993208	C9orf3	0.956	0.42	5.41x10 <sup>-5</sup>	0.917	0.955	NLT < NASH-W
cg01994308	PLAG1	0.956	0.253	2.02x10 <sup>-8</sup>	0.861	0.955	NLT < NASH-W
cg02788013	INPP5D	0.956	0.662	2.65x10 <sup>-5</sup>	0.806	1	NLT > NASH-W
cg03008165	N/A	0.956	0.796	9.94x10 <sup>-9</sup>	0.861	0.955	NLT > NASH-W
cg03274739	N/A	0.956	0.844	1.60x10 <sup>-2</sup>	0.833	1	NLT > NASH-W
cg05060577	N/A	0.956	0.565	3.20x10 <sup>-3</sup>	0.833	1	NLT > NASH-W
cg05484985	N/A	0.956	0.637	8.65x10 <sup>-5</sup>	0.972	0.864	NLT < NASH-W
cg05742286	N/A	0.956	0.704	1.35x10 <sup>-8</sup>	0.889	0.909	NLT > NASH-W
cg07628073	N/A	0.956	0.611	1.28x10 <sup>-7</sup>	0.944	0.909	NLT < NASH-W
cg07762785	ZNF486	0.956	0.683	1.30x10 <sup>-6</sup>	0.944	0.909	NLT > NASH-W
cg08775137	N/A	0.956	0.736	4.85x10 <sup>-4</sup>	0.972	0.909	NLT > NASH-W
cg09686800	IPMK	0.956	0.679	6,74x10 <sup>-6</sup>	0.972	0.818	NLT < NASH-W
cg10752406	AZU1	0.956	0.592	1.08x10 <sup>-6</sup>	0.833	1	NLT > NASH-W
cg12828313	N/A	0.956	0.197	1.37x10 <sup>-9</sup>	0.889	0.955	NLT < NASH-W
cg18210511	ZC3H3	0.956	0.521	1.20x10 <sup>-5</sup>	0.889	0.909	NLT < NASH-W
cg19015611	VAX2	0.956	0.463	3.57x10 <sup>-10</sup>	0.806	1	NLT < NASH-W
cg19556901	SNORD115-1	0.956	0.789	6.59x10 <sup>-6</sup>	0.889	0.909	NLT > NASH-W
cg19955284	SLC44A4	0.956	0.609	1.60x10 <sup>-6</sup>	0.889	0.955	NLT < NASH-W
cg23157419	PTPN9	0.956	0.672	1.39x10 <sup>-6</sup>	0.833	1	NLT < NASH-W
cg23465426	PPP1R2P1	0.956	0.597	3.17x10 <sup>-7</sup>	0.806	1	NLT > NASH-W
cg23476209	LOC100133315	0.956	0.574	1.72x10 <sup>-4</sup>	0.861	1	NLT < NASH-W
cg24599650	RPL8	0.956	0.638	1.48x10 <sup>-5</sup>	0.889	0.909	NLT > NASH-W
cg27055601	LAMP1	0.956	0.504	4.30x10 <sup>-3</sup>	0.806	1	NLT < NASH-W
cg00236302	RAP1B	0.955	0.461	4.57x10 <sup>-7</sup>	0.889	0.955	NLT < NASH-W
cg03092271	RPSAP58	0.955	0.594	1.67x10 <sup>-6</sup>	0.914	0.864	NLT > NASH-W
cg04010872	N/A	0.955	0.752	2.70x10 <sup>-3</sup>	0.861	0.955	NLT > NASH-W
cg04892437	TSNAX-DISC1	0.955	0.494	3.84x10 <sup>-5</sup>	0.972	0.909	NLT < NASH-W
cg07102320	N/A	0.955	0.504	1.02x10 <sup>-6</sup>	0.944	0.864	NLT < NASH-W
cg07475178	LDHD	0.955	0.742	3.75x10 <sup>-7</sup>	0.944	0.909	NLT < NASH-W
cg09141413	GPRC5B	0.955	0.233	8.96x10 <sup>-6</sup>	0.972	0.818	NLT < NASH-W
cg10690677	CLCA4	0.955	0.843	4.62x10 <sup>-7</sup>	0.917	0.955	NLT > NASH-W
cg12538597	N/A	0.955	0.677	2.11x10 <sup>-7</sup>	0.861	0.955	NLT > NASH-W
cg14058010	N/A	0.955	0.31	1.28x10 <sup>-6</sup>	0.917	0.864	NLT > NASH-W
cg17424859	N/A	0.955	0.704	9.04x10 <sup>-7</sup>	0.861	0.955	NLT > NASH-W
cg19751754	N/A	0.955	0.564	4.96x10 <sup>-6</sup>	0.889	0.864	NLT > NASH-W
cg21518151	N/A	0.955	0.628	3.86x10 <sup>-8</sup>	0.944	0.909	NLT > NASH-W
cg22685816	MUC6	0.955	0.505	1.45x10 <sup>-3</sup>	0.917	0.864	NLT < NASH-W
cg22921692	FBXL12	0.955	0.68	2.19x10 <sup>-7</sup>	0.889	0.909	NLT > NASH-W
cg24192846	PPP1R11	0.955	0.674	5.74x10 <sup>-9</sup>	0.861	0.955	NLT > NASH-W
cg24946729	DTNA	0.955	0.607	2.24x10 <sup>-5</sup>	0.889	0.955	NLT < NASH-W
cg26111913	FARP1	0.955	0.71	2.46x10 <sup>-7</sup>	0.889	0.909	NLT > NASH-W
cg27048142	IGFL4	0.955	0.674	8.63x10 <sup>-5</sup>	0.889	0.955	NLT > NASH-W
cg22306579	ZBTB12	0.955	0.385	2.35x10 <sup>-5</sup>	0.917	0.909	NLT < NASH-W
cg01214458	MN1	0.953	0.302	1.84x10 <sup>-3</sup>	0.833	0.955	NLT < NASH-W
cg01488306	F13B	0.953	0.61	1.18x10 <sup>-4</sup>	1	0.773	NLT > NASH-W
cg02072589	N/A	0.953	0.583	9.33x10 <sup>-7</sup>	0.861	0.955	NLT > NASH-W
cg02438164	N/A	0.953	0.52	2.65x10 <sup>-6</sup>	0.889	0.864	NLT > NASH-W
cg02596190	BNIP2	0.953	0.439	2.19x10 <sup>-5</sup>	1	0.818	NLT < NASH-W
cg03488113	N/A	0.953	0.685	1.61x10 <sup>-6</sup>	0.861	0.955	NLT > NASH-W
cg04628742	HLA-J	0.953	0.762	1.34x10 <sup>-3</sup>	0.833	1	NLT > NASH-W
cg05998816	PCNT	0.953	0.803	6.79x10 <sup>-6</sup>	0.972	0.818	NLT > NASH-W
cg06752157	MYST4	0.953	0.55	1.65x10 <sup>-2</sup>	0.861	0.909	NLT < NASH-W
cg08008286	SULT1A1	0.953	0.467	5.12x10 <sup>-5</sup>	0.833	1	NLT < NASH-W
cg08450091	N/A	0.953	0.704	7.64x10 <sup>-11</sup>	0.889	0.955	NLT > NASH-W
cg08858272	NALCN	0.953	0.412	4.4x10 <sup>-6</sup>	0.889	0.955	NLT > NASH-W

cg10195415	TRIM65	0.953	0.557	2.04x10 <sup>-2</sup>	0.889	0.909	NLT < NASH-W
cg10888281	CEP68	0.953	0.322	1.42x10 <sup>-5</sup>	0.778	1	NLT < NASH-W
cg11010178	C6orf174	0.953	0.203	1.23x10 <sup>-6</sup>	0.861	0.955	NLT < NASH-W
cg11820154	N/A	0.953	0.513	1.70x10 <sup>-5</sup>	0.972	0.909	NLT < NASH-W
cg11822175	N/A	0.953	0.692	3.75x10 <sup>-2</sup>	0.944	0.818	NLT > NASH-W
cg11957128	LOC150786	0.953	0.607	1.20x10 <sup>-6</sup>	0.806	1	NLT > NASH-W
cg13560760	PMPCA	0.953	0.635	7.01x10 <sup>-7</sup>	0.806	1	NLT > NASH-W
cg14072016	DIP2C	0.953	0.395	4.09x10 <sup>-2</sup>	0.833	1	NLT < NASH-W
cg15371806	KIF25	0.953	0.692	1.37x10 <sup>-4</sup>	0.889	0.955	NLT > NASH-W
cg15945209	N/A	0.953	0.594	3.86x10 <sup>-5</sup>	1	0.773	NLT > NASH-W
cg17304646	N/A	0.953	0.346	6.11x10 <sup>-4</sup>	0.944	0.864	NLT < NASH-W
cg23932332	DUSP10	0.953	0.6	1.52x10 <sup>-3</sup>	0.833	1	NLT < NASH-W
cg24939819	GPN2	0.953	0.473	7.25x10 <sup>-5</sup>	0.861	0.955	NLT < NASH-W
cg25270498	METRNL	0.953	0.194	9.85x10 <sup>-8</sup>	0.861	0.955	NLT < NASH-W
cg26385097	N/A	0.953	0.366	4.22x10 <sup>-6</sup>	0.944	0.864	NLT > NASH-W
cg26414000	C1orf52	0.953	0.336	1.73x10 <sup>-3</sup>	0.833	0.955	NLT < NASH-W
cg26583598	ZSWIM6	0.953	0.727	9.95x10 <sup>-7</sup>	0.972	0.864	NLT < NASH-W
cg09232069	SEC14L1	0.953	0.319	1.27x10 <sup>-3</sup>	0.943	0.864	NLT < NASH-W
cg00334245	N/A	0.952	0.136	7.97x10 <sup>-4</sup>	0.861	1	NLT < NASH-W
cg02642549	LHFPL2	0.952	0.382	6.44x10 <sup>-8</sup>	0.833	0.955	NLT > NASH-W
cg03674076	CSNK2A1	0.952	0.291	3.79x10 <sup>-6</sup>	0.917	0.909	NLT < NASH-W
cg05341610	ZNF264	0.952	0.687	2.32x10 <sup>-5</sup>	0.972	0.818	NLT > NASH-W
cg06852575	ZNF257	0.952	0.264	3.68x10 <sup>-8</sup>	0.889	0.955	NLT < NASH-W
cg07039975	DCTN1	0.952	0.507	7.93x10 <sup>-3</sup>	0.944	0.864	NLT < NASH-W
cg07058086	KIF13B	0.952	0.212	1.01x10 <sup>-7</sup>	0.889	0.955	NLT < NASH-W
cg07100957	ZNF324	0.952	0.722	3.73x10 <sup>-6</sup>	0.972	0.773	NLT > NASH-W
cg08072980	IKZF1	0.952	0.653	8.63x10 <sup>-9</sup>	0.861	1	NLT > NASH-W
cg08914926	CLIP1	0.952	0.683	4.82x10 <sup>-6</sup>	0.917	0.909	NLT < NASH-W
cg11354266	LOC285954	0.952	0.409	4.12x10 <sup>-2</sup>	0.972	0.864	NLT < NASH-W
cg11527367	C1orf152	0.952	0.638	3.23x10 <sup>-9</sup>	0.917	0.909	NLT > NASH-W
cg12728623	COMT	0.952	0.467	6.76x10 <sup>-4</sup>	0.917	0.909	NLT < NASH-W
cg12895701	N/A	0.952	0.73	3.65x10 <sup>-7</sup>	0.972	0.818	NLT < NASH-W
cg15164048	ARHGEF10	0.952	0.749	4.66x10 <sup>-6</sup>	1	0.818	NLT > NASH-W
cg17806401	LYN	0.952	0.572	2.14x10 <sup>-5</sup>	0.917	0.909	NLT > NASH-W
cg18440889	SHANK2	0.952	0.767	1.00x10 <sup>-8</sup>	0.833	1	NLT > NASH-W
cg18593660	NAV2	0.952	0.425	2.18x10 <sup>-6</sup>	0.917	0.909	NLT < NASH-W
cg20023538	N/A	0.952	0.639	7.73x10 <sup>-6</sup>	1	0.773	NLT > NASH-W
cg24738257	N/A	0.952	0.646	3.42x10 <sup>-6</sup>	0.889	0.955	NLT > NASH-W
cg24958366	N/A	0.952	0.459	2.03x10 <sup>-6</sup>	0.944	0.864	NLT > NASH-W
cg25098401	LCE2B	0.952	0.687	4.78x10 <sup>-3</sup>	0.861	1	NLT > NASH-W
cg26215406	MCF2L2	0.952	0.652	1.70x10 <sup>-3</sup>	0.917	0.909	NLT > NASH-W
cg26520012	N/A	0.952	0.288	9.16x10 <sup>-5</sup>	0.917	0.909	NLT < NASH-W
cg13719443	LOC285847	0.952	0.413	9.08x10 <sup>-8</sup>	0.943	0.909	NLT > NASH-W
cg14288091	NIPAL2	0.952	0.186	7.29x10 <sup>-6</sup>	0.914	0.909	NLT > NASH-W
cg16898066	HIST1H2BA	0.952	0.718	3.70x10 <sup>-6</sup>	0.857	0.955	NLT > NASH-W
cg00316520	N/A	0.951	0.727	1.40x10 <sup>-5</sup>	0.889	0.909	NLT > NASH-W
cg00318436	PAR6A	0.951	0.528	7.33x10 <sup>-7</sup>	0.944	0.909	NLT < NASH-W
cg01554453	ENPP1	0.951	0.275	8.65x10 <sup>-8</sup>	0.861	1	NLT < NASH-W
cg02539829	PGAP1	0.951	0.866	2.09x10 <sup>-5</sup>	1	0.818	NLT < NASH-W
cg02718464	SUGT1L1	0.951	0.806	5.15x10 <sup>-5</sup>	0.861	0.955	NLT > NASH-W
cg03611809	N/A	0.951	0.769	1.33x10 <sup>-6</sup>	0.917	0.864	NLT < NASH-W
cg03853620	PK4	0.951	0.566	4.64x10 <sup>-5</sup>	0.861	0.955	NLT < NASH-W
cg04020984	LOC100270746	0.951	0.259	9.48x10 <sup>-8</sup>	0.889	1	NLT < NASH-W
cg04396721	MOSC1	0.951	0.499	2.73x10 <sup>-2</sup>	0.889	0.864	NLT < NASH-W
cg05064489	SEC31B	0.951	0.47	1.10x10 <sup>-4</sup>	0.944	0.909	NLT < NASH-W
cg05234035	N/A	0.951	0.245	2.40x10 <sup>-5</sup>	0.944	0.864	NLT < NASH-W
cg05861743	APOM	0.951	0.808	1.64x10 <sup>-7</sup>	0.944	0.909	NLT < NASH-W
cg07223240	N/A	0.951	0.701	2.90x10 <sup>-7</sup>	0.889	0.909	NLT > NASH-W

cg09212610	<i>GABARAPL3</i>	0.951	0.791	$2.04 \times 10^{-7}$	0.917	0.909	NLT > NASH-W
cg09580859	<i>ZC3H3</i>	0.951	0.653	$4.45 \times 10^{-5}$	0.889	0.909	NLT < NASH-W
cg11586591	<i>SORL1</i>	0.951	0.577	$4.19 \times 10^{-4}$	0.833	0.955	NLT < NASH-W
cg11772086	<i>MCC</i>	0.951	0.509	$1.14 \times 10^{-3}$	0.889	0.909	NLT < NASH-W
cg14579098	<i>ILF3</i>	0.951	0.645	$2.92 \times 10^{-5}$	0.833	0.955	NLT > NASH-W
cg16074383	<i>ZNF219</i>	0.951	0.713	$3.19 \times 10^{-6}$	0.889	0.909	NLT < NASH-W
cg16117273	<i>PRKD1</i>	0.951	0.29	$2.73 \times 10^{-6}$	0.889	0.955	NLT < NASH-W
cg16282910	<i>N/A</i>	0.951	0.657	$4.96 \times 10^{-8}$	0.833	1	NLT > NASH-W
cg16478145	<i>TFPI</i>	0.951	0.544	$3.53 \times 10^{-4}$	0.917	0.909	NLT < NASH-W
cg17461271	<i>N/A</i>	0.951	0.695	$8.05 \times 10^{-8}$	0.917	0.955	NLT > NASH-W
cg18642567	<i>RPGRIP1</i>	0.951	0.722	$7.52 \times 10^{-8}$	0.833	1	NLT > NASH-W
cg18690712	<i>DNAH12</i>	0.951	0.645	$1.91 \times 10^{-6}$	0.944	0.864	NLT > NASH-W
cg19912309	<i>N/A</i>	0.951	0.639	$2.96 \times 10^{-5}$	0.917	0.864	NLT > NASH-W
cg20414217	<i>HSD3B2</i>	0.951	0.616	$4.64 \times 10^{-8}$	0.806	1	NLT > NASH-W

<sup>a</sup>Probe ID of the Infinium HumanMethylation450 BeadChip. <sup>b</sup>National Center for Biotechnology Information (NCBI) database (Genome Build 37). <sup>c</sup>The Youden index was used as a cutoff value for discriminating NASH-W samples from NLT samples for each probe. <sup>d</sup>Sensitivity was defined as the ratio of the number of tissue samples diagnosed as NASH-W based on the criteria relative to the exact number of the NASH-W samples. <sup>e</sup>Specificity was defined as the ratio of the number of tissue samples not diagnosed as NASH-W based on the criteria relative to the exact number of the NLT samples. <sup>f</sup>NASH-W < NLT: the sample was predicted to be NASH-W and/or carcinogenic risk-positive when its DNA methylation level was lower than the cutoff value; NASH-W > NLT: the sample was predicted to be NASH-W and/or carcinogenic risk-positive when its DNA methylation level was higher than the cutoff value. *N/A*, not annotated (designed in the intergenic regions).

**Additional file 5: Supplementary Table S4** Seventy statistically significant pathway maps in which the 415 probes showing area under the curve (AUC) values more than 0.95 for discrimination of non-cancerous liver tissue samples showing non-alcoholic steatohepatitis from patients with hepatocellular carcinoma (NASH-W) from normal liver tissue (NLT) samples, and were designed for the 339 genes, were significantly ( $P < 0.05$ ) accumulated, as revealed by Reactome pathway analysis (<https://reactome.org>).

ID	Description	P	Involved genes showing AUC values of more than 0.95 for discrimination of MASH-W samples from NLT samples
R-HSA-210990	PECAM1 interactions	0.000672	<i>INPP5D, LYN, SRC</i>
R-HSA-3247509	Chromatin modifying enzymes	0.000904	<i>NSD2, SMARCA4, H2AC13, H2BC13, H3C3, KAT6B, RCOR1, ELP5, MRGBP, EHMT1, H2BC1, H2AC1</i>
R-HSA-4839726	Chromatin organization	0.000904	<i>NSD2, SMARCA4, H2AC13, H2BC13, H3C3, KAT6B, RCOR1, ELP5, MRGBP, EHMT1, H2BC1, H2AC1</i>
R-HSA-1632852	Macroautophagy	0.001041	<i>WIPI2, PARK7, CSNK2A1, SRC, PCNT, TOMM20, PRKAG2, WDR45B</i>
R-HSA-3214847	HATs acetylate histones	0.001375	<i>H2AC13, H2BC13, H3C3, KAT6B, ELP5, MRGBP, H2BC1, H2AC1</i>
R-HSA-9663891	Selective autophagy	0.001375	<i>PARK7, CSNK2A1, SRC, PCNT, TOMM20, PRKAG2</i>
R-HSA-68886	M Phase	0.001629	<i>PPP2R2D, CKAP5, DCTN1, RCC2, CTDNEP1, CSNK2A1, CLIP1, UBE2I, H2BC13, H3C3, PCNT, RAN, GORASP2, H2BC1, TUBB</i>
R-HSA-9612973	Autophagy	0.002030	<i>WIPI2, PARK7, CSNK2A1, SRC, PCNT, TOMM20, PRKAG2, WDR45B</i>
R-HSA-3214815	HDACs deacetylate histones	0.002940	<i>H2AC13, H2BC13, H3C3, RCOR1, H2BC1, H2AC1</i>
R-HSA-9620244	Long-term potentiation	0.005412	<i>GRIN2A, DLG2, SRC</i>
R-HSA-5693565	Recruitment and ATM-mediated phosphorylation of repair and signaling proteins at DNA double strand breaks	0.006073	<i>NSD2, UBE2I, H2BC13, BRCA1, H2BC1</i>
R-HSA-5693606	DNA Double Strand Break Response	0.006411	<i>NSD2, UBE2I, H2BC13, BRCA1, H2BC1</i>
R-HSA-373752	Netrin-1 signaling	0.006715	<i>NEO1, SRC, PTPNA, MYO10</i>
R-HSA-1221632	Meiotic synapsis	0.006763	<i>ACD, UBE2I, H2BC13, BRCA1, H2BC1</i>
R-HSA-2559582	Senescence-Associated Secretory Phenotype (SASP)	0.006925	<i>RPS6KA2, CDK6, H2BC13, H3C3, EHMT1, H2BC1</i>
R-HSA-438064	Post NMDA receptor activation events	0.007128	<i>GRIN2A, RPS6KA2, DLG2, SRC, PRKAG2</i>
R-HSA-1483191	Synthesis of PC	0.008382	<i>PHOSPHO1, CSNK2A1, SLC44A4</i>
R-HSA-1500620	Meiosis	0.008863	<i>ACD, UBE2I, H2BC13, H3C3, BRCA1, H2BC1</i>
R-HSA-5205647	Mitophagy	0.009247	<i>CSNK2A1, SRC, TOMM20</i>
R-HSA-8934903	Receptor Mediated Mitophagy	0.011386	<i>CSNK2A1, SRC</i>
R-HSA-442755	Activation of NMDA receptors and postsynaptic events	0.013191	<i>GRIN2A, RPS6KA2, DLG2, SRC, PRKAG2</i>
R-HSA-112308	Presynaptic depolarization and calcium channel opening	0.013528	<i>CACNB3, CACNG2</i>
R-HSA-2029481	FCGR activation	0.013528	<i>LYN, SRC</i>
R-HSA-5693567	HDR through Homologous Recombination (HRR) or Single Strand Annealing (SSA)	0.014844	<i>NSD2, RAD51B, UBE2I, H2BC13, BRCA1, H2BC1</i>
R-HSA-1268020	Mitochondrial protein import	0.015756	<i>CHCHD7, TOMM20, PMPCA, LDHD</i>
R-HSA-5693607	Processing of DNA double-strand break ends	0.016240	<i>NSD2, UBE2I, H2BC13, BRCA1, H2BC1</i>
R-HSA-5689901	Metalloprotease DUBs	0.018015	<i>H2AC13, BRCA1, H2AC1</i>
R-HSA-5693538	Homology Directed Repair	0.018108	<i>NSD2, RAD51B, UBE2I, H2BC13, BRCA1, H2BC1</i>
R-HSA-5693571	Nonhomologous End-Joining (NHEJ)	0.020240	<i>NSD2, H2BC13, BRCA1, H2BC1</i>
R-HSA-68875	Mitotic Prophase	0.020539	<i>PPP2R2D, CTDNEP1, H2BC13, H3C3, GORASP2, H2BC1</i>
R-HSA-354194	GRB2:SOS provides linkage to MAPK signaling for Integrins	0.020895	<i>RAP1B, SRC</i>
R-HSA-372708	p130Cas linkage to MAPK signaling for integrins	0.020895	<i>RAP1B, SRC</i>
R-HSA-3772470	Negative regulation of TCF-dependent signaling by WNT ligand antagonists	0.020895	<i>LRP5, DKK1</i>
R-HSA-1474165	Reproduction	0.021180	<i>ACD, UBE2I, H2BC13, H3C3, BRCA1, H2BC1</i>
R-HSA-112315	Transmission across Chemical Synapses	0.021203	<i>CACNB3, COMT, GRIN2A, RPS6KA2, DLG2, GABBR1, SRC, CACNG2, PRKAG2</i>
R-HSA-380259	Loss of Nlp from mitotic centrosomes	0.021221	<i>CKAP5, DCTN1, PCNT, TUBB</i>
R-HSA-380284	Loss of proteins required for interphase microtubule organization from the centrosome	0.021221	<i>CKAP5, DCTN1, PCNT, TUBB</i>
R-HSA-1433559	Regulation of KIT signaling	0.023647	<i>LYN, SRC</i>
R-HSA-2730905	Role of LAT2/NTALLAB on calcium mobilization	0.023647	<i>LYN, LAT2</i>
R-HSA-8854518	AURKA Activation by TPX2	0.024338	<i>CKAP5, DCTN1, PCNT, TUBB</i>
R-HSA-1912422	Pre-NOTCH Expression and Processing	0.024516	<i>RFNG, H2BC13, H3C3, MAML3, H2BC1</i>
R-HSA-8934593	Regulation of RUNX1 Expression and Activity	0.026538	<i>CDK6, SRC</i>
R-HSA-157118	Signaling by NOTCH	0.026624	<i>RFNG, H2BC13, H3C3, SMAD3, HDAC4, IKZF1, MAML3, H2BC1</i>
R-HSA-1839117	Signaling by cytosolic FGFR1 fusion mutants	0.029563	<i>LRRFIP1, CUX1</i>
R-HSA-2559583	Cellular Senescence	0.029720	<i>RPS6KA2, ACD, CDK6, H2BC13, H3C3, EHMT1, H2BC1</i>
R-HSA-5663202	Diseases of signal transduction by growth factor receptors and second messengers	0.030938	<i>RAP1B, LYN, DCTN1, LRRFIP1, CUX1, LRP5, SRC, SMAD3, HDAC4, DUSP10, DKK1, MAML3</i>
R-HSA-9610379	HCMV Late Events	0.030981	<i>H2AC13, H2BC13, H3C3, H2BC1, H2AC1</i>
R-HSA-3214858	RMTs methylate histone arginines	0.031367	<i>SMARCA4, H2AC13, H3C3, H2AC1</i>
R-HSA-69231	Cyclin D associated events in G1	0.033724	<i>LYN, CDK6, SRC</i>
R-HSA-69236	G1 Phase	0.033724	<i>LYN, CDK6, SRC</i>
R-HSA-68877	Mitotic Prometaphase	0.034953	<i>CKAP5, DCTN1, RCC2, CSNK2A1, CLIP1, PCNT, TUBB</i>
R-HSA-380270	Recruitment of mitotic centrosome proteins and complexes	0.035284	<i>CKAP5, DCTN1, PCNT, TUBB</i>
R-HSA-380287	Centrosome maturation	0.035284	<i>CKAP5, DCTN1, PCNT, TUBB</i>
R-HSA-112314	Neurotransmitter receptors and postsynaptic signal transmission	0.035748	<i>GRIN2A, RPS6KA2, DLG2, GABBR1, SRC, CACNG2, PRKAG2</i>
R-HSA-9013695	NOTCH4 Intracellular Domain Regulates Transcription	0.036001	<i>SMAD3, MAML3</i>
R-HSA-9669938	Signaling by KIT in disease	0.036001	<i>LYN, SRC</i>
R-HSA-9670439	Signaling by phosphorylated juxtamembrane, extracellular and kinase domain KIT mutants	0.036001	<i>LYN, SRC</i>
R-HSA-5688426	Deubiquitination	0.036707	<i>TNIP2, H2AC13, H2BC13, SMAD3, BRCA1, TOMM20, INO80, H2BC1, H2AC1</i>
R-HSA-389513	CTLA4 inhibitory signaling	0.039404	<i>LYN, SRC</i>
R-HSA-5620916	VxPx cargo-targeting to cilium	0.039404	<i>ARF4, EXOC2</i>
R-HSA-9008059	Interleukin-37 signaling	0.039404	<i>PTPN9, SMAD3</i>
R-HSA-5693532	DNA Double-Strand Break Repair	0.040819	<i>NSD2, RAD51B, UBE2I, H2BC13, BRCA1, H2BC1</i>
R-HSA-912446	Meiotic recombination	0.040930	<i>H2BC13, H3C3, BRCA1, H2BC1</i>
R-HSA-438066	Unblocking of NMDA receptors, glutamate binding and activation	0.042923	<i>GRIN2A, DLG2</i>
R-HSA-9613829	Chaperone Mediated Autophagy	0.042923	<i>PARK7, PCNT</i>

R-HSA-9617324	Negative regulation of NMDA receptor-mediated neuronal transmission	0.042923	<i>GRIN2A, DLG2</i>
R-HSA-171306	Packaging Of Telomere Ends	0.043546	<i>ACD, H2BC13, H2BC1</i>
R-HSA-2565942	Regulation of PLK1 Activity at G2/M Transition	0.043934	<i>CKAP5, DCTN1, PCNT, TUBB</i>
R-HSA-449147	Signaling by Interleukins	0.046945	<i>RPS6KA2, RAP1B, INPP5D, LYN, SMARCA4, TNIP2, PTPN9, H3C3, SMAD3, PITPNA, IL20, TOLLIP</i>
R-HSA-201722	Formation of the beta-catenin:TCF transactivating complex	0.048667	<i>SMARCA4, H2BC13, H3C3, H2BC1</i>

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**Additional file 6: Supplementary Table S5** Correlation between levels of DNA methylation and expression for the 13 genes included in Table 2 and for which expression data are available in the The Cancer Genome Atlas database (<https://www.cancer.gov/about-nci/organization/ccg/research/structural-genomics/tcga>).

Probe ID	Gene symbol	<i>P</i>	Correlation coefficient (r)
cg05861743	<i>APOM*</i>	1.35x10 <sup>-29</sup>	-0.533
cg19861632	<i>GPR125*</i>	1.19x10 <sup>-8</sup>	-0.286
cg14950303	<i>FOXD4L1*</i>	2.33x10 <sup>-5</sup>	0.214
cg09580859	<i>ZC3H3</i>	7.68x10 <sup>-4</sup>	0.171
cg14288091	<i>NIPAL2</i>	5.19x10 <sup>-3</sup>	-0.142
cg13719443	<i>LOC285847</i>	8.21x10 <sup>-3</sup>	-0.135
cg26894854	<i>SLC45A3</i>	4.52x10 <sup>-2</sup>	-0.102
cg23785719	<i>STK17A</i>	0.12	-0.079
cg26583598	<i>ZSWIM6</i>	0.269	-0.057
cg05393736	<i>NRBF2</i>	0.354	0.047
cg18210511	<i>ZC3H3</i>	0.664	0.022
cg22083325	<i>LOC440461</i>	0.687	-0.021
cg00431813	<i>C7orf50</i>	0.749	0.016

\*Genes showing *P* values of less than 0.05 and r values of less than -0.2 or more than 0.2.

**Additional file 7: Supplementary Table S6** Comparison of DNA methylation levels based on the Infinium assay between samples of normal healthy liver tissue (GSE107038) deposited in the GEO database (<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE107038>) and non-cancerous liver tissue samples showing non-alcoholic steatohepatitis from our cohort of patients with hepatocellular carcinoma (NASH-W).

Probe ID	GSE107038 (mean± standard deviation [SD])			NASH-W (mean±SD)			$\Delta\beta_{\text{NASH-W-GSE107038}}$	<i>P</i> (Welch's <i>t</i> test)
cg00431813	0.452	±	0.069	0.629	±	0.085	0.177	5.23x10 <sup>-10</sup>
cg04662828	0.682	±	0.073	0.506	±	0.053	-0.176	2.27x10 <sup>-15</sup>
cg05393736	0.675	±	0.049	0.749	±	0.039	0.074	3.00x10 <sup>-8</sup>
cg05861743	0.717	±	0.065	0.843	±	0.049	0.126	1.46x10 <sup>-11</sup>
cg08912801	0.647	±	0.065	0.531	±	0.07	-0.116	1.03x10 <sup>-7</sup>
cg09580822	0.837	±	0.076	0.599	±	0.109	-0.239	1.90x10 <sup>-10</sup>
cg09580859	0.609	±	0.119	0.784	±	0.113	0.175	7.53x10 <sup>-7</sup>
cg11152384	0.538	±	0.09	0.36	±	0.083	-0.178	4.69x10 <sup>-10</sup>
cg11820154	0.456	±	0.056	0.546	±	0.054	0.09	1.98x10 <sup>-7</sup>
cg13719443	0.462	±	0.082	0.35	±	0.063	-0.112	1.79x10 <sup>-7</sup>
cg14288091	0.279	±	0.075	0.146	±	0.049	-0.133	1.33x10 <sup>-11</sup>
cg14950303	0.489	±	0.043	0.583	±	0.045	0.094	6.36x10 <sup>-10</sup>
cg15050398	0.752	±	0.039	0.479	±	0.058	-0.273	1.61x10 <sup>-19</sup>
cg16319310	0.808	±	0.064	0.587	±	0.027	-0.221	3.33x10 <sup>-26</sup>
cg18210511	0.464	±	0.076	0.603	±	0.078	0.14	2.68x10 <sup>-8</sup>
cg19861632	0.512	±	0.058	0.605	±	0.056	0.093	2.14x10 <sup>-7</sup>
cg22083325	0.163	±	0.056	0.289	±	0.052	0.125	2.16x10 <sup>-11</sup>
cg23785719	0.133	±	0.028	0.319	±	0.043	0.186	2.36x10 <sup>-18</sup>
cg26385097	0.504	±	0.116	0.293	±	0.105	-0.211	2.85x10 <sup>-9</sup>
cg26583598	0.642	±	0.097	0.776	±	0.087	0.134	1.12x10 <sup>-6</sup>
cg26894854	0.464	±	0.051	0.54	±	0.052	0.075	2.07x10 <sup>-6</sup>

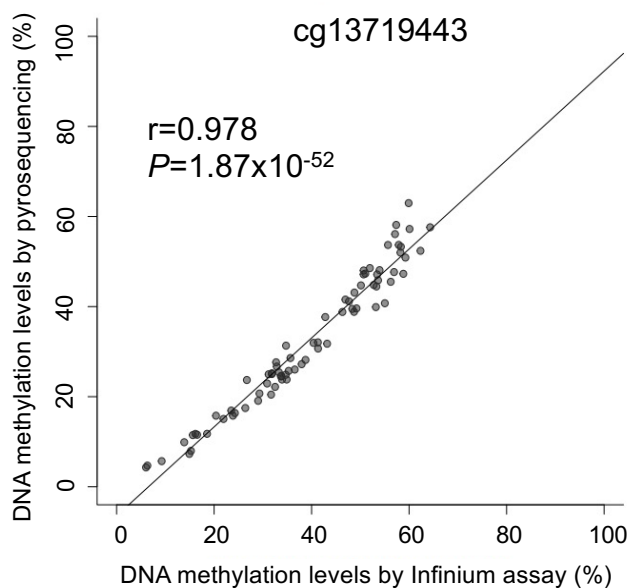
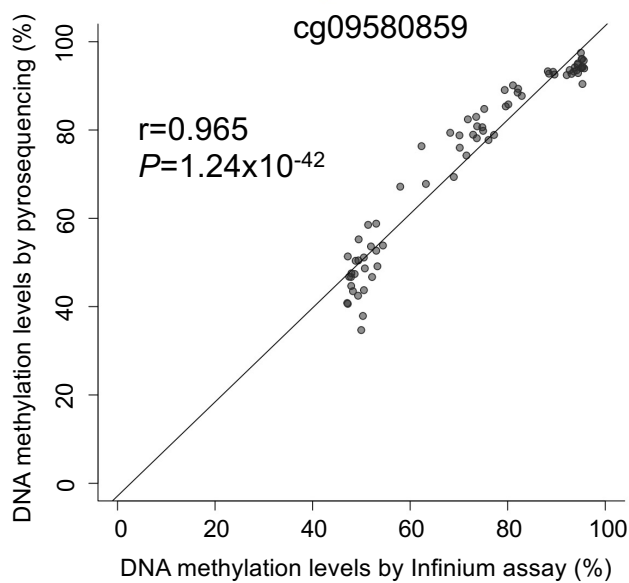
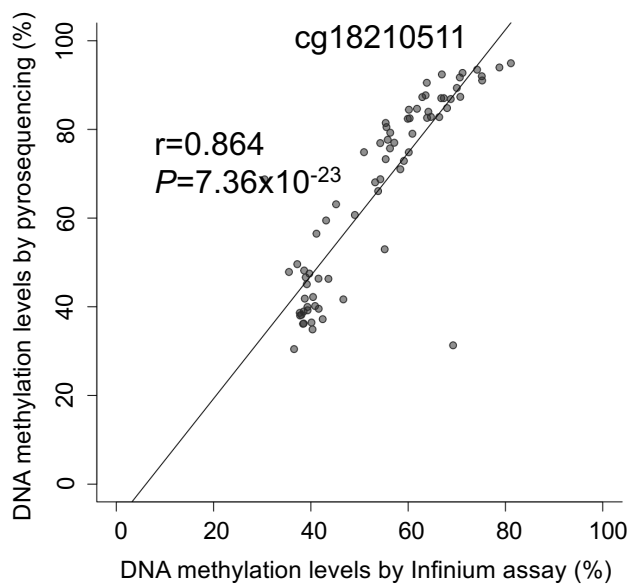
**Additional file 8: Supplementary Table S7** Multivariate analysis using the 91 samples of non-cancerous liver tissue showing non-alcoholic steatohepatitis (NASH) derived from biopsy specimens of patients with morbid obesity but without hepatocellular carcinoma (HCC) (NASH-O samples) and the 22 samples of non-cancerous liver tissue showing NASH derived from partial hepatectomy specimens of patients with HCC (NASH-W samples) in the initial cohorts.

Probe ID <sup>a</sup>	Independent variable	Odds ratio <sup>b</sup>	95% confidence interval	P value <sup>c</sup>
cg00431813	Ballooning <sup>d</sup>	5.786	0.132-252.827	0.362
	Brunt classification <sup>e</sup>	0.686	0.275-1.714	0.420
	DNA methylation quantification	232.059	31.166-1727.915	<u>1.05x10<sup>-7</sup></u>
cg05393736	Ballooning <sup>d</sup>	4.286	0.269-68.340	0.303
	Brunt classification <sup>c</sup>	0.972	0.472-2.001	0.938
	DNA methylation quantification	44.977	10.934-185.009	<u>1.33x10<sup>-7</sup></u>
cg09580822	Ballooning <sup>d</sup>	1.378	0.124-15.383	0.795
	Brunt classification <sup>e</sup>	0.553	0.248-1.235	0.148
	DNA methylation quantification	180.610	23.957-1361.603	<u>4.61x10<sup>-7</sup></u>
cg11820154	Ballooning <sup>d</sup>	0.460	0.031-6.765	0.571
	Brunt classification <sup>c</sup>	0.347	0.100-1.207	0.096
	DNA methylation quantification	1138.492	52.740-24576.521	<u>7.13x10<sup>-6</sup></u>
cg14950303	Ballooning <sup>d</sup>	1.256	0.114-13.824	0.853
	Brunt classification <sup>c</sup>	0.702	0.315-1.565	0.387
	DNA methylation quantification	144.050	21.556- 962.621	<u>2.92x10<sup>-7</sup></u>
cg15050398	Ballooning <sup>d</sup>	7.485	0.656-85.377	0.105
	Brunt classification <sup>e</sup>	1.772	0.873-3.600	0.113
	DNA methylation quantification	39.410	10.225-151.901	<u>9.44x10<sup>-8</sup></u>
cg23785719	Ballooning <sup>d</sup>	2.288	0.048-109.285	0.675
	Brunt classification <sup>e</sup>	2.717	0.959-7.697	0.060
	DNA methylation quantification	245.432	30.392-1981.975	<u>2.42x10<sup>-7</sup></u>
cg26583598	Ballooning <sup>d</sup>	0.692	0.051-9.460	0.782
	Brunt classification <sup>e</sup>	0.286	0.090-0.915	<u>0.035</u>
	DNA methylation quantification	1035.707	54.365-19731.273	<u>3.89x10<sup>-6</sup></u>
cg18210511	Ballooning <sup>d</sup>	8.990	0.219-369.308	0.247
	Brunt classification <sup>e</sup>	0.482	0.207-1.123	0.091
	DNA methylation quantification	248.725	30.517-2027.198	<u>2.56x10<sup>-7</sup></u>
cg05861743	Ballooning <sup>d</sup>	1.491	0.133-16.687	0.746
	Brunt classification <sup>e</sup>	0.503	0.229-1.106	0.088
	DNA methylation quantification	190.885	24.574-1482.750	<u>5.14x10<sup>-7</sup></u>
cg14288091	Ballooning <sup>d</sup>	1.606	0.152-16.949	0.694
	Brunt classification <sup>e</sup>	0.759	0.344-1.675	0.494



	DNA methylation quantification	99.726	16.280-610.913	<u>6.46x10<sup>-7</sup></u>
cg26385097	Ballooning <sup>d</sup>	1.577	0.145-17.140	0.708
	Brunt classification <sup>e</sup>	0.595	0.275-1.288	0.188
	DNA methylation quantification	141.119	20.394-976.513	<u>5.30x10<sup>-7</sup></u>
cg22083325	Ballooning <sup>d</sup>	6.795	0.307-150.345	0.225
	Brunt classification <sup>e</sup>	0.632	0.286-1.397	0.257
	DNA methylation quantification	90.209	16.093-505.661	<u>3.07x10<sup>-7</sup></u>
cg09580859	Ballooning <sup>d</sup>	9.892	0.299-327.815	0.200
	Brunt classification <sup>e</sup>	0.506	0.226-1.133	0.098
	DNA methylation quantification	180.393	24.567-1324.612	<u>3.27x10<sup>-7</sup></u>
cg13719443	Ballooning <sup>d</sup>	1.774	0.166-18.957	0.635
	Brunt classification <sup>e</sup>	0.609	0.278-1.335	0.216
	DNA methylation quantification	120.359	17.878-810.272	<u>8.48x10<sup>-7</sup></u>
cg26894854	Ballooning <sup>d</sup>	1.782	0.169-18.816	0.631
	Brunt classification <sup>e</sup>	0.586	0.273-1.261	0.172
	DNA methylation quantification	83.537	14.260-489.391	<u>9.28x10<sup>-7</sup></u>
cg04662828	Ballooning <sup>d</sup>	14.655	1.172-183.220	0.037
	Brunt classification <sup>e</sup>	1.036	0.544-1.973	0.915
	DNA methylation quantification	35.014	8.406-145.841	<u>1.04x10<sup>-6</sup></u>
cg11152384	Ballooning <sup>d</sup>	1.865	0.172-20.186	0.608
	Brunt classification <sup>e</sup>	0.528	0.248-1.125	0.098
	DNA methylation quantification	140.210	19.811-992.306	<u>7.38x10<sup>-7</sup></u>
cg08912801	Ballooning <sup>d</sup>	9.581	0.420-218.813	0.157
	Brunt classification <sup>e</sup>	0.662	0.324-1.352	0.258
	DNA methylation quantification	91.389	15.135-551.828	<u>8.58x10<sup>-7</sup></u>
cg16319310	Ballooning <sup>d</sup>	4.220	0.268-66.499	0.306
	Brunt classification <sup>e</sup>	2.148	0.963-4.788	0.062
	DNA methylation quantification	70.412	12.597-393.575	<u>1.26x10<sup>-6</sup></u>
cg19861632	Ballooning <sup>d</sup>	2.047	0.191-21.929	0.554
	Brunt classification <sup>e</sup>	0.610	0.302-1.232	0.168
	DNA methylation quantification	207.072	20.883-2053.237	<u>5.20x10<sup>-6</sup></u>

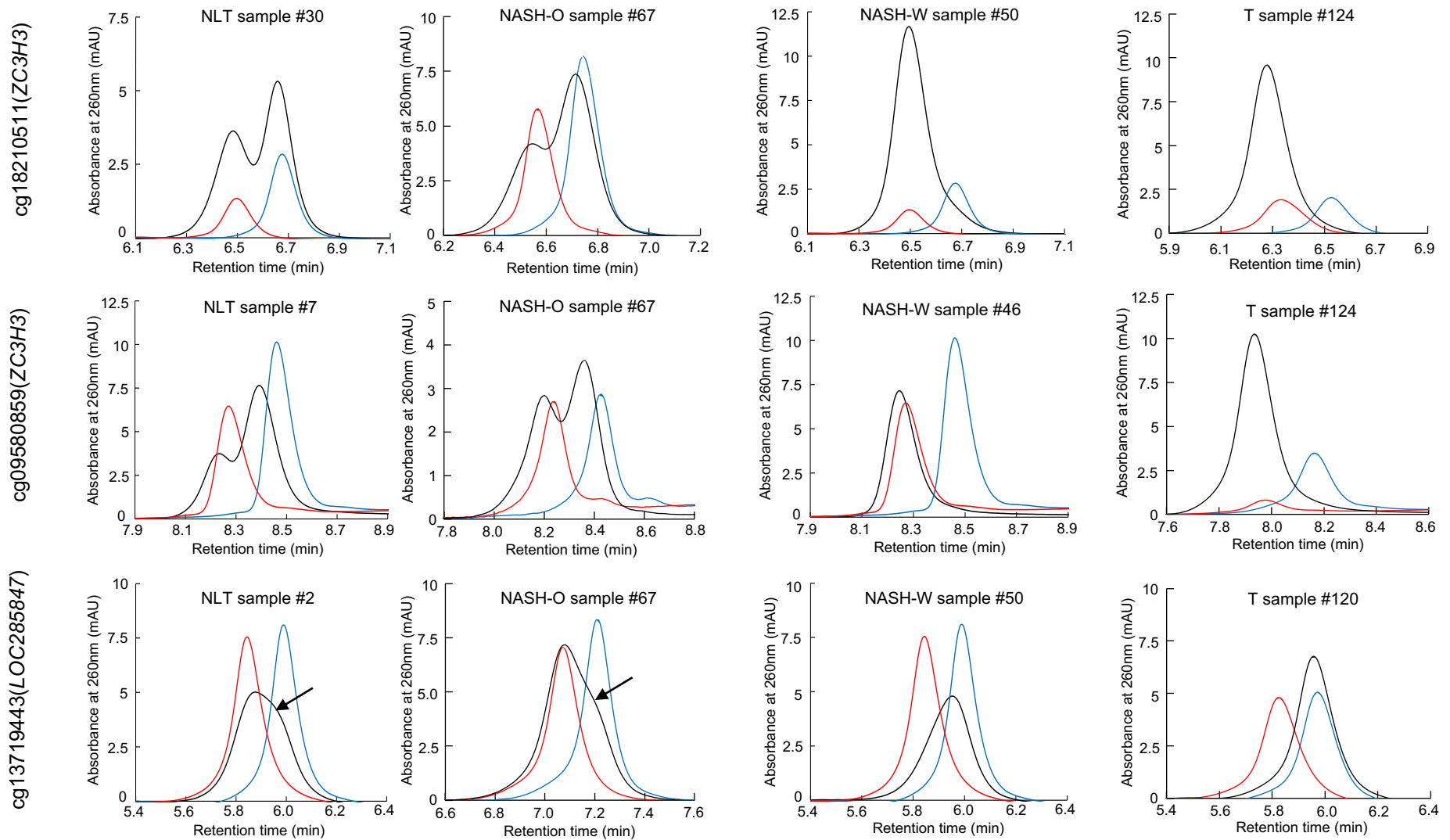
<sup>a</sup>Probe ID of the Infinium HumanMethylation450 BeadChip. <sup>b</sup>Top 10 CpG sites showing the highest odds ratio of being NASH-W samples are summarized in Table 3. <sup>c</sup>P values less than 0.05 are underlined. <sup>d</sup>Ballooning was evaluated according to the non-alcoholic fatty disease (NAFLD) activity score (NAS) (Ref. 26) <sup>e</sup>Fibrosis stage was defined according to the Brunt classification (Ref. 27).



**Additional file 9: Supplementary Figure S2** Correlation between DNA methylation levels based on the Infinium assay and such levels based on pyrosequencing using samples of normal liver tissue (n=34), non-cancerous liver tissue showing non-alcoholic steatohepatitis from partial hepatectomy specimens from patients with hepatocellular carcinoma (n=22), and cancerous tissue samples (n = 22) in the initial cohort. Infinium data were successfully verified by pyrosequencing. ( $P < 7.36 \times 10^{-23}$  and Pearson correlation coefficient [ $r$ ] > 0.864).

**Additional file 10: Supplementary Table S8** Correlation between DNA methylation levels based on the Infinium assay of the 21 marker CpG sites included in Table 2 and obesity in patients with nonalcoholic steatohepatitis (NASH) with and without hepatocellular carcinoma in the initial and validation cohorts.

Probe ID	DNA methylation levels based on Infinium assay (mean±standard deviation)		
	Non-obese NASH patients (body mass index [BMI]<25) (n=17)	Obese NASH patients (BMI≥25) (n=22)	<i>P</i> (Welch's <i>t</i> test)
cg00431813	0.591 ± 0.106	0.614 ± 0.109	0.519
cg04662828	0.512 ± 0.045	0.503 ± 0.041	0.522
cg05393736	0.725 ± 0.037	0.708 ± 0.056	0.240
cg05861743	0.815 ± 0.061	0.831 ± 0.055	0.403
cg08912801	0.560 ± 0.078	0.528 ± 0.102	0.276
cg09580822	0.617 ± 0.106	0.613 ± 0.131	0.923
cg09580859	0.749 ± 0.145	0.750 ± 0.138	0.974
cg11152384	0.399 ± 0.099	0.359 ± 0.109	0.237
cg11820154	0.524 ± 0.067	0.528 ± 0.063	0.877
cg13719443	0.374 ± 0.096	0.376 ± 0.11	0.950
cg14288091	0.178 ± 0.071	0.160 ± 0.075	0.463
cg14950303	0.560 ± 0.048	0.577 ± 0.052	0.302
cg15050398	0.460 ± 0.043	0.462 ± 0.052	0.886
cg16319310	0.579 ± 0.019	0.575 ± 0.041	0.670
cg18210511	0.583 ± 0.104	0.579 ± 0.088	0.901
cg19861632	0.587 ± 0.045	0.597 ± 0.061	0.560
cg22083325	0.266 ± 0.042	0.282 ± 0.056	0.304
cg23785719	0.313 ± 0.037	0.282 ± 0.041	0.016
cg26385097	0.332 ± 0.124	0.298 ± 0.136	0.411
cg26583598	0.729 ± 0.107	0.727 ± 0.111	0.939
cg26894854	0.525 ± 0.046	0.529 ± 0.073	0.854



**Additional file 11: Supplementary Figure S3** Representative chromatograms obtained by high-performance liquid chromatography analysis using a newly developed anion-exchange column for marker CpG sites in specimens of normal liver tissue (NLT), non-cancerous liver tissue (N) showing non-alcoholic steatohepatitis (NASH) derived from partial hepatectomy specimens from patients without hepatocellular carcinoma (HCC) (NASH-O), N samples showing NASH from patients with HCC (NASH-W), and cancerous tissue (T) samples. The chromatogram patterns (bimodal peak or single peak with a shoulder [indicated by an arrow]) for most of the NASH-O samples are similar to those for NLT samples, whereas those for T samples (single peak) are similar to those for NASH-W samples.

**Additional file 12: Supplementary Table S9** Correlation between relative methylation rates based on high-performance liquid chromatography (HPLC) and the sex and age of nonalcoholic steatohepatitis (NASH) patients with and without hepatocellular carcinoma in the initial and validation cohorts from whom HPLC data had been obtained (n=34).

Probe ID	Correlation with sex			Correlation with age	
	Relative methylation rates (mean±standard deviation)		<i>P</i> (Welch's <i>t</i> test)	<i>P</i>	Correlation coefficient ( <i>r</i> )
	Male (n=29)	Female (n=5)			
cg18210511	83.6 ± 20.3	100.4 ± 14.1	0.0540	0.0994	0.287
cg09580859	96.1 ± 17.2	108.7 ± 11.1	0.0663	0.0345	0.364
cg13719443	32.4 ± 10.0	30.6 ± 9.1	0.7147	0.6018	-0.093