

**Supplementary table 1**, SNPs that have strong linkage disequilibrium with lead SNP rs1997243. The linkage disequilibrium (LD,  $r^2$ ) was calculated using European population datasets from 1000 genome phase 3 as described in Methods. LD with  $r^2 > 0.8$  are listed and SNPs located in genome active regions are highlighted and subjected to further function studies.

Variant 1	Variant 1 location	Variant 2	Variant 2 location	LD ( $r^2$ )
rs1997243	7:1044141	rs6951245	7:1018557	1
rs1997243	7:1044141	rs75280240	7:1018875	1
rs1997243	7:1044141	rs57068908	7:1020448	1
rs1997243	7:1044141	rs11763020	7:1020652	1
rs1997243	7:1044141	rs11763765	7:1020874	1
rs1997243	7:1044141	rs1881128	7:1023677	1
rs1997243	7:1044141	rs11766669	7:1023957	1
rs1997243	7:1044141	rs11768895	7:1024055	0.803571
rs1997243	7:1044141	rs79067319	7:1025912	1
rs1997243	7:1044141	rs884977	7:1026774	1
rs1997243	7:1044141	rs74360401	7:1027767	1
rs1997243	7:1044141	rs143361185	7:1028127	1
rs1997243	7:1044141	rs118132455	7:1028596	1
rs1997243	7:1044141	rs78628466	7:1028817	1
rs1997243	7:1044141	rs144042633	7:1029715	1
rs1997243	7:1044141	rs11768761	7:1030171	1
rs1997243	7:1044141	rs76833820	7:1030642	1
rs1997243	7:1044141	rs28379681	7:1030903	1
rs1997243	7:1044141	rs28399710	7:1030995	1
rs1997243	7:1044141	rs28528096	7:1031276	1
rs1997243	7:1044141	rs112425403	7:1031895	0.961981
rs1997243	7:1044141	rs74369356	7:1032075	1
rs1997243	7:1044141	rs77083167	7:1032187	1
rs1997243	7:1044141	rs199718264	7:1032483	1
rs1997243	7:1044141	rs74347384	7:1032804	1
rs1997243	7:1044141	rs78308415	7:1032998	1
rs1997243	7:1044141	rs75493422	7:1033254	1
rs1997243	7:1044141	rs118059236	7:1033566	1
rs1997243	7:1044141	rs113858334	7:1033840	1
rs1997243	7:1044141	rs79765398	7:1034128	1
rs1997243	7:1044141	rs79443843	7:1035609	1
rs1997243	7:1044141	rs113713890	7:1036436	1
rs1997243	7:1044141	rs78896566	7:1040546	1
rs1997243	7:1044141	rs79422648	7:1040605	1
rs1997243	7:1044141	rs113119264	7:1040928	1
rs1997243	7:1044141	rs140138013	7:1041233	0.960947
rs1997243	7:1044141	rs186044114	7:1041261	0.922562
rs1997243	7:1044141	rs145122769	7:1041289	0.960947
rs1997243	7:1044141	rs181094051	7:1041317	0.960947
rs1997243	7:1044141	rs185931365	7:1041345	1
rs1997243	7:1044141	rs117800627	7:1041439	0.852872
rs1997243	7:1044141	rs76804143	7:1042385	1
rs1997243	7:1044141	rs77760339	7:1044291	1
rs1997243	7:1044141	rs113575110	7:1044758	1
rs1997243	7:1044141	rs1881123	7:1045070	1
rs1997243	7:1044141	rs77569514	7:1045872	1

rs1997243	7:1044141	rs148758091	7:1046716	1
rs1997243	7:1044141	rs11770909	7:1047080	1
rs1997243	7:1044141	rs74785791	7:1048858	1
rs1997243	7:1044141	rs74366004	7:1048994	1
rs1997243	7:1044141	rs77702926	7:1049202	1
rs1997243	7:1044141	rs78573577	7:1049451	1
rs1997243	7:1044141	rs76129108	7:1049523	1
rs1997243	7:1044141	rs78523927	7:1049822	1
rs1997243	7:1044141	rs74652290	7:1050473	1
rs1997243	7:1044141	rs78185558	7:1050547	1
rs1997243	7:1044141	rs78158942	7:1050804	1
rs1997243	7:1044141	rs2363286	7:1051989	1
rs1997243	7:1044141	rs11764937	7:1052438	0.926339
rs1997243	7:1044141	rs79808627	7:1052883	0.860168
rs1997243	7:1044141	rs56048221	7:1052897	0.821014
rs1997243	7:1044141	rs77868187	7:1054332	0.961981
rs1997243	7:1044141	rs75016635	7:1054485	0.961981
rs1997243	7:1044141	rs113066613	7:1054492	0.961981
rs1997243	7:1044141	rs11763793	7:1054706	0.961981
rs1997243	7:1044141	rs11764748	7:1054872	0.961981
rs1997243	7:1044141	rs11763835	7:1054877	0.961981
rs1997243	7:1044141	rs78861357	7:1055782	0.961981
rs1997243	7:1044141	rs76713558	7:1056230	0.961981
rs1997243	7:1044141	rs79658522	7:1056241	0.961981
rs1997243	7:1044141	rs76525951	7:1056377	0.961981
rs1997243	7:1044141	rs79683221	7:1056503	0.961981
rs1997243	7:1044141	rs78185801	7:1056731	0.961981
rs1997243	7:1044141	rs80031817	7:1057157	0.961981
rs1997243	7:1044141	rs78143408	7:1057210	0.961981
rs1997243	7:1044141	rs78351779	7:1057387	0.961981
rs1997243	7:1044141	rs11761941	7:1057547	0.961981
rs1997243	7:1044141	rs11767527	7:1057758	0.961981
rs1997243	7:1044141	rs61910751	7:1058259	0.961981
rs1997243	7:1044141	rs77434655	7:1058769	0.961981
rs1997243	7:1044141	rs75398423	7:1058778	0.961981
rs1997243	7:1044141	rs112309216	7:1060660	0.961981
rs1997243	7:1044141	rs76161580	7:1060671	0.961981
rs1997243	7:1044141	rs76388414	7:1061058	0.961981
rs1997243	7:1044141	rs77305932	7:1061225	0.961981
rs1997243	7:1044141	rs79788515	7:1061443	0.926339
rs1997243	7:1044141	rs11768486	7:1061654	0.961981
rs1997243	7:1044141	rs11766526	7:1061797	0.961981
rs1997243	7:1044141	rs76214082	7:1062461	0.961981
rs1997243	7:1044141	rs75488469	7:1062486	0.961981
rs1997243	7:1044141	rs80094748	7:1064322	0.961981
rs1997243	7:1044141	rs113146460	7:1065528	0.961981
rs1997243	7:1044141	rs61753396	7:1065736	0.961981
rs1997243	7:1044141	rs113642700	7:1066018	0.961981
rs1997243	7:1044141	rs149125341	7:1066258	0.961981
rs1997243	7:1044141	rs553221139	7:1066867	0.961981
rs1997243	7:1044141	rs111705570	7:1067106	0.961981
rs1997243	7:1044141	rs79327308	7:1068505	0.961981
rs1997243	7:1044141	rs117729148	7:1068895	0.961981
rs1997243	7:1044141	rs113221697	7:1069107	0.961981

rs1997243	7:1044141	rs113365567	7:1069149	0.961981
rs1997243	7:1044141	rs113448118	7:1069318	0.961981
rs1997243	7:1044141	rs79143504	7:1070576	0.961981
rs1997243	7:1044141	rs574980713	7:1070621	0.961981
rs1997243	7:1044141	rs111161354	7:1070686	0.961981
rs1997243	7:1044141	rs532319453	7:1070844	0.961981
rs1997243	7:1044141	rs558665380	7:1070854	0.961981
rs1997243	7:1044141	rs190638559	7:1070869	0.961981
rs1997243	7:1044141	rs200416508	7:1070909	0.961981
rs1997243	7:1044141	rs74887741	7:1071022	0.961981
rs1997243	7:1044141	rs79617366	7:1072322	0.961981
rs1997243	7:1044141	rs111899361	7:1072712	0.961981
rs1997243	7:1044141	rs80212261	7:1074376	0.961981
rs1997243	7:1044141	rs77346188	7:1074387	0.961981
rs1997243	7:1044141	rs77943789	7:1100522	0.831632
rs1997243	7:1044141	rs10266519	7:1103341	0.86134
rs1997243	7:1044141	rs74976697	7:1120869	0.803571
rs1997243	7:1044141	rs28600085	7:1130000	0.803571
rs1997243	7:1044141	rs28483034	7:1130535	0.803571
rs1997243	7:1044141	rs183256883	7:1135851	0.803571
rs1997243	7:1044141	rs6952546	7:948373	0.883578
rs1997243	7:1044141	rs113184427	7:950403	0.922546
rs1997243	7:1044141	rs113766238	7:950606	0.922546
rs1997243	7:1044141	rs79672483	7:955120	0.922546
rs1997243	7:1044141	rs113464035	7:955606	0.922546

Note: LD data were generated on Ensemble using 1000 genome phase 3 data, with European population. The window is 200kb. Highlighted SNPs are the one localized in genomic active regions and used for function studies.

**Supplementary Table 2: This table contains sequence information used in this study.**

**shRNA sequence for mouse *gpr146*.**

Target Gene	Sequence
<i>Gpr146</i>	GCTTAGGCTATAATGCTCTTC

**gRNA sequence for rs1997243 site**

Target Site	Sequence
rs1997243	GCAAACCTTCGGTGAAGAAAG

**Primers for qRT-PCR.**

Human	Forward	Reverse
<i>CYP2W1</i>	CCGATTTGACTACCGGGACC	CGTCCACATAGCTGCACAC
<i>GPER1</i>	CACCAGCAGTACGTGATCGG	CATCTTCTCGCGGAAGCTGAT
<i>C7orf50</i>	AGCTGAAAAAGGAACGGAAGAA	TGGAGAAGTGCTCATCGGGAA
<i>COX19</i>	TTTCGGGACCAAGAGCTTCC	GCATCAATTTTCTCTCCATCTGC
<i>ZFAND2A</i>	TGTGACTCTCACCTGGGAA	GGGTGAGCACCCAGCTT
<i>GPR146</i>	TGAGCCTCGACCACTACATC	GCTTCTGCGTTCTGCATCTTG
<i>36B4</i>	TGCATCAGTACCCCATCTATCA	AAGGTGTAATCCGTCTCCACAGA
Mouse	Forward	Reverse
<i>Albumin</i>	CGAGAAGCTTGGAGAATATGGA	CTTGGTGCCCACTCTTCCTA
<i>Apob</i>	CGTGGGCTCCAGCATTCTA	TCACCAGTCATTTCTGCCTTTG
<i>F4/80</i>	CTTTGGCTATGGGCTTCCAGTC	GCAAGGAGGACAGAGTTTATCGTG
<i>Gpr146</i>	TGACCATGTACTCCACTGCAC	AAGACACGTGACTGCAGATGT
<i>36b4</i>	CACTGGTCTAGGACCCGAGAAG	GGTGCCTCTGGAGATTTTCG
<i>Gapdh</i>	TGTGTCCGTCGTGGATCTGA	CCTGCTTACCACCTTCTTGAT
<i>Cyclophilin</i>	TGGAGAGCACCAAGACAGACA	TGCCGGAGTCGACAATGAT

**Primers used to amplify genome sequence from HepG2 cells and primers used to introduce mutations for each SNPs.**

Figures	Primer sequence
Fig 1b-c	<b>Reference allele primer</b> F:ATTTCTCTATCGATAGGTACCATGGTGACCTATCTCATTGACGC R:ACTTAGATCGCAGATCTCGAGGAATGGAGGACTCAAGTACATCTTCA
	<b>Primers for mutagenesis</b>
	rs1997243 F:AAACTTCGGTGAAGAAGGAGGGGCAGGTGT R:CTTCTTACCAGGTTTGTCTGCTGTTTCCA
	rs77760339 F:CCGCGCTGGGCACTAAGATAATTCTCAA R:ATCTTAGTGCCCAGCGCGTTTC
	rs113575110 F:TCCCACGGCGGACGCTGCGCTTACTG R:CAGCGTCCGCGTGGGAGCCACAGCAGCTT
	rs1881123 F:TGGATCTGCTGTCAGTTGTCTTGGACAGTT R:ACAACTGACAGCAGATCCTACACCTCCATGTA

Fig S3b	<p><b>Reference allele primer</b>  F:ATTTCTCTATCGATAGGTACCCTCTGCCAACACAATGGAC  R:ACTTAGATCGCAGATCTCGAGGAGCGGGAGAAGACCTCAGG</p> <p><b>Primers for mutagenesis</b>  F:ACATACATAGGCCCTGCAAGAGC  R:GCCTATGTATGTCTGCAGCCAGG</p>
Fig S3d	<p><b>Reference allele primer</b>  F:ATTTCTCTATCGATAGGTACCGCCACCGCCTCCTCAGAA  R:ACTTAGATCGCAGATCTCGAGCTGTGTGGGCTGGCGCAT</p> <p><b>Primers for mutagenesis</b></p> <p>rs74360401 F:CGGCACAGGGAGAGGGCAGGGCGGCG  R:CGCCGCCTCGCCTCTCCCTGTGCCG</p> <p>rs143361185 F:CGGAGCGGGGCCGAGCAGCGTCTG  R:CAGACGCTGCTGCGGCCCGCTCCG</p> <p>rs118132455 F:GAACTGCGGGGAGGGCGAACCCCGCCCGCGCAG  R:CTGCGCGGGCGGGGGTTCGCCCTCCCGCAGTTC</p> <p>rs78628466 F:CAATCTGACTCCATGCCCCCATCTCCTCC  R:GGAGGAGATGGGGGCATGGAGTCAGATTG</p> <p>rs144042633 F:GGTCGCGGGCCTGCTCTGGAGGCC  R:GGCCTCCAGAGCAGGCCCGCGACC</p>
Fig S3e	<p><b>Reference allele primer</b>  F:ATTTCTCTATCGATAGGTACCGGAGGATGAGCAAAGGCAGA  R:ACTTAGATCGCAGATCTCGAGCCACGCCTGCTGATGTGATA</p> <p><b>Primers for mutagenesis</b></p> <p>rs181094051 Minor allele sequence was synthesized due to multi-repeats near this SNP</p> <p>rs185931365 Minor allele sequence was synthesized due to multi-repeats near this SNP</p> <p>rs76804143 F:TCCAGCTCCTGACCAGCA  R:AGATTGGGGCGTAGGGGGGCATGTGGCCCTGACTCAGC</p>
Fig S3f	<p><b>Reference allele primer</b>  F:ATTTCTCTATCGATAGGTACCAATAGGACTTGGGCTCCGCA  R:ACTTAGATCGCAGATCTCGAGAGACAGCATGTCATCATCTGACACT</p> <p>rs117800627 Minor allele sequence was synthesized directly due to multi-repeats near this SNP. The sequence was further confirmed by sanger sequencing.</p>
Fig S3g	<p><b>Reference allele primer</b>  F:ATTTCTCTATCGATAGGTACCGTTAGTATTACAAACCTGGCAAGTCAG  R:ACTTAGATCGCAGATCTCGAGGGATTCCAGGTGACATCCTAGG</p> <p><b>Primers for mutagenesis</b></p> <p>rs77569514 F:ACACATCCGTGCTGGCATCCACGTGTCATCCTGCC  R:GGCAGGATGACACGTGGATGCCAGCACGGATGTGT</p>
Fig S3h	<p><b>Reference allele primer</b>  F:ATTTCTCTATCGATAGGTACCCAGAGAAGCGCAGCAGCG  R:ACTTAGATCGCAGATCTCGAGCGCACAGTGATTCCCGAAGT</p>

	<p><b>Primers for mutagenesis</b></p> <p>rs78861357 F:GAGACAGCCCTCCCGTTCCGATCTTCTAATC R:GATTAGAAGATCGGAACGGGAGGGCTGTCTC</p> <p>rs76713558 F:GTGTTAGTGAGGGGCTAGACAAGATG R:CATCTTGTCTAGCCCCTCACTAACAC</p> <p>rs79658522 F:GAGCTAGACAAGGTGAGCACGTGAG R:CTCACGTGCTCACCTTGTCTAGCTC</p> <p>rs76525951 F:CACCTGACCCTCATTGCGGCTGCTGG R:CCAGCAGCCGCAATGAGGGTCAGGTG</p> <p>rs79683221 F:GCCTGCATGCCTGGCCGAGGGCCG R:CGGCCCTGCGGCCAGGCATGCAGGC</p> <p>rs78185801 F:GGGAACGATGCCATCTGCTCGTCTG R:CAGACGAGCAGATGGCATCGTTCCC</p>
Fig S3j	<p><b>Reference allele primer</b></p> <p>F:ATTTCTCTATCGATAGGTACCCCCGGGGTACTGATGCC R:ACTTAGATCGCAGATCTCGAGAAGATGCTTCTAGGCTGCGG</p>
	<p><b>Primers for mutagenesis</b></p> <p>rs74785791 F:CAGGTTCTCCTTCCCAGTCCCATGTTC R:GAACATGGGACTGGGAAGGAGAACCTG</p> <p>rs74366004 F:GAACATAAAAACCATACAACCTGCAAAGCCTCTGC R:GCAGAGGCTTTGCAGTTGTATGGTTTTTATGTTC</p> <p>rs77702926 F:CACCCTGCCCCACATTTCCCCTGCAC R:GTGCAGGGGAAATGTGGGGCAGGGTG</p> <p>rs78573577 F:GCAAGGATGTCACATGCCTGCAAAGGC R:GCCTTTGCAGGCATGTGACATCCTTGC</p> <p>rs76129108 F:CATGCTTGCTGCCACTCCGGAGCCCAG R:CTGGGCTCCGGAGTGGGCAGCAAGCATG</p> <p>rs78523927 F:GGCACCCTGTACCGGGTTCTATGAC R:GTCATAGAACCCGGTACAGTGGTGCC</p>
Fig S3k	<p><b>Reference allele primer</b></p> <p>F:ATTTCTCTATCGATAGGTACCAAACGATTGAAACTGGGCCA R:ACTTAGATCGCAGATCTCGAGACTGTGGACGCCCTCCC</p>
	<p><b>Primers for mutagenesis</b></p> <p>rs11764937 F:GGGGGAGGGTTTTGGGGGAGATGC R:GCATCTCCCCCAAACCCCTCCCC</p> <p>rs79808627 F:GAGCTCCAGAATCTTTCATCGCCGC R:GCGGCGATGAAAGATTCTGGAGGCTC</p> <p>rs56048221 F:GTTTCATCGCCGCCACAACAACTCAGG R:CCTGAGTTTGTGTGGCGGCGATGAAAC</p>