

Figure S1 Expression of TP53 in hepatocellular carcinoma tissues by immunohistochemical staining.

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|---|---|
| Study participants | <ul style="list-style-type: none"> ○ HCC with dual exposure of HBV and AFB1 in Guangxi |
| Inclusion criteria | <ul style="list-style-type: none"> ○ 1. HCC with positive for hepatitis B surface antigen ○ 2. Epidemiology & clinical pathology data were complete ○ 3. TP53 249Ser mutation detection was successful |
| Exclusion criteria | <ul style="list-style-type: none"> ○ 1. Combined HCV infection ○ 2. Recurrence of HCC |
| Genome-wide association study | |
| Phase one | <ul style="list-style-type: none"> ○ 1. 165 mutation and 320 non-mutation cases were enrolled ○ 2. Genotyped using Illumina HumanExome BeadChip-12-1_A |
| Phase two | <ul style="list-style-type: none"> ○ 1. 180 mutation and 178 non-mutation cases were enrolled ○ 2. Genotyped using iPLEX Gold SNP typing technology |
| Quality control (QC) | <ul style="list-style-type: none"> ○ 1. Samples were excluded under the following conditions. <ul style="list-style-type: none"> (i) genotyping rate < 95%, (ii) ambiguous gender (iii) genome-wide identity-by-descent (IBD) > 0.1875 (iv) outliers in principal components analysis ○ 2. SNPs were removed under the following conditions. <ul style="list-style-type: none"> (i) genotype call rate < 95% (ii) P value in HWE < 1×10^{-6} (iii) MAF < 0.05 |
| Expression quantitative trait loci (eQTL) | <ul style="list-style-type: none"> ○ Candidate SNP loci for eQTL analysis |

Figure S2 Study flowchart.

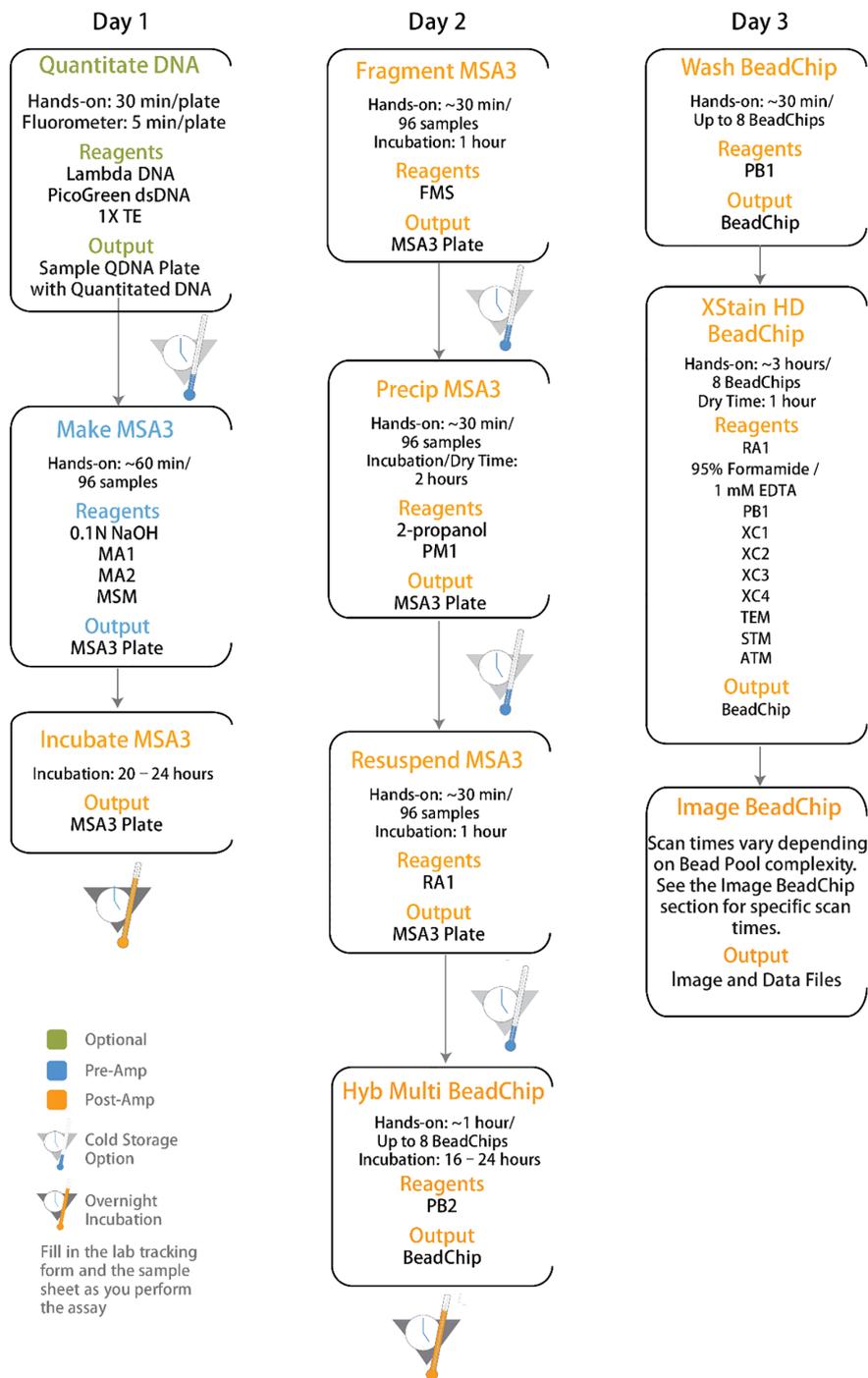


Figure S3 Genotyping procedure of BeadChip-12-1_A in the GWAS. GWAS, genome-wide association study.

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459 founders and 0 non-founders found
2637 heterozygous haploid genotypes; set to missing
Writing list of heterozygous haploid genotypes to [ chd_clean2.hh ]
Total genotyping rate in remaining individuals is 0.983547
0 SNPs failed missingness test < GENO > 1 >
0 SNPs failed frequency test < MAF < 0 >
After frequency and genotyping pruning, there are 21501 SNPs
After filtering, 159 cases, 300 controls and 0 missing
After filtering, 407 males, 52 females, and 0 of unspecified sex
Writing main association results to [ chd_clean2.assoc ]

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QC: Genotype failure rate vs heterozygosity across all individuals.

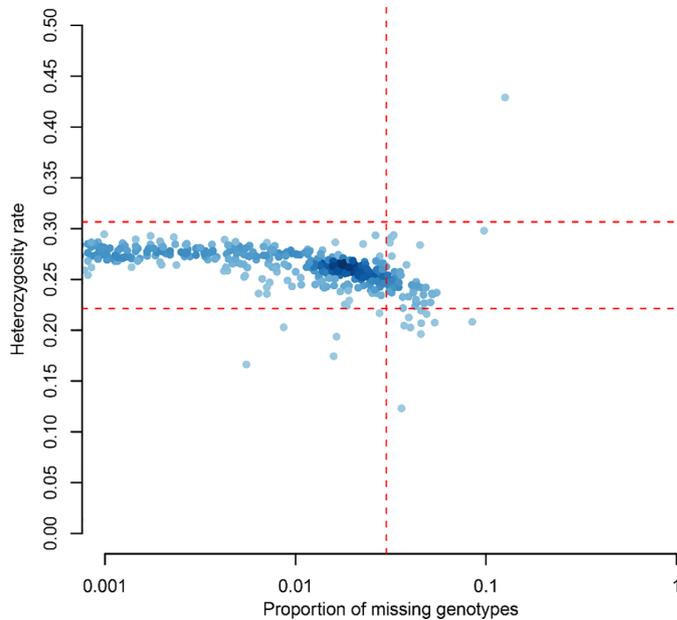


Figure S4 Quality control overview chart. (A) Overall overview of BeadChip-12-1_A after QC. (B) Genotype failure rate and heterozygosity across all individuals.

Table S1 Primers for TP53 R249S mutation detection

| Gene | Primers | Sequences |
|------|---------|----------------------------|
| TP53 | Forward | 5'-CTTGCCACAGGTCTCCCCAA-3' |
| | Reverse | 5'-AGGGGTCAGAGGCAAGCAGA-3' |

The following conditions were applied: 35 cycles of denaturation for 30 sec at 94 °C; 30 sec of annealing at 62 °C; and primer extension for 1 min at 72 °C.

Table S2 Associations between TP53 R249S mutation and whole-exon SNPs (TOP-29)

| SNP | Chr | Position and gene | Number | HWE | MAF | P* | Mutation group | Non-mutation group | AF of mutation group | AF of non-mutation group |
|-------------|-----|--|--------|-------|-------|-----------|----------------|--------------------|----------------------|--------------------------|
| rs3758354 | 9 | 9:75764565_A/C_Intergenic | 447 | 0.974 | 0.109 | 0.0000543 | 155 | 292 | 0.048 | 0.140 |
| rs10001249 | 4 | 4:1535004_G/A_Intergenic | 447 | 0.974 | 0.272 | 0.0000627 | 154 | 293 | 0.351 | 0.230 |
| rs6104 | 18 | 18:61570529_C/G_ Nonsynonymous:SERPINB2 | 448 | 0.976 | 0.462 | 0.000168 | 155 | 293 | 0.626 | 0.491 |
| rs4646450 | 7 | 7:99266318_G/A_ Intron:CYP3A5 | 453 | 0.987 | 0.328 | 0.000249 | 156 | 297 | 0.407 | 0.286 |
| rs9895154 | 17 | 17:42267949_G/A_ Nonsynonymous:TMUB2 | 459 | 1.000 | 0.063 | 0.000261 | 159 | 300 | 0.104 | 0.042 |
| rs6585827 | 10 | 10:124165615_G/A_ Intron:PLEKHA1 | 444 | 0.967 | 0.368 | 0.000270 | 151 | 293 | 0.715 | 0.589 |
| rs7414489 | 1 | 1:64165243_C/A_Intergenic | 444 | 0.967 | 0.452 | 0.000285 | 152 | 292 | 0.536 | 0.408 |
| rs2288101 | 2 | 2:31135184_G/T_ Nonsynonymous:GALNT14 | 458 | 0.998 | 0.216 | 0.000285 | 159 | 299 | 0.283 | 0.181 |
| rs9930984 | 16 | 16:77353973_G/T_ Nonsynonymous:ADAMTS18 | 437 | 0.952 | 0.126 | 0.000334 | 148 | 289 | 0.936 | 0.843 |
| rs5951426 | X | X:22291606_C/A_ Nonsynonymous:ZNF645 | 437 | 0.952 | 0.489 | 0.000460 | 154 | 283 | 0.620 | 0.452 |
| rs75218075 | 3 | 3:167320010_T/C_ Nonsynonymous:WDR49 | 459 | 1.000 | 0.179 | 0.00047 | 159 | 300 | 0.120 | 0.210 |
| rs1619714 | 11 | 11:115552918_A/G_ Intron:AP000797.3 | 443 | 0.965 | 0.409 | 0.000609 | 152 | 291 | 0.671 | 0.550 |
| rs12012519 | X | X:87190349_T/C_Intergenic | 459 | 1.000 | 0.107 | 0.000648 | 159 | 300 | 0.170 | 0.073 |
| rs11901030 | 2 | 2:40998751_A/G_Intergenic | 451 | 0.983 | 0.269 | 0.000728 | 156 | 295 | 0.340 | 0.232 |
| rs11640912 | 16 | 16:77359919_A/T_ Nonsynonymous:ADAMTS18 | 443 | 0.965 | 0.138 | 0.000749 | 151 | 292 | 0.921 | 0.832 |
| rs714106 | 19 | 19:42083849_C/A_ Nonsynonymous:CEACAM21 | 453 | 0.987 | 0.373 | 0.000783 | 156 | 297 | 0.551 | 0.667 |
| rs3745936 | 19 | 19:42092815_T/A_Essential_ Splice_Site:CEACAM21 | 437 | 0.952 | 0.365 | 0.000798 | 149 | 288 | 0.557 | 0.675 |
| rs893817 | 15 | 15:74229065_G/A_ Intron:LOXL1 | 457 | 0.996 | 0.479 | 0.000832 | 158 | 299 | 0.405 | 0.518 |
| rs11023787 | 11 | 11:15952294_C/T_Intergenic | 447 | 0.974 | 0.497 | 0.000999 | 155 | 292 | 0.571 | 0.457 |
| rs55752830 | 11 | 11:124947396_A/G_ Nonsynonymous:SLC37A2 | 452 | 0.985 | 0.108 | 0.00109 | 156 | 296 | 0.154 | 0.084 |
| rs2056822 | 19 | 19:15739597_A/C_ Exon:CYP4F8 | 444 | 0.967 | 0.274 | 0.00139 | 149 | 295 | 0.792 | 0.693 |
| rs3812629 | 10 | 10:75407290_G/A_ Nonsynonymous:SYNPO2L | 453 | 0.987 | 0.205 | 0.00154 | 156 | 297 | 0.141 | 0.239 |
| rs34051490 | 16 | 16:20966362_T/C_ Nonsynonymous:DNAH3 | 442 | 0.963 | 0.181 | 0.00154 | 155 | 287 | 0.126 | 0.211 |
| rs8022091 | 14 | 14:70655751_A/C_ Utr5:SLC8A3 | 437 | 0.952 | 0.360 | 0.00155 | 148 | 289 | 0.561 | 0.680 |
| rs1442801 | 15 | 15:98768182_C/T_Intron:CTD- 2544M6.1 | 449 | 0.978 | 0.296 | 0.00161 | 155 | 294 | 0.639 | 0.738 |
| rs922948 | 3 | 3:69442637_G/A_ Intron:FRMD4B | 451 | 0.983 | 0.369 | 0.00174 | 155 | 296 | 0.700 | 0.595 |
| rs10842496 | 12 | 12:25311489_G/T_ Nonsynonymous:CASC1 | 453 | 0.987 | 0.171 | 0.00177 | 155 | 298 | 0.226 | 0.143 |
| rs117866676 | 12 | 12:123342706_C/T_ Nonsynonymous:HIP1R | 457 | 0.996 | 0.053 | 0.00183 | 157 | 300 | 0.083 | 0.037 |
| rs12192544 | 6 | 6:46620252_C/G_ Nonsynonymous:CYP39A1 | 459 | 1.000 | 0.149 | 0.00294 | 159 | 300 | 0.195 | 0.125 |

*, adjusted for age, sex, race, smoking status, and drinking status. SNP, single nucleotide polymorphism; Chr, chromosome; MAF, minor allele frequency; AF, allele frequency; HWE, Hardy-Weinberg equilibrium.

Table S3 Primers of candidate SNPs in the GWAS (TOP-29)

| SNP | 5' to 3' | | Product (bp) | Tm (°C) |
|-------------|----------------------------|------------------------------|--------------|---------|
| | Forward primer | Reverse primer | | |
| rs10001249 | GCCTGCCAGGAACATCAGTT | GTGGCGATTTCGGCGTTA | 477 | 62 |
| rs10842496 | ATTACTGGTAGCTATGGGCTGAGA | TCTTGAAGAAAGGAGAACTGACACT | 358 | 60 |
| rs11023787 | ATGGAAGCACATTCATTTGGG | AGGGCATTTCGACCGTGAG | 332 | 60 |
| rs11640912 | TTTGATACAAGCAGCAATTTCTTCTG | TGAGTGAACAGTGGTAATGAAAAGAA | 507 | 62 |
| rs117866676 | GTGGCCCATGGGTCATTCCAG | TCTGTAAACCTCCCCAAAAGGCAAGA | 508 | 62 |
| rs11901030 | TTGTAAATGGCAGAGTTGAGTGTTG | CTTGTGCAGGGGAATGACG | 556 | 63 |
| rs12012519 | AAGGCGTCAAAGGTCAGGAA | GCATCGGATATGCCATAGAGTG | 315 | 60 |
| rs12192544 | TGTTCTAGCCCTGCACTTAAGAGT | CGCGCTGGCTGAGATTCAAAGA | 495 | 62 |
| rs1442801 | CGTTATGGCTGTAGGCTGTTTG | GGCTCCAATTTCTTTGTTTTCC | 291 | 60 |
| rs1619714 | GCCAGGGTGGTAGGAATGAG | GGGAGGCTGAGGTAGGACAA | 398 | 60 |
| rs2056822 | ATCCCCAAAGGTGCCCTCCAT | AAGTCAGGCATCTGACAAGGCA | 493 | 62 |
| rs2288101 | TTTCTCTCTTTCTGCTCATCAGA | TTGTTGTTTCAGACTCCTGCCCAA | 505 | 62 |
| rs34051490 | ACCGTATCTTACTGGCAACCCATC | GCTCTAAAACGTTGGGTCCATTGT | 394 | 60 |
| rs3745936 | GCAGTGAATAACAGGAGGTGGTGA | GCCATAGGCCCATTCACCTTCC | 502 | 62 |
| rs3758354 | ATGAGGAAGCTGTGGGGAGA | TGTTGCTGCTATTACCAGTGCC | 793 | 62 |
| rs3812629 | ACCACATACTGTCCGCACG | CTCGCGAGCAGCGCATCT | 496 | 60 |
| rs4646450 | ACAGGACCTCTATGCTGAAAATAT | GTGTCAATTCAACTGTCCGTGAT | 635 | 60 |
| rs55752830 | GGGACATAGAATCTGGTAGGAGGCA | GGATGGCTGTGGGTGGATTGTA | 536 | 60 |
| rs5951426 | TGAACAAGATGCCTGCTGGTGA | GCATATGTTGCACAGACGGTAGTGA | 588 | 60 |
| rs6104 | TCTGAGAAGCATGGGCATGGA | GGGTAGCAGAAGTTGTTCCAGAAGAGCA | 411 | 62 |
| rs6585827 | TCCTCTTCTCTCTCCCCTCT | ACCTTGCTAAGTTCAACACCGT | 592 | 60 |
| rs714106 | GTGAAGAGACCTGCACCCAGGA | TGACAATCCTGCGTATGTGAAGCA | 509 | 60 |
| rs7414489 | TGATTCCCTTCGCCTCAAG | ACCACAATAAACACCACTCCAAC | 658 | 60 |
| rs75218075 | TCAGAGAAATTCAGATCCCAGAGTT | GGGACTATATGTTTTCTTTCACCTCAT | 502 | 60 |
| rs8022091 | CAGCTGTCAGGGAGCTGCG | TCCCAGCTGATAGGGTGACGTT | 493 | 60 |
| rs893817 | CCCGCTCAGCACATATTTCA | TCTCACAACCCCTACAGACGAT | 377 | 62 |
| rs922948 | TGGAGGTGGGAGGTCAGTCA | CCTATTCAGCGTCTATTCTTTGG | 420 | 62 |
| rs9895154 | GCCTGTTTGCCTTCTCATTCC | CTGCCACATTGACACCAAG | 274 | 62 |
| rs9930984 | CCTTTGAACTAGAAGGACTGGAGTT | GCCACATACATTTTCTCTAGTGTCT | 545 | 60 |

SNP, single nucleotide polymorphism; GWAS, genome-wide association study.

Table S4 Association results of SNPs in the replication study

| SNP | Chr | Position and gene | Number | HWE | MAF | P | Mutation group | Non-mutation group | AF of mutation group | AF of Non-mutation group |
|-------------|-----|--|--------|-------|-------|--------|----------------|--------------------|----------------------|--------------------------|
| rs8022091 | 14 | 14:70655751_A/C_Utr5:SLC8A3 | 248 | 0.961 | 0.347 | 0.0232 | 78 | 170 | 0.731 | 0.618 |
| rs9930984 | 16 | 16:77353973_G/T_ Nonsynonymous:ADAMTS18 | 252 | 0.977 | 0.091 | 0.0255 | 78 | 174 | 0.962 | 0.885 |
| rs75218075 | 3 | 3:167320010_T/C_ Nonsynonymous:WDR49 | 252 | 0.977 | 0.147 | 0.0295 | 79 | 173 | 0.095 | 0.171 |
| rs11023787 | 11 | 11:15952294_C/T_Intergenic | 251 | 0.973 | 0.478 | 0.0592 | 78 | 173 | 0.545 | 0.448 |
| rs117866676 | 12 | 12:123342706_C/T_ Nonsynonymous:HIP1R | 256 | 0.992 | 0.064 | 0.0858 | 79 | 177 | 0.095 | 0.051 |
| rs12012519 | X | X:87190349_T/C_Intergenic | 258 | 1.000 | 0.118 | 0.130 | 80 | 178 | 0.163 | 0.098 |
| rs6104 | 18 | 18:61570529_C/G_ Nonsynonymous:SERPINB2 | 255 | 0.988 | 0.410 | 0.154 | 78 | 177 | 0.468 | 0.384 |
| rs3758354 | 9 | 9:75764565_A/C_Intergenic | 250 | 0.969 | 0.142 | 0.167 | 78 | 172 | 0.109 | 0.157 |
| rs5951426 | X | X:22291606_C/A_ Nonsynonymous:ZNF645 | 258 | 1.000 | 0.426 | 0.223 | 80 | 178 | 0.519 | 0.598 |
| rs11640912 | 16 | 16:77359919_A/T_ Nonsynonymous:ADAMTS18 | 249 | 0.965 | 0.094 | 0.259 | 79 | 170 | 0.930 | 0.894 |
| rs893817 | 15 | 15:74229065_G/A_Intron:LOXL1 | 253 | 0.981 | 0.476 | 0.338 | 77 | 176 | 0.442 | 0.491 |
| rs9895154 | 17 | 17:42267949_G/A_ Nonsynonymous:TMUB2 | 250 | 0.969 | 0.062 | 0.377 | 76 | 174 | 0.046 | 0.069 |
| rs55752830 | 11 | 11:124947396_A/G_ Nonsynonymous:SLC37A2 | 252 | 0.977 | 0.099 | 0.414 | 79 | 173 | 0.082 | 0.107 |
| rs10842496 | 12 | 12:25311489_G/T_ Nonsynonymous:CASC1 | 243 | 0.942 | 0.200 | 0.425 | 77 | 166 | 0.221 | 0.190 |
| rs2056822 | 19 | 19:15739597_A/C_Exon:CYP4F8 | 247 | 0.957 | 0.292 | 0.487 | 76 | 171 | 0.730 | 0.699 |
| rs3745936 | 19 | 19:42092815_T/A_Essential_ Splice_Site:CEACAM21 | 247 | 0.957 | 0.370 | 0.501 | 75 | 172 | 0.607 | 0.640 |
| rs2288101 | 2 | 2:31135184_G/T_ Nonsynonymous:GALNT14 | 254 | 0.985 | 0.209 | 0.639 | 79 | 175 | 0.222 | 0.203 |
| rs3812629 | 10 | 10:75407290_G/A_ Nonsynonymous:SYNPO2L | 252 | 0.977 | 0.177 | 0.653 | 77 | 175 | 0.188 | 0.171 |
| rs34051490 | 16 | 16:20966362_T/C_ Nonsynonymous:DNAH3 | 247 | 0.957 | 0.200 | 0.677 | 77 | 170 | 0.188 | 0.206 |
| rs7414489 | 1 | 1:64165243_C/A_Intergenic | 248 | 0.961 | 0.413 | 0.726 | 80 | 168 | 0.425 | 0.408 |
| rs1442801 | 15 | 15:98768182_C/T_Intron:CTD- 2544M6.1 | 251 | 0.973 | 0.299 | 0.730 | 78 | 173 | 0.712 | 0.697 |
| rs4646450 | 7 | 7:99266318_G/A_Intron:CYP3A5 | 257 | 0.996 | 0.296 | 0.785 | 79 | 178 | 0.304 | 0.292 |
| rs714106 | 19 | 19:42083849_C/A_ Nonsynonymous:CEACAM21 | 257 | 0.996 | 0.181 | 0.860 | 80 | 177 | 0.825 | 0.816 |
| rs922948 | 3 | 3:69442637_G/A_Intron:FRMD4B | 250 | 0.969 | 0.418 | 0.862 | 79 | 171 | 0.576 | 0.585 |
| rs11901030 | 2 | 2:40998751_A/G_Intergenic | 252 | 0.977 | 0.266 | 0.917 | 78 | 174 | 0.263 | 0.267 |
| rs10001249 | 4 | 4:1535004_G/A_Intergenic | 255 | 0.988 | 0.235 | 0.938 | 80 | 175 | 0.238 | 0.234 |
| rs1619714 | 11 | 11:115552918_A/G_ Intron:AP000797.3 | 249 | 0.965 | 0.392 | 0.987 | 78 | 171 | 0.609 | 0.608 |
| rs12192544 | 6 | 6:46620252_C/G_ Nonsynonymous:CYP39A1 | 254 | 0.985 | 0.152 | 0.992 | 76 | 178 | 0.151 | 0.152 |
| rs6585827 | 10 | 10:124165615_G/A_ Intron:PLEKHA1 | 245 | 0.950 | 0.400 | 1.000 | 75 | 170 | 0.600 | 0.600 |

*, adjusted for age, sex, race, smoking status and drinking status. SNP, single nucleotide polymorphism.

Table S5 Primers for MassARRAY genotyping

| SNP | 2ND-PCR | 1ST-PCR | Product (bp) | UEP_SEQ | EXT1_SEQ | EXT2_SEQ |
|-------------|--------------------------------|---------------------------------|--------------|-------------------------------|-------------------------------|-------------------------------|
| rs8022091 | ACGTTGGATGCATTAAGCTGCCGGAAGAAG | ACGTTGGATGTGTCTCCCAGCTGATAGGGT | 102 | ATCTCCAAGCCTCCA | ATCTCCAAGCCTCCAC | ATCTCCAAGCCTCCAA |
| rs75218075 | ACGTTGGATGTTGGACGGCTATTACTG | ACGTTGGATGTTGCCTTTGGAATCCCTATG | 99 | GGACACCCACTGGTT | GGACACCCACTGGTTC | GGACACCCACTGGTTT |
| rs7414489 | ACGTTGGATGTTCCCAGCCTTGATCCATAC | ACGTTGGATGAAGACTCATGCCAGCATAAC | 105 | CCTTGCCTGCCTGCAC | CCTTGCCTGCCTGCAGG | CCTTGCCTGCCTGCACT |
| rs55752830 | ACGTTGGATGACCTGATGAACATGCCGATG | ACGTTGGATGCCATCTGCTTTCAGACAAGG | 115 | ACGATGGCATAGGCGA | ACGATGGCATAGGCGAC | ACGATGGCATAGGCGAT |
| rs4646450 | ACGTTGGATGGCCTTGTCCAGAATACACAC | ACGTTGGATGTAACAAAGAGCGAGAGGACG | 103 | ATCACTTCACGTGGCA | ATCACTTCACGTGGCAC | ATCACTTCACGTGGCAT |
| rs11023787 | ACGTTGGATGATGGCATGTCCTACCTTCTG | ACGTTGGATGAACATTGAGGGAAGGGTCAG | 99 | TCCTACCTTCTGCTCCTT | TCCTACCTTCTGCTCCTTC | TCCTACCTTCTGCTCCTTT |
| rs3812629 | ACGTTGGATGTTACAAGACCCTGCCTCAGG | ACGTTGGATGGAGTCTTAGGAGTCATAGGG | 103 | CGACACCTAAGACCCCCC | CGACACCTAAGACCCCCC | CGACACCTAAGACCCCCCT |
| rs34051490 | ACGTTGGATGCCATTCTGGAGAATGCTGAC | ACGTTGGATGCGTTGGTCCATTGTTCTTC | 100 | GGAAACTTCTCTGATGGA | GGAAACTTCTCTGATGGAC | GGAAACTTCTCTGATGGAT |
| rs2288101 | ACGTTGGATGTCTCTTCTCCCCAGGTATG | ACGTTGGATGACAAGGTGATGACTGACAGG | 102 | GGCCTTCACATACACCAG | GGCCTTCACATACACCAGC | GGCCTTCACATACACCAGA |
| rs12012519 | ACGTTGGATGCTGTATTCTTGACAGAGGG | ACGTTGGATGAAGAAGGACCGCTTCTAGAC | 90 | ACAGGGTGCCTTTAATTTA | ACAGGGTGCCTTTAATTTAC | ACAGGGTGCCTTTAATTTAT |
| rs117866676 | ACGTTGGATGAGCTTGCTCACGGCATCCTG | ACGTTGGATGAGGCTGCTGGACGAGCAGTT | 103 | GGAGCGGCAGCAGCGCCCC | GGAGCGGCAGCAGCGCCCCA | GGAGCGGCAGCAGCGCCCCG |
| rs10001249 | ACGTTGGATGATGTGAGATGCGCCCGAGA | ACGTTGGATGAAATCCACCTGGACGCGAAC | 120 | CACACCCAGGCCAGAAAAC | CACACCCAGGCCAGAAAACC | CACACCCAGGCCAGAAAACCT |
| rs1619714 | ACGTTGGATGAAGGATGACTGTCTCTG | ACGTTGGATGCAGTATCCTGCTTCCCTAAG | 99 | GGGTCGTTATGAGGATTCAA | GGGTCGTTATGAGGATTCAAC | GGGTCGTTATGAGGATTCAAT |
| rs922948 | ACGTTGGATGTCTCCCTTAAAGAAGGTGGC | ACGTTGGATGAAAAGCATCCAAATGGGAGG | 101 | ACCATGATCCACTGGACTTCC | ACCATGATCCACTGGACTTCCC | ACCATGATCCACTGGACTTCT |
| rs3745936 | ACGTTGGATGATCTGCTTTGTGGTCGATCC | ACGTTGGATGGGGTCAAGACCTTCTCTG | 103 | TCGTCAGAGTGTAGCAATTCC | TCGTCAGAGTGTAGCAATTCCA | TCGTCAGAGTGTAGCAATTCT |
| rs3758354 | ACGTTGGATGCTCCAGAGAAATGACTCACC | ACGTTGGATGGTTTGTAAAGTAAAGTGGAGC | 94 | GCTGTTTCTAGAAGATGATGA | GCTGTTTCTAGAAGATGATGAG | GCTGTTTCTAGAAGATGATGAT |
| rs714106 | ACGTTGGATGTGCATTTCCAGAACGTCACC | ACGTTGGATGGGTGAGATGCCTGTTCAATC | 110 | GGGAGGGACACGGGATACTACA | GGGAGGGACACGGGATACTACAC | GGGAGGGACACGGGATACTACAA |
| rs6585827 | ACGTTGGATGCCATTACATTCTACCAAC | ACGTTGGATGCAGGTGCTAACAACCAGTTC | 97 | ACCACATACACATTTTATTTTCAT | ACCACATACACATTTTATTTTCATC | ACCACATACACATTTTATTTTCATT |
| rs1442801 | ACGTTGGATGCTGATTTCTGAGCCAAGTCC | ACGTTGGATGCCCTGTAAAATCTAAATGC | 111 | ATTTATGAGCCAAGTCCACTGTT | ATTTATGAGCCAAGTCCACTGTTA | ATTTATGAGCCAAGTCCACTGTTG |
| rs11640912 | ACGTTGGATGAATACGGCTAGAACCTGGAC | ACGTTGGATGTGAGCCCTTTGATTACTAAC | 110 | ACGTCTAGAACCTGGACAGAATA | ACGTCTAGAACCTGGACAGAATAA | ACGTCTAGAACCTGGACAGAATAT |
| rs893817 | ACGTTGGATGAAACAGGTGAGGTGTGGACG | ACGTTGGATGAAATCTGTTCCCTCCTGCC | 120 | AAGTTGTGGACGAGCAATGGGAA | AAGTTGTGGACGAGCAATGGGAAA | AAGTTGTGGACGAGCAATGGGAAG |
| rs9930984 | ACGTTGGATGGGTGGAATTCAGACATGTTT | ACGTTGGATGCTCCTGGATTTTCGATGCTTC | 112 | GGTTGAGAATATTATCCGGTGGTC | GGTTGAGAATATTATCCGGTGGTCC | GGTTGAGAATATTATCCGGTGGTCA |
| rs6104 | ACGTTGGATGGTGGCAGATCATCTTTTCT | ACGTTGGATGAGCAGCACGCTTAGTTTTAG | 120 | TGCCTTTATTTTTCGGCAGATTTT | TGCCTTTATTTTTCGGCAGATTTTC | TGCCTTTATTTTTCGGCAGATTTTG |
| rs5951426 | ACGTTGGATGTAGCTTAGATGGTCCCTGTC | ACGTTGGATGGTTCGTCTCATATTGCTCC | 100 | CCATGTCTTGCAGTCTTTTAGGGAT | CCATGTCTTGCAGTCTTTTAGGGATG | CCATGTCTTGCAGTCTTTTAGGGATT |
| rs2056822 | ACGTTGGATGATCAGCAGCCTTAACTTGCC | ACGTTGGATGAAGCCATAGGTGACCTTTC | 108 | CTCGATGACCCCTTCCGCTTCGACCC | CTCGATGACCCCTTCCGCTTCGACCCC | CTCGATGACCCCTTCCGCTTCGACCCA |
| rs10842496 | ACGTTGGATGGCTGTATTTCAAGCCTTTCC | ACGTTGGATGACAGTGATCTATTCACTGAG | 119 | CCGTTCTTCTTCTCATATTTCAAAC | CCGTTCTTCTTCTCATATTTCAAACG | CCGTTCTTCTTCTCATATTTCAAACCT |
| rs12192544 | ACGTTGGATGCCTTGCTCTGTTCTTACTCC | ACGTTGGATGCTCCAATCCAAGGAATCCAG | 100 | GACTGGCTCTGTTCTTACTCCTTCAGC | GACTGGCTCTGTTCTTACTCCTTCAGCC | GACTGGCTCTGTTCTTACTCCTTCAGCG |
| rs11901030 | ACGTTGGATGTGGTTTCAGACACTAAAAGC | ACGTTGGATGGGACTGCAGTTTCTCAGAAC | 106 | AAAATCAACTAATGTTGACACTTAAAT | AAAATCAACTAATGTTGACACTTAAATA | AAAATCAACTAATGTTGACACTTAAATG |
| rs9895154 | ACGTTGGATGTGAAACTGATCTACCAGGGC | ACGTTGGATGGTGAATCACACAGTTGTCGG | 106 | ATGCGACAAGACCCAGCCCGCACACTGCG | ATGCGACAAGACCCAGCCCGCACACTGCA | ATGCGACAAGACCCAGCCCGCACACTGCG |

Table S6 Primers used in quantitative RT-PCR assays

| Genes | Primers | Sequences |
|----------|---------|------------------------|
| GAPDH | Forward | GTCAGCCGCATCTTCTTT |
| | Reverse | CGCCAATACGACCAAAT |
| ADAMTS18 | Forward | GAGGTGCAGCAATGCTTCTAT |
| | Reverse | CAGCACACGTAGACACAGC |
| WDR49 | Forward | CCATTATGAGTTGCCAGAAAGC |
| | Reverse | CCCACGCTGAGTTGGTTTT |
| SLC8A3 | Forward | GACGACAAAGGGCTACTGGAA |
| | Reverse | AGCATTAGGAAGCAAGAGCGT |