

Table S3. Testing for antagonistic pleiotropy for SNPs with significant effects on lifetime reproductive success (LRS) and coronary artery disease (CAD). *Left table:* provides statistics for CAD index SNPs derived directly from the CARDIoGRAMplusC4D 1000 Genomes-based GWAS meta-analysis (see [1] or <http://www.cardiogramplusc4d.org/data-downloads/> for further details of data and variables). *Right table:* provides corresponding FaST-LMM regression statistics of these SNPs on LRS based on Framingham Heart Study women (first six columns), rows correspond to SNPs in the left table. Last four columns test for antagonistic effects between CAD and LRS with the last two providing these tests only when the LRS beta was significant. This shows that when SNPs with significant effects on both LRS and CAD are considered, most (5 of 6, or 83%) were antagonistic, i.e. the allele that increases LRS also increases CAD risk.

| index SNP | chr | gene | locus name | Nikpay Statistics (additive) | | | | | | FaST-LMM results (LRS) | | | | | Antagonistic effect checks (LRS beta corrected for Nikpay effect allele) | | | |
|------------|-----|------------|---------------------|------------------------------|---------------|-------------------|---------|--------|----------|------------------------|---------|--------|----------|--------|--|--------------------|---------------|--------------|
| | | | | b37 position | effect allele | non-effect allele | beta | se_dgc | p_dgc | het_pvalue | beta | se | p value | allele | MAF | beta (any p value) | beta (p<0.05) | |
| rs7212798 | 17 | BCAS3 | BCAS3 | 59013488 | T | C | -0.0800 | 0.0142 | 1.88E-08 | 2.11E-01 | 0.0035 | 0.0165 | 8.32E-01 | C | T | 0.1355 | -0.0035 | antagonistic |
| rs12413409 | 10 | CNNM2 | CYP17A1-CNNM2-NTSC2 | 104719096 | G | A | 0.0752 | 0.0141 | 1.07E-07 | 1.13E-01 | -0.0143 | 0.0159 | 3.70E-01 | A | G | 0.0820 | 0.0143 | antagonistic |
| rs2252641 | 2 | TEX41 | ZEB2-AC074093.1 | 145801461 | C | T | 0.0333 | 0.0096 | 5.16E-04 | 7.11E-02 | 0.0104 | 0.0159 | 5.15E-01 | C | T | 0.4636 | 0.0104 | antagonistic |
| rs216172 | 17 | SMG6 | SMG6 | 2126504 | G | C | -0.0480 | 0.0096 | 5.07E-07 | 2.00E-01 | 0.0216 | 0.0160 | 1.76E-01 | C | G | 0.3495 | -0.0216 | antagonistic |
| rs12526453 | 6 | PHACTR1 | PHACTR1 | 12927544 | C | G | 0.0968 | 0.0105 | 2.14E-20 | 4.58E-01 | -0.0073 | 0.0160 | 6.49E-01 | G | C | 0.3245 | 0.0073 | antagonistic |
| rs1122608 | 19 | LDLR | LDLR | 11163601 | G | T | 0.0732 | 0.0110 | 2.73E-11 | 7.48E-02 | 0.0262 | 0.0159 | 1.01E-01 | T | G | 0.2498 | -0.0262 | - |
| rs10947789 | 6 | KCNK5 | KCNK5 | 39174922 | T | C | 0.0531 | 0.0111 | 1.63E-06 | 5.55E-01 | 0.0088 | 0.0160 | 5.86E-01 | C | T | 0.2387 | -0.0088 | - |
| rs579459 | 9 | ABO | ABO | 136154168 | T | C | -0.0730 | 0.0113 | 1.14E-10 | 2.58E-02 | 0.0117 | 0.0160 | 4.66E-01 | C | T | 0.1889 | -0.0117 | antagonistic |
| rs10840293 | 11 | SWAP70 | SWAP70 | 9751196 | A | G | 0.0547 | 0.0096 | 1.28E-08 | 1.58E-01 | -0.0039 | 0.0182 | 8.32E-01 | G | A | 0.4218 | 0.0039 | antagonistic |
| rs3184504 | 12 | SH2B3 | SH2B3 | 111884608 | C | T | -0.0642 | 0.0105 | 1.03E-09 | 6.76E-03 | -0.0056 | 0.0198 | 7.77E-01 | T | C | 0.4839 | 0.0056 | - |
| rs12936587 | 17 | PEMT | RAI1-PEMT-RASD1 | 17543722 | G | A | 0.0333 | 0.0099 | 8.24E-04 | 1.98E-01 | 0.0079 | 0.0176 | 6.52E-01 | A | G | 0.4467 | -0.0079 | - |
| rs9818870 | 3 | MRAS | MRAS | 138122122 | C | T | -0.0646 | 0.0137 | 2.21E-06 | 4.61E-01 | -0.0013 | 0.0159 | 9.35E-01 | T | C | 0.1403 | 0.0013 | - |
| rs2505083 | 10 | KIAA1462 | KIAA1462 | 30335122 | T | C | -0.0610 | 0.0095 | 1.57E-10 | 2.36E-01 | 0.0035 | 0.0181 | 8.46E-01 | C | T | 0.3981 | -0.0035 | antagonistic |
| rs7692387 | 4 | GUCY1A3 | GUCY1A3 | 156635309 | G | A | 0.0679 | 0.0117 | 7.35E-09 | 7.64E-01 | 0.0155 | 0.0160 | 3.32E-01 | A | G | 0.1805 | -0.0155 | - |
| rs3217992 | 9 | CDKN2B-AS1 | CDKN2BAS1 | 22003223 | C | T | -0.1283 | 0.0094 | 1.03E-42 | 3.25E-04 | 0.0173 | 0.0164 | 2.94E-01 | T | C | 0.3939 | -0.0173 | antagonistic |
| rs17609940 | 6 | ANKS1A | ANKS1A | 35034800 | G | C | 0.0276 | 0.0125 | 2.65E-02 | 3.59E-01 | 0.0237 | 0.0160 | 1.40E-01 | C | G | 0.1857 | -0.0237 | - |
| rs974819 | 11 | PDGFD | PDGFD | 103660567 | C | T | -0.0634 | 0.0100 | 2.44E-10 | 2.17E-01 | 0.0070 | 0.0163 | 6.66E-01 | T | C | 0.3082 | -0.0070 | antagonistic |
| rs11830157 | 12 | KSR2 | KSR2 | 118265441 | T | G | -0.0347 | 0.0098 | 3.88E-04 | 1.39E-01 | 0.0220 | 0.0184 | 2.32E-01 | G | T | 0.3703 | -0.0220 | antagonistic |
| rs9319428 | 13 | FLT1 | FLT1 | 28973621 | G | A | -0.0396 | 0.0100 | 7.13E-05 | 3.90E-01 | 0.0415 | 0.0169 | 1.43E-02 | A | G | 0.2877 | -0.0415 | antagonistic |
| rs6544713 | 2 | ABCG5 | ABCG5-ABCG8 | 44073881 | C | T | -0.0515 | 0.0105 | 8.88E-07 | 5.40E-02 | 0.0161 | 0.0163 | 3.23E-01 | T | C | 0.3303 | -0.0161 | antagonistic |
| rs11556924 | 7 | ZC3HC1 | ZC3HC1 | 129663496 | C | T | 0.0726 | 0.0111 | 5.34E-11 | 8.44E-02 | 0.0057 | 0.0160 | 7.21E-01 | T | C | 0.3797 | -0.0057 | - |
| rs56062135 | 15 | SMAD3 | SMAD3 | 67455630 | C | T | 0.0697 | 0.0119 | 4.52E-09 | 6.68E-01 | -0.0109 | 0.0171 | 5.24E-01 | T | C | 0.2080 | 0.0109 | antagonistic |
| rs17087335 | 4 | REST | REST-NOA1 | 57838583 | G | T | -0.0608 | 0.0111 | 4.59E-08 | 1.14E-01 | -0.0140 | 0.0159 | 3.79E-01 | T | G | 0.1811 | 0.0140 | - |
| rs17114036 | 1 | PPAP2B | PPAP2B | 56962821 | A | G | 0.1231 | 0.0168 | 2.22E-13 | 6.45E-02 | 0.0199 | 0.0161 | 2.17E-01 | G | A | 0.0940 | -0.0199 | - |
| rs17464857 | 1 | MIA3 | MIA3 | 222762709 | T | G | 0.0573 | 0.0140 | 4.18E-05 | 4.71E-01 | 0.0142 | 0.0159 | 3.69E-01 | G | T | 0.1457 | -0.0142 | - |
| rs4845625 | 1 | IL6R | IL6R | 154422067 | C | T | -0.0507 | 0.0092 | 3.93E-08 | 6.40E-01 | 0.0018 | 0.0161 | 9.09E-01 | T | C | 0.4178 | -0.0018 | antagonistic |
| rs2023938 | 7 | HDAC9 | HDAC9 | 19036775 | T | C | -0.0591 | 0.0155 | 1.36E-04 | 2.97E-01 | 0.0436 | 0.0159 | 6.24E-03 | C | T | 0.0892 | 0.0436 | - |
| rs9515203 | 13 | COL4A1 | COL4A1-COL4A2 | 111049623 | T | C | 0.0711 | 0.0116 | 9.33E-10 | 1.39E-01 | 0.0176 | 0.0184 | 3.39E-01 | C | T | 0.1985 | -0.0176 | - |
| rs8042271 | 15 | ABHD2 | MFG8-ABHD2 | 89574218 | A | G | -0.0967 | 0.0176 | 3.68E-08 | 1.86E-01 | -0.0264 | 0.0162 | 1.03E-01 | A | G | 0.0470 | -0.0264 | antagonistic |
| rs602633 | 1 | SORT1 | SORT1 | 109821511 | G | T | 0.0960 | 0.0115 | 6.97E-17 | 7.33E-03 | -0.0073 | 0.0163 | 6.53E-01 | T | G | 0.2171 | 0.0073 | antagonistic |
| rs264 | 8 | LPL | LPL | 19813180 | G | A | 0.0583 | 0.0132 | 1.06E-05 | 9.78E-01 | 0.0188 | 0.0160 | 2.40E-01 | A | G | 0.1355 | -0.0188 | - |
| rs7173743 | 15 | ADAMT57 | ADAMT57 | 79141784 | T | C | 0.0755 | 0.0093 | 5.55E-16 | 2.12E-01 | 0.0188 | 0.0163 | 2.48E-01 | C | T | 0.4627 | -0.0188 | - |
| rs46522 | 17 | UBE2Z | UBE2Z | 46988597 | C | T | -0.0398 | 0.0093 | 1.84E-05 | 6.44E-01 | 0.0028 | 0.0159 | 8.60E-01 | C | T | 0.4658 | 0.0028 | - |
| rs273909 | 5 | SLC22A4 | SLC22A4-SLC22A5 | 131667353 | A | G | -0.0559 | 0.0146 | 1.24E-04 | 4.79E-01 | -0.0027 | 0.0166 | 8.69E-01 | G | A | 0.0726 | -0.0027 | antagonistic |
| rs12976411 | 19 | LOC400684 | ZNF507-LOC400684 | 32882020 | A | T | 0.0478 | 0.0183 | 9.12E-03 | 1.03E-01 | 0.0010 | 0.0164 | 9.50E-01 | T | A | 0.0385 | 0.0010 | antagonistic |
| rs2047009 | 10 | CXCL12 | CXCL12 | 44539913 | T | G | -0.0613 | 0.0092 | 2.75E-11 | 1.54E-01 | 0.0041 | 0.0159 | 7.97E-01 | T | G | 0.4769 | 0.0041 | - |
| rs515135 | 2 | APOB | APOB | 21286057 | C | T | 0.0675 | 0.0122 | 3.09E-08 | 9.42E-01 | 0.0159 | 0.0160 | 3.23E-01 | T | C | 0.1979 | -0.0159 | - |
| rs1878406 | 4 | EDNRA | EDNRA | 148393664 | C | T | -0.0604 | 0.0125 | 1.24E-06 | 3.59E-02 | -0.0137 | 0.0160 | 3.93E-01 | T | C | 0.1399 | 0.0137 | - |
| rs4252120 | 6 | PLG | PLG | 161143608 | T | C | 0.0329 | 0.0112 | 3.32E-03 | 8.71E-01 | -0.0468 | 0.0159 | 3.32E-03 | C | T | 0.2967 | 0.0468 | antagonistic |
| rs11206510 | 1 | PCSK9 | PCSK9 | 55496039 | T | C | 0.0745 | 0.0133 | 2.34E-08 | 5.58E-01 | -0.0012 | 0.0159 | 9.39E-01 | C | T | 0.1932 | 0.0012 | antagonistic |
| rs17514846 | 15 | FES | FURIN-FES | 91416550 | C | A | -0.0509 | 0.0100 | 3.10E-07 | 2.42E-01 | -0.0372 | 0.0344 | 2.79E-01 | A | C | 0.4834 | 0.0372 | - |
| rs6725887 | 2 | WDR12 | WDR12 | 203745885 | T | C | -0.1329 | 0.0155 | 9.51E-18 | 3.93E-01 | -0.0214 | 0.0159 | 1.78E-01 | C | T | 0.1308 | 0.0214 | - |
| rs1561198 | 2 | VAMP5 | VAMP5-VAMP8-GGCX | 85809989 | C | T | -0.0584 | 0.0095 | 6.37E-10 | 4.03E-01 | 0.0216 | 0.0161 | 1.79E-01 | T | C | 0.4663 | -0.0216 | antagonistic |
| rs2954029 | 8 | TRIB1 | TRIB1 | 126490972 | A | T | 0.0439 | 0.0093 | 2.61E-06 | 2.42E-01 | 0.0169 | 0.0162 | 2.96E-01 | T | A | 0.4396 | -0.0169 | - |
| rs12190287 | 6 | TCF21 | TCF21 | 134214525 | C | G | 0.0580 | 0.0177 | 1.07E-03 | 1.24E-09 | -0.0435 | 0.0176 | 1.33E-02 | G | C | 0.3670 | 0.0435 | antagonistic |
| rs180803 | 22 | POM121L9P | POM121L9P-ADORA2A | 24658858 | T | G | -0.1809 | 0.0283 | 1.64E-10 | 6.68E-01 | - | - | - | - | 0.0092 | - | - | |
| rs663129 | 18 | PMAIP1 | PMAIP1-MC4R | 57838401 | G | A | -0.0582 | 0.0105 | 3.20E-08 | 5.95E-01 | 0.0106 | 0.0160 | 5.06E-01 | A | G | 0.2172 | -0.0106 | antagonistic |
| rs3918226 | 7 | NOS3 | NOS3 | 150690176 | C | T | -0.1333 | 0.0221 | 1.69E-09 | 1.94E-01 | 0.0364 | 0.0175 | 3.84E-02 | T | C | 0.0278 | -0.0364 | antagonistic |
| rs2048327 | 6 | LPA | SLC22A3-LPAL2-LPA | 160863532 | T | C | -0.0575 | 0.0096 | 2.46E-09 | 8.72E-03 | -0.0418 | 0.0160 | 8.94E-03 | C | T | 0.3648 | -0.0418 | antagonistic |
| rs11203042 | 10 | LIPA | LIPA | 90989109 | C | T | -0.0355 | 0.0092 | 1.22E-04 | 3.10E-01 | 0.0238 | 0.0165 | 1.50E-01 | T | C | 0.4519 | 0.0238 | - |
| rs9982601 | 21 | KCNE2 | KCNE2 | 35599128 | C | T | -0.1098 | 0.0148 | 1.33E-13 | 5.43E-02 | -0.0084 | 0.0161 | 6.02E-01 | T | C | 0.1369 | 0.0084 | - |
| rs2895811 | 14 | HHLPL1 | HHLPL1 | 100133942 | T | C | -0.0408 | 0.0095 | 1.86E-05 | 3.75E-02 | -0.0209 | 0.0202 | 3.01E-01 | C | T | 0.3636 | 0.0209 | - |
| rs445925 | 19 | APOC1 | ApoE-ApoC1 | 45415640 | G | A | 0.0858 | 0.0187 | 4.23E-06 | 5.30E-02 | 0.0169 | 0.0204 | 4.09E-01 | A | G | 0.0356 | -0.0169 | - |
| rs9326246 | 11 | APOA1 | ZNF259-APOA5-APOA1 | 116611733 | G | C | -0.0458 | 0.0151 | 2.46E-03 | 2.56E-02 | -0.0253 | 0.0159 | 1.12E-01 | C | G | 0.0739 | 0.0253 | - |

5 of 6 (83%) antagonistic

References
 1. Nikpay, M., et al., *A comprehensive 1000 Genomes-based genome-wide association meta-analysis of coronary artery disease.* Nature Genetics, 2015. **47**(10): p. 1121-+.