**Supplemental Digital Content 1. Single nucleotide polymorphisms included in construction of genetic scores for physical fitness**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Gene** | **Location** | **SNP** | **Fitness Allele** | **Fitness Allele Frequency**  **in WGHS** | **Genotyped/**  **Imputed**  **(R-squared)** | **Reference Number** | **CHD Risk per Allele**  **in WGHS** | | | | **SNP X PA Interaction\***  **in WGHS** | |
| HR (95% CI) | | | P-value | β (SE) | P-value |
| **Endurance Phenotypes** | | | | | | | | | | | | |
| *ACE* | 17q23 | rs1800764 | T | 0.54 | Imputed (0.925) | 3 | | 0.92 (0.78, 1.09) | | 0.34 | 0.09 (0.06) | 0.09 |
| *ADRA2A* | 10q24-q26 | rs553668 | G | 0.84 | Genotyped | 50 | | 0.98 (0.79, 1.22) | | 0.88 | 0.13 (0.08) | 0.10 |
| *ADRB1* | 10q24-q26 | rs1801253 | C | 0.73 | Genotyped | 7, 33, 46 | | 1.00 (0.84, 1.20) | | 0.97 | -0.02 (0.06) | 0.72 |
| *ADRB2* | 5q31-q32 | rs1800888 | C | 0.99 | Genotyped | 47 | | 1.12 (0.55, 2.25) | | 0.76 | -0.15 (0.22) | 0.48 |
| *ADRB2* | 5q31-q32 | rs1042713 | A | 0.37 | Genotyped | 47, 51 | | 1.03 (0.88, 1.21) | | 0.74 | 0.12 (0.05) | 0.03 |
| *ADRB2* | 5q31-q32 | rs1042714 | C | 0.56 | Genotyped | 21, 22 | | 0.97 (0.83, 1.14) | | 0.73 | 0.09 (0.05) | 0.09 |
| *AMPD1* | 1p13 | rs17602729 | G | 0.85 | Genotyped | 28, 32 | | 1.21 (0.96, 1.54) | | 0.11 | 0.09 (0.08) | 0.30 |
| *EPHX1* | 1q42.1 | rs1051740 | T | 0.70 | Genotyped | 19 | | 0.98 (0.82, 1.17) | | 0.78 | -0.10 (0.06) | 0.07 |
| *GABPB2* | 15q21.2 | rs12594956 | A | 0.59 | Imputed (0.999) | 16 | | 1.03 (0.88, 1.21) | | 0.72 | -0.03 (0.05) | 0.52 |
| *GABPB2* | 15q21.2 | rs8031031 | T | 0.02 | Imputed (0.990) | 16 | | 0.62 (0.29, 1.30) | | 0.21 | 0.11 (0.23) | 0.62 |
| *HBB* | 11p15.5 | rs10768683 | C | 0.16 | Imputed (0.998) | 17 | | 0.96 (0.77, 1.19) | | 0.72 | -0.10 (0.08) | 0.18 |
| *LTBP4* | 19q13.1-q13.2 | rs2303729 | A | 0.44 | Genotyped | 19 | | 1.02 (0.88, 1.20) | | 0.78 | -0.06 (0.05) | 0.28 |
| *LTBP4* | 19q13.1-q13.2 | rs1051303 | G | 0.42 | Genotyped | 19 | | 1.07 (0.92, 1.26) | | 0.38 | -0.04 (0.05) | 0.50 |
| *NOS3* | 7q36 | [rs1799983](http://www.pharmgkb.org/redirect.jsp?p=http%3A%2F%2Fwww.ncbi.nlm.nih.gov%2Fentrez%2Fquery.fcgi%3Fdb%3Dsnp%26cmd%3Dsearch%26term%3Drs1799983) | T | 0.34 | Imputed (0.753) | 35 | | 1.00 (0.83, 1.21) | | 0.99 | 0.06 (0.06) | 0.37 |
| *PPARA* | 22q13.31 | rs4253778 | G | 0.82 | Imputed (0.981) | 1 | | 1.11 (0.90, 1.37) | | 0.33 | -0.05 (0.07) | 0.48 |
| *PPARD* | 6p21.2-p21.1 | rs2016520 | T | 0.81 | Genotyped | 15 | | 0.94 (0.78, 1.14) | | 0.52 | 0.05 (0.07) | 0.43 |
| *PPARD* | 6p21.2-p21.1 | rs2267668 | A | 0.83 | Genotyped | 39 | | 0.90 (0.74, 1.09) | | 0.27 | 0.05 (0.07) | 0.43 |
| *PPARGC1A* | 4p15.1 | rs8192678 | C | 0.65 | Imputed (0.923) | 20, 39 | | 0.99 (0.84, 1.18) | | 0.93 | -0.03 (0.06) | 0.63 |
| *SCGB1A1* | 11q12.3-q13.1 | rs3741240 | G | 0.63 | Imputed (0.851) | 38 | | 0.90 (0.75, 1.07) | | 0.22 | -0.003 (0.06) | 0.95 |
| *UCP2* | 11q13 | rs660339 | A | 0.996 | Genotyped | 5 | | 1.45 (0.18, 11.49) | | 0.72 | -0.13 (0.63) | 0.83 |
| **Muscle Strength Phenotypes** | | | | | | | | | | | | |
| *ACTN3* | 11q13-q14 | rs1815739 | C | 0.55 | Genotyped | 6, 8, 23, 44, 52 | | | 0.90 (0.77, 1.06) | 0.20 | 0.09 (0.05) | 0.10 |
| *ACVR2B* | 3p22 | rs2268757 | C | 0.43 | Imputed (0.976) | 45 | | | 0.96 (0.82, 1.13) | 0.65 | -0.01 (0.05) | 0.87 |
| *AMPD1* | 1p13 | rs17602729 | G | 0.85 | Genotyped | 11 | | | 1.21 (0.96, 1.54) | 0.11 | 0.09 (0.08) | 0.30 |
| *CNTF* | 11q12.2 | rs1800169 | G | 0.86 | Genotyped | 2, 31 | | | 0.84 (0.68, 1.04) | 0.11 | 0.05 (0.07) | 0.51 |
| *CNTFR* | 9p13 | rs3808871 | A | 0.24 | Imputed (0.977) | 9 | | | 0.92 (0.76, 1.11) | 0.35 | -0.09 (0.07) | 0.19 |
| *CNTFR* | 9p13 | rs2070802 | T | 0.14 | Imputed (0.991) | 9 | | | 0.96 (0.76, 1.21) | 0.73 | -0.16 (0.09) | 0.07 |
| *DIO1* | 1p33-p32 | rs11206244 | T | 0.32 | Imputed (0.799) | 25 | | | 0.79 (0.65, 0.96) | 0.02 | 0.01 (0.07) | 0.86 |
| *GDF8* | 2q32.2 | rs1805086 | T | 0.992 | Imputed (0.605) | 37 | | | 1.35 (0.46, 3.92) | 0.58 | 0.23 (0.44) | 0.61 |
| *IGF2* | 11p15.5 | rs3213221 | G | 0.62 | Imputed (0.993) | 10 | | | 0.98 (0.83, 1.14) | 0.75 | -0.04 (0.05) | 0.48 |
| *IGF2* | 11p15.5 | rs7924316 | T | 0.45 | Genotyped | 10 | | | 0.97 (0.83, 1.14) | 0.75 | 0.09 (0.05) | 0.09 |
| *PPARA* | 22q13.31 | rs4253778 | G | 0.82 | Imputed (0.981) | 1 | | | 1.11 (0.90, 1.37) | 0.33 | -0.05 (0.07) | 0.48 |
| *RETN* | 19p13.2 | rs1862513 | C | 0.70 | Genotyped | 26 | | | 1.02 (0.86, 1.21) | 0.83 | -0.05 (0.06) | 0.40 |
| *TNF* | 6p21.3 | rs1800629 | G | 0.83 | Genotyped | 24 | | | 0.85 (0.70, 1.04) | 0.11 | -0.01 (0.07) | 0.90 |

**Supplemental Digital Content 1 (continued). Single nucleotide polymorphisms included in construction of genetic scores for physical fitness**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Gene** | **Location** | **SNP** | **Fitness Allele** | **Fitness Allele Frequency**  **in WGHS** | **Genotyped/**  **Imputed**  **(R-squared)** | | | **Reference Number** | | | **CHD Risk per Allele**  **in WGHS** | | | | **SNP X PA Interaction\***  **in WGHS** | | |
| HR (95% CI) | | P-value | | β (SE) | | P-value |
| *VDR* | 12q13.11 | rs1544410 | T | 0.41 | Imputed (0.998) | | | 12, 13, 48, 49 | | | 0.91 (0.78, 1.07) | | 0.24 | | -0.02 (0.05) | | 0.77 |
| **Vo2max Training Response** | | | | | | | | | | | | | | | | | |
| *BTAF1* | 10q22-q23 | rs2792022 | G | 0.28 | Genotyped | | | 41 | 1.01 (0.85, 1.21) | | | | 0.87 | | 0.01 (0.06) | | 0.85 |
| *CPVL* | 7p15-p14 | rs4257918 | G | 0.86 | Imputed (0.997) | | | 41 | 1.08 (0.86, 1.35) | | | | 0.53 | | -0.01 (0.08) | | 0.90 |
| *DEPDC6* | 8q24.12 | rs7386139 | A | 0.81 | Genotyped | | | 41 | 1.04 (0.85, 1.28) | | | | 0.68 | | -0.04 (0.07) | | 0.53 |
| *DIS3L* | 15q22.31 | rs1546570 | A | 0.24 | Imputed (0.968) | | | 41 | 0.86 (0.71, 1.04) | | | | 0.12 | | 0.08 (0.06) | | 0.22 |
| *H19* | 11p15.5 | rs2251375 | C | 0.71 | Imputed (0.862) | | | 41 | 0.98 (0.81, 1.17) | | | | 0.80 | | -0.03 (0.06) | | 0.67 |
| *ID3* | 1p36.13-p36.12 | rs11574 | G | 0.76 | Genotyped | | | 41 | 0.89 (0.75, 1.06) | | | | 0.20 | | -0.02 (0.06) | | 0.73 |
| *MIPEP* | 13q12 | rs7324557 | A | 0.35 | Imputed (0.892) | | | 41 | 0.91 (0.77, 1.09) | | | | 0.31 | | -0.02 (0.06) | | 0.74 |
| *NRP2* | 2q33.3 | rs3770991 | A | 0.11 | Imputed (0.830) | | | 41 | 0.92 (0.69, 1.21) | | | | 0.53 | | 0.09 (0.09) | | 0.31 |
| *SLC22A3* | 6q26-q27 | rs2457571 | G | 0.49 | Genotyped | | | 41 | 1.07 (0.92, 1.25) | | | | 0.38 | | 0.04 (0.05) | | 0.46 |
| *SVIL* | 10p11.2 | rs6481619 | G | 0.28 | Imputed (0.962) | | | 41 | 0.93 (0.78, 1.11) | | | | 0.42 | | -0.06 (0.06) | | 0.31 |
| *TTN* | 2q31 | rs10497520 | G | 0.87 | Genotyped | | | 41 | 1.29 (1.00, 1.66) | | | | 0.05 | | -0.03 (0.08) | | 0.73 |
| *PRDM1* | 6q21 | rs10499043 | A | 0.12 | Genotyped | | | 4 | 1.05 (0.82, 1.33) | | | | 0.71 | | -0.06 (0.08) | | 0.45 |
| *GRIN3A* | 9q31.1 | rs1535628 | A | 0.08 | Genotyped | | | 4 | 0.96 (0.72, 1.28) | | | | 0.77 | | 0.05 (0.09) | | 0.59 |
| *KCNH8* | 3p24.3 | rs4973706 | A | 0.75 | Genotyped | | | 4 | 0.93 (0.78, 1.11) | | | | 0.41 | | 0.05 (0.06) | | 0.42 |
| *C9orf27* | 9q33.1 | rs12115454 | G | 0.91 | Genotyped | | | 4 | 1.09 (0.83, 1.45) | | | | 0.53 | | 0.02 (0.10) | | 0.85 |
| *ACSL1* | 4q35.1 | rs6552828 | G | 0.60 | Genotyped | | | 4 | 0.93 (0.80, 1.09) | | | | 0.40 | | 0.05 (0.05) | | 0.36 |
| *ZIC4* | 3q24 | rs11715829 | G | 0.07 | Genotyped | | | 4 | 0.94 (0.69, 1.28) | | | | 0.69 | | -0.07 (0.11) | | 0.53 |
| *CAMTA1* | 1p36.31 | rs884736 | G | 0.55 | Genotyped | | | 4 | 1.08 (0.92, 1.26) | | | | 0.35 | | -0.003 (0.05) | | 0.96 |
| *RGS18* | 1q31.2 | rs10921078 | A | 0.18 | Genotyped | | | 4 | 1.06 (0.87, 1.29) | | | | 0.59 | | 0.11 (0.06) | | 0.07 |
| *BIRC7* | 20q13.33 | rs6090314 | A | 0.16 | Genotyped | | | 4 | 1.29 (1.06, 1.57) | | | | 0.01 | | 0.02 (0.07) | | 0.72 |
| *DBX1* | 11p15.1 | rs10500872 | A | 0.84 | Genotyped | | | 4 | 0.92 (0.75, 1.14) | | | | 0.45 | | -0.14 (0.07) | | 0.03 |
| *DAAM1* | 14q23.1 | rs1956197 | G | 0.14 | Genotyped | | | 4 | 0.88 (0.70, 1.11) | | | | 0.28 | | -0.09 (0.08) | | 0.27 |
| *NDN* | 15q11.2 | rs824205 | A | 0.18 | Genotyped | | | 4 | 0.88 (0.72, 1.09) | | | | 0.24 | | -0.001 (0.07) | | 0.99 |
| *CXCR5* | 11q23.3 | rs7933007 | G | 0.24 | Genotyped | | | 4 | 0.76 (0.62, 0.92) | | | | 0.005 | | 0.07 (0.06) | | 0.25 |
| *TTC6* | 14q21.1 | rs12896790 | C | 0.10 | Genotyped | | | 4 | 1.07 (0.83, 1.38) | | | | 0.61 | | -0.05 (0.09) | | 0.57 |
| *LOC400950* | 2p21 | rs4952535 | G | 0.63 | Genotyped | | | 4 | 1.01 (0.86, 1.18) | | | | 0.93 | | -0.05 (0.05) | | 0.36 |
| **SNPs Not Available (Not Genotyped or Imputed)** | | | | | | | | | | | | | | | | | |
| *ADRB1* | 10q24-q26 | rs1801252 |  |  |  | | | 7, 46 |  | | | |  | |  | |  |
| *APOE* | 19q13.2 | rs429358 |  |  |  | | | 14, 40 |  | | | |  | |  | |  |
| *APOE* | 19q13.2 | rs7412 |  |  |  | | | 14, 40 |  | | | |  | |  | |  |
| *CKM* | 19q13.2-q13.3 | rs1803285 |  |  |  | | | 29, 30, 53 |  | | | |  | |  | |  |
| *COL1A1* | 17q21.3-q22.1 | rs1800012 |  |  |  | | | 42 |  | | | |  | |  | |  |
| *EPAS1* | 2p21-p16 | rs895436 |  |  |  | | | 18 |  | | | |  | |  | |  |
| **Supplemental Digital Content 1 (continued). Single nucleotide polymorphisms included in construction of genetic scores for physical fitness** | | | | | | | | | | | | | | | | | |
| **Gene** | **Location** | **SNP** | **Fitness Allele** | **Fitness Allele Frequency**  **in WGHS** | **Genotyped/**  **Imputed**  **(R-squared)** | | | **Reference Number** | **CHD Risk per Allele**  **in WGHS** | | | | | | **SNP X PA Interaction\***  **in WGHS** | | |
| HR (95% CI) | | | | P-value | | β (SE) | | P-value |
| *EPAS1* | 2p21-p16 | rs4035887 |  |  | |  | 18 | | |  | |  | |  | |  | |
| *IGF2* | 11p15.5 | rs680 |  |  | |  | 10, 34, 36 | | |  | |  | |  | |  | |
| *LTBP4* | 19q13.1-q13.2 | rs2077407 |  |  | |  | 16 | | |  | |  | |  | |  | |
| *NR3C1* | 5q21 | rs6189 |  |  | |  | 43 | | |  | |  | |  | |  | |
| *NR3C1* | 5q21 | rs6190 |  |  | |  | 43 | | |  | |  | |  | |  | |
| *VDR* | 12q13.11 | rs2228570 |  |  | |  | 49 | | |  | |  | |  | |  | |
| *VEGFA* | 6p21 | rs1570360 |  |  | |  | 27 | | |  | |  | |  | |  | |
| *VEGFA* | 6p21 | rs2010963 |  |  | |  | 27 | | |  | |  | |  | |  | |

\*β (SE) for interaction between SNP and physical activity in multivariable-adjusted model with CHD as the outcome.