

**ESM Table 7 51 associations for eight metabolic traits selected for replication in stage 3**

| Trait               | Gene            | rs-number  | Chr-Pos      | Effect allele | Non effect allele | MAF  | MAF-HapMap | Function | Mutation | <i>n</i> | Effect (95% CI)     | <i>P</i> -value      |
|---------------------|-----------------|------------|--------------|---------------|-------------------|------|------------|----------|----------|----------|---------------------|----------------------|
| Type 2 diabetes     | <i>COBLL1</i>   | rs7607980  | 2-165259447  | C             | T                 | 13   | 16         | Nonsyn   | N939D    | 12177    | 0.80 (0.74 to 0.87) | 3×10 <sup>-7</sup>   |
| Type 2 diabetes     | <i>KIR3DL3</i>  | rs16985907 | 19-59938624  | C             | G                 | 4.1  | 4.2        | Nonsyn   | A348P    | 12179    | 1.31 (1.16 to 1.49) | 7.5×10 <sup>-5</sup> |
| Type 2 diabetes     | <i>C1orf222</i> | rs28633659 | 1-1844406    | T             | C                 | 3.9  |            | Nonsyn   | E187K    | 12179    | 0.76 (0.66 to 0.87) | 2×10 <sup>-4</sup>   |
| Type 2 diabetes     | <i>GPSM1</i>    | rs60980157 | 9-138355236  | T             | C                 | 25   |            | Nonsyn   | S368L    | 12175    | 0.89 (0.84 to 0.94) | 0.00028              |
| Type 2 diabetes     | <i>AQP8</i>     |            | 16-25147310  | A             | G                 | 2.4  |            | Nonsyn   | R261Q    | 12175    | 0.71 (0.59 to 0.85) | 0.00038              |
| Type 2 diabetes     | <i>C9</i>       | rs34882957 | 5-39367651   | A             | G                 | 0.97 |            | Nonsyn   | P167S    | 12177    | 0.58 (0.44 to 0.77) | 0.00043              |
| Type 2 diabetes     | <i>NISCH</i>    | rs9856575  | 3-52485632   | G             | A                 | 2.1  | 0.4        | Nonsyn   | I299V    | 12177    | 1.40 (1.17 to 1.68) | 0.00055              |
| Type 2 diabetes     | <i>GPNMB</i>    |            | 7-23272666   | A             | G                 | 2.2  |            | Nonsyn   | A354T    | 12179    | 1.39 (1.16 to 1.65) | 0.00055              |
| Type 2 diabetes     | <i>MACF1</i>    | rs2296172  | 1-39608404   | G             | A                 | 23   | 18         | Nonsyn   | M2290V   | 12175    | 1.12 (1.05 to 1.19) | 0.00065              |
| Type 2 diabetes     | <i>LMTK2</i>    | rs56204700 | 7-97659791   | C             | T                 | 2.2  |            | Nonsyn   | I693T    | 12179    | 1.38 (1.16 to 1.65) | 0.00076              |
| Type 2 diabetes     | <i>ELOVL3</i>   | rs36103207 | 10-103978255 | A             | G                 | 3.7  |            | Nonsyn   | D109N    | 12178    | 1.28 (1.12 to 1.47) | 0.00083              |
| Type 2 diabetes     | <i>PHF15</i>    |            | 5-133929838  | T             | G                 | 1.4  |            | Nonsyn   | G368V    | 12151    | 0.66 (0.52 to 0.83) | 0.00089              |
| Obesity             | <i>ACP1</i>     | rs11553746 | 2-262203     | T             | C                 | 38   | 30         | Nonsyn   | T95I     | 10324    | 0.89 (0.84 to 0.94) | 9.4×10 <sup>-5</sup> |
| Obesity             | <i>TCERG1L</i>  |            | 10-132851444 | T             | C                 | 3.7  |            | Nonsyn   | G322E    | 10346    | 1.37 (1.18 to 1.59) | 0.00013              |
| Obesity             | <i>INHA</i>     | rs12720062 | 2-220148160  | A             | G                 | 2.1  |            | Nonsyn   | A257T    | 10306    | 0.68 (0.56 to 0.83) | 0.00038              |
| Obesity             | <i>GDAP1L1</i>  | rs2425632  | 20-42325348  | T             | C                 | 4.2  |            | Syn      |          | 10346    | 0.78 (0.68 to 0.89) | 0.00049              |
| Obesity             | <i>C10orf47</i> | rs2147439  | 10-11951710  | A             | G                 | 1.5  |            | Nonsyn   | E203K    | 10346    | 1.53 (1.22 to 1.93) | 0.00057              |
| Obesity             | <i>ANKH</i>     |            | 5-14924560   | T             | C                 | 7.7  |            | 5'UTR    |          | 10346    | 0.83 (0.75 to 0.92) | 0.00073              |
| Obesity             | <i>SLC27A4</i>  | rs2240953  | 9-130150713  | A             | G                 | 4.2  |            | Nonsyn   | G209S    | 10308    | 1.29 (1.12 to 1.48) | 0.00073              |
| Obesity             | <i>TOMM40</i>   | rs157581   | 19-50087554  | C             | T                 | 24   |            | Syn      |          | 10344    | 0.89 (0.83 to 0.95) | 0.00076              |
| Obesity             | <i>PML</i>      | rs743581   | 15-72115194  | T             | G                 | 37   |            | Nonsyn   | G780V    | 10346    | 1.11 (1.05 to 1.17) | 0.00079              |
| Obesity             | <i>MED20</i>    |            | 6-41982766   | A             | C                 | 1.6  |            | 3'UTR    |          | 10345    | 0.67 (0.54 to 0.84) | 0.00085              |
| Obesity             | <i>OR2Y1</i>    | rs11960429 | 5-180099283  | A             | G                 | 1.2  | 2.1        | Nonsyn   | R128C    | 10346    | 0.64 (0.5 to 0.82)  | 0.00098              |
| BMI                 | <i>ACP1</i>     | rs11553746 | 2-262203     | T             | C                 | 38   | 30         | Nonsyn   | T95I     | 14793    | -0.06 (0.01)        | 1.1×10 <sup>-5</sup> |
| BMI                 | <i>SLC27A4</i>  | rs2240953  | 9-130150713  | A             | G                 | 4.2  |            | Nonsyn   | G209S    | 14776    | 0.12 (0.03)         | 0.00017              |
| BMI                 | <i>CCDC165</i>  | rs35739383 | 18-8773835   | T             | C                 | 40   |            | Nonsyn   | M242T    | 14820    | -0.04 (0.01)        | 0.00051              |
| BMI                 | <i>TGIF1</i>    | rs4468717  | 18-3447606   | T             | C                 | 7.2  |            | Nonsyn   | P163S    | 14759    | 0.08 (0.02)         | 0.00064              |
| BMI                 | <i>SIM2</i>     |            | 21-37003350  | T             | C                 | 5.1  |            | Nonsyn   | A63V     | 14827    | -0.09 (0.03)        | 0.00076              |
| Waist circumference | <i>SLC27A4</i>  | rs2240953  | 9-130150713  | A             | G                 | 4.2  |            | Nonsyn   | G209S    | 14496    | 0.12 (0.03)         | 4.1×10 <sup>-5</sup> |

| Trait                         | Gene            | rs-number  | Chr-Pos      | Effect allele | Non effect allele | MAF | MAF-HapMap | Function | Mutation | <i>n</i> | Effect (95% CI) | <i>P</i> -value      |
|-------------------------------|-----------------|------------|--------------|---------------|-------------------|-----|------------|----------|----------|----------|-----------------|----------------------|
| Waist circumference           | <i>ACP1</i>     | rs11553746 | 2-262203     | T             | C                 | 38  | 30         | Nonsyn   | T95I     | 14513    | -0.05 (0.01)    | 0.00011              |
| Waist circumference           | <i>OR10Z1</i>   | rs41273513 | 1-156843597  | G             | A                 | 1.5 |            | Nonsyn   | I249V    | 14544    | -0.17 (0.05)    | 0.00045              |
| Waist circumference           | <i>ELOVL3</i>   | rs36103207 | 10-103978255 | A             | G                 | 3.7 |            | Nonsyn   | D109N    | 14545    | 0.10 (0.03)     | 0.00083              |
| Fasting plasma glucose        | <i>CASP4</i>    | rs1801319  | 11-104330859 | T             | C                 | 4.3 |            | 5'UTR    |          | 9087     | 0.13 (0.03)     | 0.00019              |
| Fasting plasma glucose        | <i>EIF2B4</i>   | rs1058065  | 2-27441228   | A             | G                 | 2.1 | 4.2        | Syn      |          | 9087     | 0.18 (0.05)     | 3×10 <sup>-4</sup>   |
| Fasting plasma glucose        | <i>ELOVL3</i>   | rs36103207 | 10-103978255 | A             | G                 | 3.7 |            | Nonsyn   | D109N    | 9086     | 0.13 (0.04)     | 0.00055              |
| Fasting plasma glucose        | <i>BRD3</i>     | rs34609592 | 9-135905516  | A             | G                 | 1.7 |            | Nonsyn   | A172V    | 9087     | 0.19 (0.05)     | 0.00056              |
| Fasting plasma glucose        | <i>CSAD</i>     |            | 12-51840193  | T             | C                 | 1   |            | Nonsyn   | D382N    | 9087     | -0.24 (0.07)    | 0.00056              |
| Fasting plasma glucose        | <i>ZFAND2B</i>  | rs61750009 | 2-219780675  | A             | C                 | 4.2 |            | Nonsyn   | P71H     | 9080     | -0.12 (0.03)    | 0.00065              |
| Fasting plasma glucose        | <i>ABCC2</i>    | rs41318029 | 10-101580476 | A             | G                 | 1.6 |            | Nonsyn   | G921S    | 9087     | 0.19 (0.06)     | 0.00085              |
| Fasting plasma glucose        | <i>PTPRH</i>    | rs16986309 | 19-60401886  | A             | G                 | 11  | 17         | Nonsyn   | L543F    | 9087     | -0.08 (0.02)    | 0.00087              |
| Fasting serum insulin         | <i>GRK4</i>     | rs35605687 | 4-2985351    | A             | G                 | 15  | 16         | Nonsyn   | V215I    | 8417     | -0.10 (0.02)    | 1.1×10 <sup>-5</sup> |
| Fasting serum insulin         | <i>DST</i>      |            | 6-56588459   | C             | T                 | 3.6 |            | Nonsyn   | I2589V   | 8418     | -0.18 (0.04)    | 1.7×10 <sup>-5</sup> |
| Fasting serum insulin         | <i>ENTPD5</i>   | rs12434581 | 14-73524572  | A             | T                 | 41  |            | 5'UTR    |          | 8413     | -0.06 (0.02)    | 5.2×10 <sup>-5</sup> |
| Fasting serum insulin         | <i>AKAP12</i>   | rs41289373 | 6-151714763  | A             | G                 | 1.3 |            | Nonsyn   | A1182T   | 8381     | -0.25 (0.06)    | 9×10 <sup>-5</sup>   |
| Fasting serum insulin         | <i>C13orf35</i> |            | 13-112385690 | T             | C                 | 1.7 |            | Nonsyn   | R121W    | 8419     | -0.21 (0.06)    | 0.00042              |
| Fasting serum insulin         | <i>PHC2</i>     | rs41265897 | 1-33608751   | A             | G                 | 4   |            | Nonsyn   | A145V    | 8417     | -0.14 (0.04)    | 0.00042              |
| Fasting serum insulin         | <i>DHX58</i>    | rs35118457 | 17-37516926  | T             | C                 | 5.8 |            | Nonsyn   | R95Q     | 8418     | 0.11 (0.03)     | 9×10 <sup>-4</sup>   |
| Fasting serum insulin         | <i>FBN3</i>     |            | 19-8082890   | G             | C                 | 2.6 |            | Nonsyn   | G1311A   | 8418     | -0.16 (0.05)    | 0.001                |
| Fasting serum HDL-cholesterol | <i>CD300LG</i>  |            | 17-39281652  | T             | C                 | 3.5 |            | Nonsyn   | R82C     | 13063    | -0.18 (0.03)    | 7.1×10 <sup>-8</sup> |
| Fasting serum HDL-cholesterol | <i>SLC26A2</i>  |            | 5-149340823  | T             | C                 | 2.1 |            | Nonsyn   | R492W    | 13060    | -0.18 (0.04)    | 1.5×10 <sup>-5</sup> |
| Fasting serum triacylglycerol | <i>PRRC2A</i>   | rs41273264 | 6-31708085   | A             | C                 | 4.2 |            | Nonsyn   | S1219Y   | 13326    | 0.13 (0.03)     | 5.2×10 <sup>-5</sup> |

51 associations with metabolic phenotypes for 45 unique SNPs selected for replication in stage 3. More details on the selection process are given in ESM Methods section 4.1. Rs numbers are based on dbSNP 129. Chromosome and position based on genome build 36. All alleles are shown on the positive strand. HapMap allele frequencies are based on the HapMap CEU population release 27. All effects are shown for the minor allele. *P*-values have been corrected by genomic control.