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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNPs** | **Loci** | **Type of variant (amino acid change)** | **Minor Allele** | **Major Allele** | **Risk allele** | **Effect on serum iron1** | **Minor Allele Frequency** | | | | | | | | | | **References** |
|  |  |  |  |  |  |  | 1000 Genomes | | | | | | | HapMap | | Keneba Biobank |  |
|  |  |  |  |  |  |  | Global (All) | AFR (All) | GWD | EUR | EAS | SAS | AMR | YRI | CEU |  |  |
| rs10421768 | *HAMP* | intron variant | G | A | A | High | 0.16 | 0.19 | 0.26 | 0.24 | 0.03 | 0.20 | 0.14 | 0.21 | 0.13 | NA | (1–4) |
| rs1799945 | *HFE* | missense variant (aa: H/D) | G | C | G | High | 0.07 | 0.01 | 0.00 | 0.17 | 0.03 | 0.07 | 0.12 | 0.01 | 0.13 | 0.01 | (5–17) |
| rs1800562 | *HFE* | Missense variant (C282Y) | A | G | A | High | 0.01 | 0.00 | 0.00 | 0.04 | 0.00 | 0.00 | 0.02 | 0.00 | 0.05 | 0 | (13,15,16,18–20) |
| rs198846 | *close to HFE* | Intron variant | A | G | A | High | 0.11 | 0.12 | 0.05 | 0.18 | 0.02 | 0.07 | 0.14 | 0.21 | 0.16 | NA | (21,22) |
| rs129128 | close to *HFE* | Intron variant | C | T | C | High | 0.07 | 0.01 | 0.00 | 0.16 | 0.03 | 0.09 | 0.11 | 0.01 | 0.14 | NA | (23) |
| rs744653 | close to *SLC40A1* | regulatory region variant | C | T | T | Moderates HH2 | 0.14 | 0.21 | 0.18 | 0.16 | 0.04 | 0.19 | 0.08 | 0.18 | 0.15 | NA | (5) |
| rs1439816 | *SLC40A1* | intron variant | C | G | G | Moderates HH2 | 0.34 | 0.73 | 0.74 | 0.16 | 0.18 | 0.25 | 0.23 | 0.76 | 0.17 | NA | (4) |
| rs11568350 (Q248H) | *SLC40A1* | Missense variant (Q248H) | A | C | A | High | 0.01 | 0.05 | 0.06 | 0.00 | 0.00 | 0.00 | 0.00 | 0.05 | 0.00 | 0.05 | (24–26) |
| rs2280673 | close to *TF* | intron variant RAB6B | A | C | NA | Low | 0.49 | 0.41 | 0.38 | 0.37 | 0.61 | 0.56 | 0.47 | 0.40 | 0.34 | NA | (18) |

**S1 Table:** **Details of the fifty SNPs identified in the six genes that are associated with** **iron imbalance**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
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| **Table S1 Continued**   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **SNPs** | **Loci** | **Type of variant (amino acid change)** | **Minor Allele** | **Major Allele** | **Risk allele** | **Effect on serum iron1** | **Minor Allele Frequency** | | | | | | | | | | **References** | |  |  |  |  |  |  |  | 1000 Genomes | | | | | | | HapMap | | Keneba Biobank |  | |  |  |  |  |  |  |  | Global  (All) | AFR (All) | GWD | EUR | EAS | SAS | AMR | YRI | CEU |  |  | | rs1867504 | *TF* | Intron variant | A | G | A | High | 0.42 | 0.22 | 0.24 | 0.49 | 0.50 | 0.52 | 0.43 | 0.48 | 0.23 | NA | (2) | | rs9872999 | *TF* | Intron variant | C | T | NA | High | 0.33 | 0.35 | 0.39 | 0.47 | 0.26 | 0.25 | 0.30 | NA | NA | NA | (12) | | rs8177179 | *TF* | Intron variant | G | A | A | Moderates HH2 | 0.34 | 0.36 | 0.40 | 0.47 | 0.26 | 0.26 | 0.30 | 0.28 | 0.42 | NA | (5) | | rs1799852 | *TF* | Synonymous variant (L247L) | A | G | A | High | 0.14 | 0.05 | 0.10 | 0.14 | 0.22 | 0.19 | 0.14 | 0.06 | 0.06 | 0.07 | (2,13,18,20,27) | | ﻿rs12493168 | *TF* |  | G | A | NA | Low | 0.07 | 0.01 | 0.00 | 0.13 | 0.00 | 0.08 | 0.21 | 0.01 | 0.17 | NA | (27) | | rs1799899 (G277S) | *TF* | Missense variant (G277S) | A | G | A | Conflict3 | 0.03 | 0.00 | 0.00 | 0.07 | 0.00 | 0.05 | 0.04 | 0.00 | 0.04 | NA | (28,29) | | rs3811658 | *TF* | Intron variant | T | C | T | Conflict3 | 0.32 | 0.12 | 0.10 | 0.35 | 0.43 | 0.41 | 0.39 | 0.01 | 0.37 | NA | (2,27,30) | | rs8177248 | *TF* | intron variant | T | C | NA | Low | 0.31 | 0.08 | 0.07 | 0.35 | 0.43 | 0.41 | 0.39 | 0.04 | 0.36 | NA | (30) | | rs8177253 | *TF* | intron variant | T | C | T | Low | 0.35 | 0.22 | 0.15 | 0.35 | 0.43 | 0.41 | 0.40 | 0.22 | 0.36 | NA | (12) | | rs1405023 | *TF* | intron variant | C | T | NA | High | 0.44 | 0.62 | 0.62 | 0.44 | 0.33 | 0.38 | 0.35 | NA | NA | NA | (27) |   **Table S1 Continued**   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **SNPs** | **Loci** | **Type of variant (amino acid change)** | **Minor Allele** | **Major Allele** | **Risk allele** | **Effect on serum iron1** | **Minor Allele Frequency** | | | | | | | | | | **References** | |  |  |  |  |  |  |  | 1000 Genomes | | | | | | | HapMap | | Keneba Biobank |  | |  |  |  |  |  |  |  | Global (All) | AFR (All) | GWD | EUR | EAS | SAS | AMR | YRI | CEU |  |  | | rs1880669 | *TF* | intron variant | T | C | NA | Conflict3 | 0.50 | 0.65 | 0.66 | 0.39 | 0.50 | 0.44 | 0.44 | 0.70 | 0.39 | NA | (27,30,31) | | rs3811647 | *TF* | intron variant | A | G | A | Low | 0.34 | 0.19 | 0.15 | 0.35 | 0.42 | 0.41 | 0.39 | 0.17 | 0.36 | 0.14 | (6,12,13,18,27,32–36) | | rs1358024 | *TF* | intron variant | T | C | NA | Low | 0.19 | 0.01 | 0.00 | 0.19 | 0.39 | 0.27 | 0.17 | 0.00 | 0.18 | NA | (18,27,30,33) | | rs1525892 | *TF* | intron variant | A | G | A | Conflict3 | 0.36 | 0.26 | 0.23 | 0.35 | 0.47 | 0.41 | 0.40 | 0.37 | 0.23 | NA | (2,30,33) | | rs1049296 | *TF* | Missense variant (S589P) | T | C | NA | High | 0.16 | 0.06 | 0.02 | 0.14 | 0.26 | 0.23 | 0.12 | 0.07 | 0.16 | 0.01 | (27) | | rs7638018 | *TF* | intron variant | G | A | NA | Low | 0.33 | 0.15 | 0.14 | 0.35 | 0.42 | 0.41 | 0.40 | 0.15 | 0.36 | NA | (30) | | rs1830084 | *TF* | 3 prime UTR variant | T | A | Uncertain risk allele4 | Low | 0.32 | 0.11 | 0.08 | 0.34 | 0.46 | 0.40 | 0.40 | 0.13 | 0.35 | NA | (12,30) | | rs7385804 | *TFR2* | Intron variant | C | A | C | Conflict3 | 0.31 | 0.33 | 0.30 | 0.38 | 0.24 | 0.32 | 0.29 | 0.35 | 0.38 | NA | (2,5,6,31,32,37) | | rs2235321 | *TMPRSS6* | Synonymous variant (Y739Y) | A | G | A | Low | 0.36 | 0.41 | 0.44 | 0.42 | 0.41 | 0.26 | 0.21 | 0.38 | 0.39 | 0.44 | (38–40) | | rs855791 | *TMPRSS6* | Missense variant (A736V) | A | G | A | Low | 0.40 | 0.10 | 0.10 | 0.39 | 0.57 | 0.54 | 0.49 | 0.12 | 0.41 | 0.07 | (5,8,10,15–17,21,22,32,36,39,41–59) | | rs78174698 | *TMPRSS6* | missense variant (P555S) | A | G | NA | Low | 0.03 | 0.01 | 0.02 | 0.00 | 0.01 | 0.12 | 0.00 | 0.02 | 0.00 | 0.01 | (43) |   **Table S1 Continued**   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **SNPs** | **Loci** | **Type of variant (amino acid change)** | **Minor Allele** | **Major Allele** | **Risk allele** | **Effect on serum iron1** | **Minor Allele Frequency** | | | | | | | | | | **References** | |  |  |  |  |  |  |  | 1000 Genomes | | | | | | | HapMap | | Keneba Biobank |  | |  |  |  |  |  |  |  | Global (All) | AFR (All) | GWD | EUR | EAS | SAS | AMR | YRI | CEU |  |  | | rs5756504 | *TMPRSS6* | Intron variant | T | C | T | High | 0.43 | 0.67 | 0.65 | 0.40 | 0.42 | 0.26 | 0.24 | 0.71 | 0.33 | NA | (22,56,57,60) | | rs5756506 | *TMPRSS6* | Intron variant | C | G | C | High | 0.47 | 0.83 | 0.82 | 0.40 | 0.43 | 0.26 | 0.26 | 0.85 | 0.35 | 0.84 | (27,37,47) | | rs4820268 | *TMPRSS6* | Missense variant (D521E) | G | A | G | Low | 0.46 | 0.28 | 0.27 | 0.42 | 0.56 | 0.57 | 0.53 | 0.21 | 0.48 | 0.27 | (2,6,21,22,32,39,42,47,57,61,62) | | rs2413450 | *TMPRSS6* | Intron variant | T | C | T | Low | 0.42 | 0.12 | 0.12 | 0.41 | 0.56 | 0.56 | 0.52 | 0.12 | 0.48 | 0.17 | (2,47,53,63) | | rs2072860 | *TMPRSS6* | Intron variant | G | A | NA | Conflict3 | 0.46 | 0.28 | 0.27 | 0.42 | 0.57 | 0.57 | 0.53 | NA | NA | NA | (12,43) | | rs9610643 | *TMPRSS6* | Intron variant | A | G | NA | Low | 0.38 | 0.60 | 0.59 | 0.33 | 0.40 | 0.23 | 0.22 | NA | NA | NA | (43) | | rs855788 | *TMPRSS6* | intron variant | A | G | NA | High | 0.49 | 0.90 | 0.86 | 0.44 | 0.30 | 0.35 | 0.27 | 0.95 | 0.31 | NA | (57) | | rs2543519 | *TMPRSS6* | Intron variant | G | A | NA | Low | 0.25 | 0.40 | 0.43 | 0.21 | 0.17 | 0.25 | 0.14 | 0.36 | 0.21 | NA | (39,43) | | rs2111833 | *TMPRSS6* | Synonymous variant (S>S) | T | C | T | Conflict3 | 0.31 | 0.38 | 0.31 | 0.39 | 0.31 | 0.24 | 0.20 | 0.42 | 0.34 | NA | (4) (30) | | rs2235324 | *TMPRSS6* | Missense variant (K253E) | G | A | G | Low | 0.39 | 0.40 | 0.43 | 0.43 | 0.40 | 0.37 | 0.33 | 0.43 | 0.35 | 0.45 | (38–40,47,51,57) |   **Table S1 Continued**   |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | **SNPs** | **Loci** | **Type of variant (amino acid change)** | **Minor Allele** | **Major Allele** | **Risk allele** | **Effect on serum iron1** | **Minor Allele Frequency** | | | | | | | | | | **References** | |  |  |  |  |  |  |  | 1000 Genomes | | | | | | | HapMap | | Keneba Biobank |  | |  |  |  |  |  |  |  | Global (All) | AFR (All) | GWD | EUR | EAS | SAS | AMR | YRI | CEU |  |  | | rs1421312 | *TMPRSS6* | intron variant | G | A | NA | High | 0.47 | 0.60 | 0.58 | 0.42 | 0.40 | 0.50 | 0.35 | 0.62 | 0.47 | NA | (30,57) | | rs5756512 | *TMPRSS6* | intron variant | T | C | NA | Low | 0.33 | 0.28 | 0.26 | 0.42 | 0.33 | 0.36 | 0.23 | NA | NA | NA | (43) | | rs2160906 | *TMPRSS6* | Intron variant | A | G | NA | Low | 0.13 | 0.06 | 0.05 | 0.19 | 0.18 | 0.14 | 0.12 | 0.05 | 0.20 | NA | (36) | | rs732756 | *TMPRSS6* | Intron variant | C | T | NA | Low | 0.14 | 0.08 | 0.08 | 0.19 | 0.18 | 0.14 | 0.12 | 0.06 | 0.20 | NA | (43) | | rs228904 | *TMPRSS6* | Intron variant | G | A | NA | High | 0.14 | 0.08 | 0.08 | 0.19 | 0.18 | 0.14 | 0.12 | 0.06 | 0.20 | NA | (57) | | rs11704654 | *TMPRSS6* | Synonymous variant (P33P) | T | C | NA | Low | 0.15 | 0.15 | 0.14 | 0.19 | 0.13 | 0.16 | 0.11 | 0.16 | 0.25 | NA | (39,42) | | rs5756516 | *TMPRSS6* | Intron variant | T | C | NA | Low | 0.32 | 0.30 | 0.27 | 0.42 | 0.33 | 0.20 | 0.35 | 0.31 | 0.43 | NA | (43) | | rs228916 | *TMPRSS6* | 5 prime UTR variant | C | T | T | Low | 0.07 | 0.03 | 0.00 | 0.11 | 0.00 | 0.09 | 0.18 | 0.03 | 0.08 | NA | (5) | | rs228921 | *TMPRSS6* 2kb Upstream Variant | Intergenic variant | G | A | G | Low | 0.41 | 0.40 | 0.40 | 0.41 | 0.43 | 0.48 | 0.31 | NA | 0.40 | NA | (21,35) | | rs228918 | *TMPRSS6:* 2kb Upstream | Intergenic variant- | A | G | G | Low | 0.41 | 0.40 | 0.40 | 0.41 | 0.43 | 0.49 | 0.31 | 0.34 | 0.47 | NA | (2,21) | |

1 The documented effect of each SNP on iron status, based on its influence on iron biomarkers. High: Indicates SNPs that have been associated with elevated iron status as shown by at least iron biomarker signifying elevated iron status. Low indicates SNPs associated with decreased iron status, determined by at least one biomarker signifying low iron.

2 The only information available about this SNPs is that they modulate hemochromatosis.

3 We found contradictory information about the effects of these SNPs on iron status. Different papers reported direction of effects of these SNPs on iron status.

NA indicates SNPs that we could not establish the risk allele because it was not stated by the respective studies that reported the SNPs. In the Keneba Biobank, NA indicates SNPs whose genotype data was not present in the Biobank population.

4Indicates a SNP in which the effect of the risk allele has not been clearly described in the paper it was reported.

5The phenotype associated with the risk allele

AFR, Africans; AMR, Americans; CEU, Utah residents with Northern and Western European ancestry from the CEPH collection; EAS, East Asians; EUR, Europeans; GWD, Gambians from Western Division; HAMP, hepcidin antimicrobial peptide; Hb, haemoglobin; HCT, haematocrit; HFE, High fe; HH, hereditary hemochromatosis; IDA, iron deficiency anaemia; MCH, mean corpuscular haemoglobin; NA, not available; SAS, South Asians; SI, serum iron; *SLC40A1*, solute carrier family 40 member 1; SNP, single nucleotide polymorphism; sTfR, soluble transferrin receptor; *TF*, transferrin; *TMPRSS6*, transmembrane protease serine 6; UTR, untranslated region; YRI, Yoruba in Nigeria.

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