

Identification and Functional Characterization of Novel Nonsynonymous Variants in the

Human Multidrug and Toxin Extrusion 2-K (MATE2-K)

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Fig. 1s

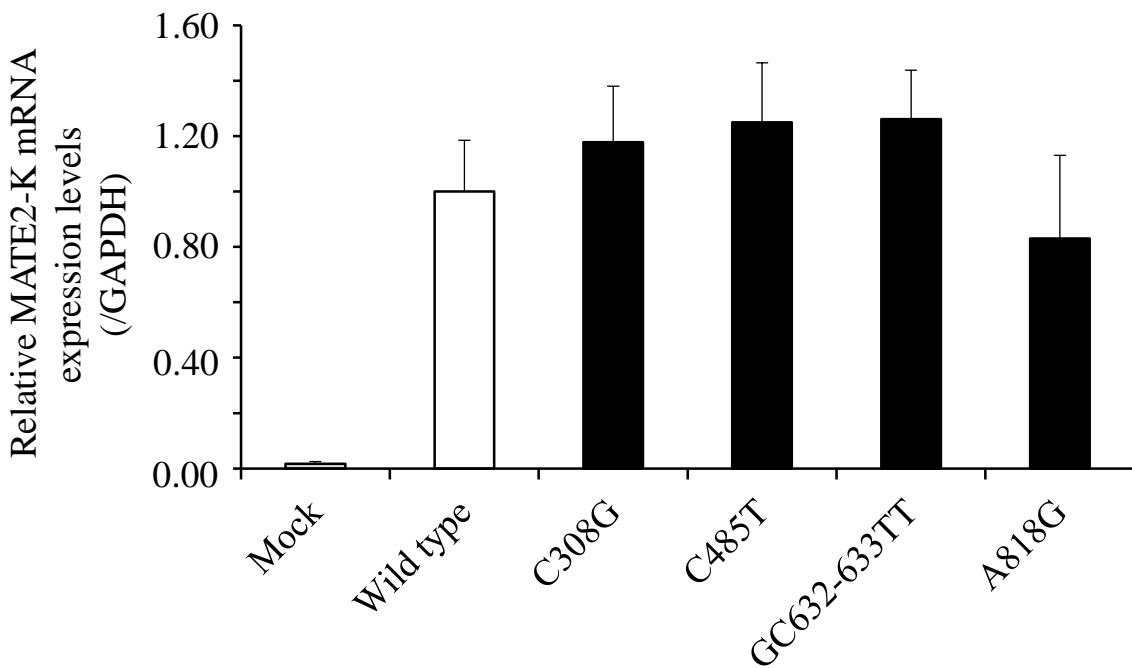


Fig. 1s. Relative MATE2-K mRNA levels of MATE2-K wild type and its variants in transfected HEK293 cells. MATE2-K mRNA expression level was normalized with glyceraldehyde 3-phosphate dehydrogenase (GAPDH). Relative MATE2-K mRNA expression levels were expressed as ratios of the relative MATE2-K mRNA in the wild type.

Fig. 2s

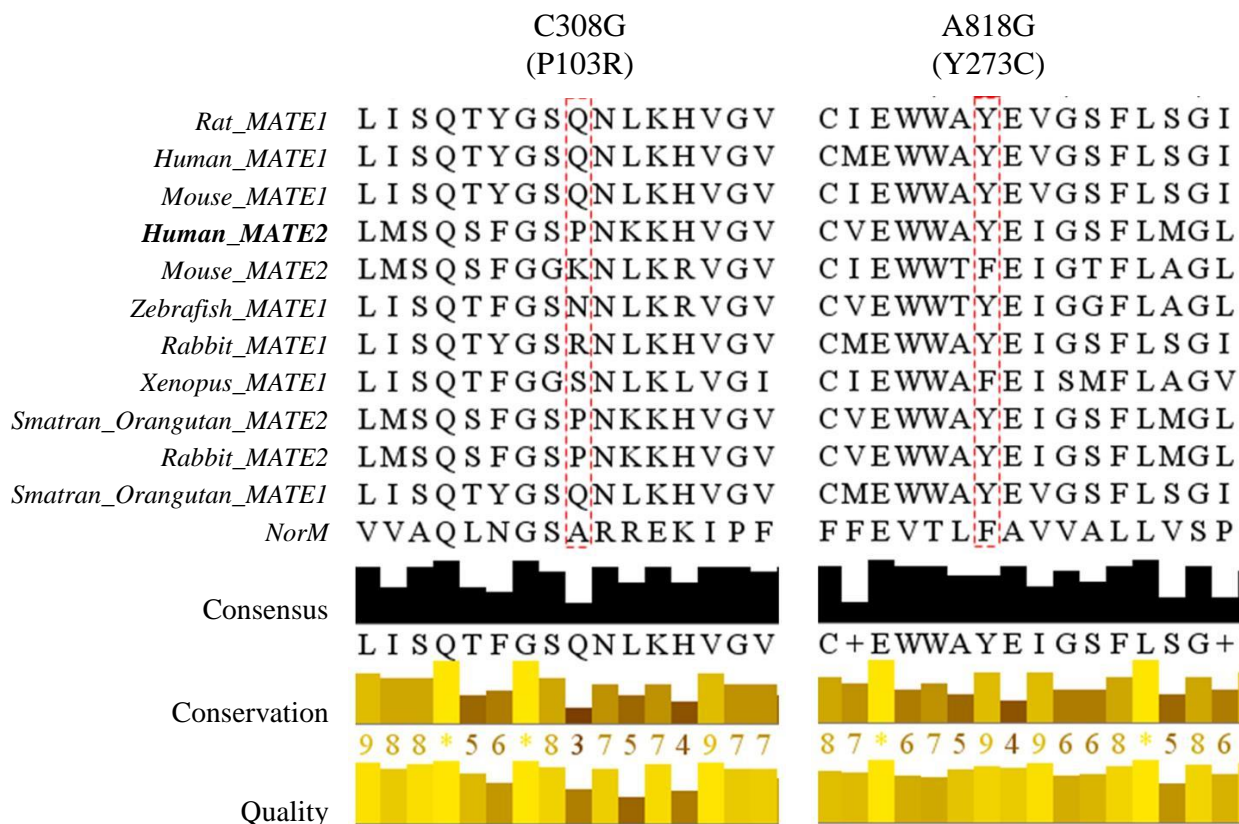


Fig. 2s. Comparison of the amino acid sequences of MATEs between organisms. The alignment file was produced from BLASTP (<http://blast.ncbi.nlm.nih.gov/Blast.cgi?PAGE=Protein>) and visualized by Jalview Version 2 (developed from 2004 at University of Dundee with support from the BBSRC).

TABLE S1-a

Oligonucleotide primers for genotyping of the *SLC47A2* (MATE2-K) gene (5' region)

| Location                              | Primer (5' to 3')                   | Direction | Position <sup>a</sup> (5') | Position <sup>a</sup> (3') | Annealing (°C) | Amplified length (bp) |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|---------------------------------------|-------------------------------------|-----------|----------------------------|----------------------------|----------------|-----------------------|-------------------------------------|---|----------|----------|------|-----|-------------------------------------|---|----------|----------|-------------------------------------|---|----------|----------|------|-----|-------------------------------------|---|----------|----------|-------------------------------------|---|----------|----------|------|-----|-------------------------------------|---|----------|----------|-------------------------------------|---|----------|----------|------|-----|-------------------------------------|---|----------|----------|-------------------------------------|---|----------|----------|------|-----|-------------------------------------|---|----------|----------|-------------------------------------|---|----------|----------|------|-----|-------------------------------------|---|----------|----------|-------------------------------------|---|----------|----------|------|-----|-------------------------------------|---|
| Promoter<br>(-2165~108 <sup>b</sup> ) | 5'- GAG TCA GTA ATC GCC CTT GCT -3' | F         | 19622033                   | 19622013                   | 55.7           | 380                   |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- GGT ATA GGC AGA AGA ATC CAT -3' | R         | 19621674                   | 19621654                   |                |                       | 5'- CTG GTC AGC TCT GGA TAA AGC -3' | F | 19621797 | 19621777 | 64.0 | 394 | 5'- AGT TCT CAT GGT CAG CCT ACC -3' | R | 19621424 | 19621404 | 5'- TGG AAG AGG TAG GCT GAC CAT -3' | F | 19621431 | 19621411 | 55.7 | 428 | 5'- GGA GAG GAG GCA GGA CAA ATA -3' | R | 19621024 | 19621004 | 5'- CCG CCC ATG GGT GTA GCA AAC -3' | F | 19621061 | 19621041 | 62.3 | 436 | 5'- TCG ACG TCC CAC AGG GTC CTC -3' | R | 19620646 | 19620626 | 5'- CAC TGC CCT GCT GGT CTT GAG -3' | F | 19620737 | 19620717 | 63.3 | 250 | 5'- CTA GGA CAC CTC GGC GGA GTC -3' | R | 19620508 | 19620488 | 5'- ATG CTG CTG AAA GGG GTG ACG -3' | F | 19620546 | 19620526 | 63.3 | 361 | 5'- AGT GGC TGT GGG AGG TGT GCT -3' | R | 19620206 | 19620186 | 5'- TTT GGG AAG GTG ACA GAG GAC -3' | F | 19620661 | 19620641 | 59.5 | 591 | 5'- CAG CCA CTA GGG AGG ACA GGT -3' | R | 19620091 | 19620071 | 5'- GAC ACA ACA GGC AGC GGT CTG -3' | F | 19620126 | 19620106 | 64.0 | 367 | 5'- GGG CAA AGA GAG TCC ACA TCT -3' | R |
|                                       | 5'- CTG GTC AGC TCT GGA TAA AGC -3' | F         | 19621797                   | 19621777                   | 64.0           | 394                   |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- AGT TCT CAT GGT CAG CCT ACC -3' | R         | 19621424                   | 19621404                   |                |                       | 5'- TGG AAG AGG TAG GCT GAC CAT -3' | F | 19621431 | 19621411 | 55.7 | 428 | 5'- GGA GAG GAG GCA GGA CAA ATA -3' | R | 19621024 | 19621004 | 5'- CCG CCC ATG GGT GTA GCA AAC -3' | F | 19621061 | 19621041 | 62.3 | 436 | 5'- TCG ACG TCC CAC AGG GTC CTC -3' | R | 19620646 | 19620626 | 5'- CAC TGC CCT GCT GGT CTT GAG -3' | F | 19620737 | 19620717 | 63.3 | 250 | 5'- CTA GGA CAC CTC GGC GGA GTC -3' | R | 19620508 | 19620488 | 5'- ATG CTG CTG AAA GGG GTG ACG -3' | F | 19620546 | 19620526 | 63.3 | 361 | 5'- AGT GGC TGT GGG AGG TGT GCT -3' | R | 19620206 | 19620186 | 5'- TTT GGG AAG GTG ACA GAG GAC -3' | F | 19620661 | 19620641 | 59.5 | 591 | 5'- CAG CCA CTA GGG AGG ACA GGT -3' | R | 19620091 | 19620071 | 5'- GAC ACA ACA GGC AGC GGT CTG -3' | F | 19620126 | 19620106 | 64.0 | 367 | 5'- GGG CAA AGA GAG TCC ACA TCT -3' | R | 19619780 | 19619760 |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- TGG AAG AGG TAG GCT GAC CAT -3' | F         | 19621431                   | 19621411                   | 55.7           | 428                   |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- GGA GAG GAG GCA GGA CAA ATA -3' | R         | 19621024                   | 19621004                   |                |                       | 5'- CCG CCC ATG GGT GTA GCA AAC -3' | F | 19621061 | 19621041 | 62.3 | 436 | 5'- TCG ACG TCC CAC AGG GTC CTC -3' | R | 19620646 | 19620626 | 5'- CAC TGC CCT GCT GGT CTT GAG -3' | F | 19620737 | 19620717 | 63.3 | 250 | 5'- CTA GGA CAC CTC GGC GGA GTC -3' | R | 19620508 | 19620488 | 5'- ATG CTG CTG AAA GGG GTG ACG -3' | F | 19620546 | 19620526 | 63.3 | 361 | 5'- AGT GGC TGT GGG AGG TGT GCT -3' | R | 19620206 | 19620186 | 5'- TTT GGG AAG GTG ACA GAG GAC -3' | F | 19620661 | 19620641 | 59.5 | 591 | 5'- CAG CCA CTA GGG AGG ACA GGT -3' | R | 19620091 | 19620071 | 5'- GAC ACA ACA GGC AGC GGT CTG -3' | F | 19620126 | 19620106 | 64.0 | 367 | 5'- GGG CAA AGA GAG TCC ACA TCT -3' | R | 19619780 | 19619760 |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- CCG CCC ATG GGT GTA GCA AAC -3' | F         | 19621061                   | 19621041                   | 62.3           | 436                   |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- TCG ACG TCC CAC AGG GTC CTC -3' | R         | 19620646                   | 19620626                   |                |                       | 5'- CAC TGC CCT GCT GGT CTT GAG -3' | F | 19620737 | 19620717 | 63.3 | 250 | 5'- CTA GGA CAC CTC GGC GGA GTC -3' | R | 19620508 | 19620488 | 5'- ATG CTG CTG AAA GGG GTG ACG -3' | F | 19620546 | 19620526 | 63.3 | 361 | 5'- AGT GGC TGT GGG AGG TGT GCT -3' | R | 19620206 | 19620186 | 5'- TTT GGG AAG GTG ACA GAG GAC -3' | F | 19620661 | 19620641 | 59.5 | 591 | 5'- CAG CCA CTA GGG AGG ACA GGT -3' | R | 19620091 | 19620071 | 5'- GAC ACA ACA GGC AGC GGT CTG -3' | F | 19620126 | 19620106 | 64.0 | 367 | 5'- GGG CAA AGA GAG TCC ACA TCT -3' | R | 19619780 | 19619760 |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- CAC TGC CCT GCT GGT CTT GAG -3' | F         | 19620737                   | 19620717                   | 63.3           | 250                   |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- CTA GGA CAC CTC GGC GGA GTC -3' | R         | 19620508                   | 19620488                   |                |                       | 5'- ATG CTG CTG AAA GGG GTG ACG -3' | F | 19620546 | 19620526 | 63.3 | 361 | 5'- AGT GGC TGT GGG AGG TGT GCT -3' | R | 19620206 | 19620186 | 5'- TTT GGG AAG GTG ACA GAG GAC -3' | F | 19620661 | 19620641 | 59.5 | 591 | 5'- CAG CCA CTA GGG AGG ACA GGT -3' | R | 19620091 | 19620071 | 5'- GAC ACA ACA GGC AGC GGT CTG -3' | F | 19620126 | 19620106 | 64.0 | 367 | 5'- GGG CAA AGA GAG TCC ACA TCT -3' | R | 19619780 | 19619760 |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- ATG CTG CTG AAA GGG GTG ACG -3' | F         | 19620546                   | 19620526                   | 63.3           | 361                   |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- AGT GGC TGT GGG AGG TGT GCT -3' | R         | 19620206                   | 19620186                   |                |                       | 5'- TTT GGG AAG GTG ACA GAG GAC -3' | F | 19620661 | 19620641 | 59.5 | 591 | 5'- CAG CCA CTA GGG AGG ACA GGT -3' | R | 19620091 | 19620071 | 5'- GAC ACA ACA GGC AGC GGT CTG -3' | F | 19620126 | 19620106 | 64.0 | 367 | 5'- GGG CAA AGA GAG TCC ACA TCT -3' | R | 19619780 | 19619760 |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- TTT GGG AAG GTG ACA GAG GAC -3' | F         | 19620661                   | 19620641                   | 59.5           | 591                   |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- CAG CCA CTA GGG AGG ACA GGT -3' | R         | 19620091                   | 19620071                   |                |                       | 5'- GAC ACA ACA GGC AGC GGT CTG -3' | F | 19620126 | 19620106 | 64.0 | 367 | 5'- GGG CAA AGA GAG TCC ACA TCT -3' | R | 19619780 | 19619760 |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- GAC ACA ACA GGC AGC GGT CTG -3' | F         | 19620126                   | 19620106                   | 64.0           | 367                   |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |
|                                       | 5'- GGG CAA AGA GAG TCC ACA TCT -3' | R         | 19619780                   | 19619760                   |                |                       |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |          |          |                                     |   |          |          |      |     |                                     |   |

<sup>a</sup>Reference sequence: NC\_000017.10 GRCh37.p9 primary assembly<sup>b</sup>Number refers to the position from the MATE2-K start codon (reference sequence: NM\_001099646.1)

TABLE S1-b

Oligonucleotide primers for genotyping of the *SLC47A2* (MATE2-K) gene (exon)

| Location                   | Primer (5' to 3')                   | Direction | Position <sup>a</sup> (5') | Position <sup>a</sup> (3') | Annealing (°C) | Amplified length (bp) |
|----------------------------|-------------------------------------|-----------|----------------------------|----------------------------|----------------|-----------------------|
| Exon 1                     | 5'- GCA GGG CTC ATC CCA CAA GTT -3' | F         | 19620030                   | 19620010                   | 65.0           | 420                   |
|                            | 5'- TCT GGA CCT GGC AGT CAA CAT -3' | R         | 19619631                   | 19619611                   |                |                       |
| Exon 2<br>(207, RFLP)      | 5'- TGA CCT CTC GGG GCA CTG GTG -3' | F         | 19618642                   | 19618622                   | 65.0           | 558                   |
|                            | 5'- TCC GCA GAC ATT GAC AAA CTG -3' | R         | 19618105                   | 19618085                   |                |                       |
| Exon 3                     | 5'- TGG TCA GGG ATG GGA AGA CAC -3' | F         | 19618343                   | 19618323                   | 65.0           | 468                   |
|                            | 5'- GCC TGT GGT CCT TGG AGG TAG -3' | R         | 19617896                   | 19617876                   |                |                       |
| IVS 3<br>(c.295-107, RFLP) | 5'- GGC TTT GTC CTG GCT CCA CTT -3' | F         | 19617564                   | 19617544                   | 65.0           | 512                   |
|                            | 5'- TGC CCG GGA CAT TCC TAA ATC -3' | R         | 19617343                   | 19617323                   |                |                       |
| Exon 4<br>(345, RFLP)      | 5'- GGC TTT GTC CTG GCT CCA CTT -3' | F         | 19617564                   | 19617544                   | 58.9           | 242                   |
|                            | 5'- TGT GAG GGC TGG GCA TCT TCA -3' | R         | 19617073                   | 19617053                   |                |                       |
| Exon 5                     | 5'- TTC ACA GTC CTG GCT GAG ACC -3' | F         | 19616183                   | 19616163                   | 65.0           | 238                   |
|                            | 5'- TAG AGT GGG AAA GCA AAA AGC -3' | R         | 19615966                   | 19615946                   |                |                       |
| Exon 6                     | 5'- CCT GGA AAG GAA TGT CTG TTA -3' | F         | 19612155                   | 19612135                   | 55.7           | 415                   |
|                            | 5'- AGG TGT GAG TGA GAT GGA TGG -3' | R         | 19611761                   | 19611741                   |                |                       |
| Exon 7                     | 5'- TGA AAG GGG TCA CTT CCA ACC -3' | F         | 19611918                   | 19611898                   | 65.0           | 419                   |
|                            | 5'- TCC ACT TCA GGA CGG CAC AGG -3' | R         | 19611520                   | 19611500                   |                |                       |
| Exon 8                     | 5'- TGG GCC CTG GTT GAG TCT GAT -3' | F         | 19611306                   | 19611286                   | 65.0           | 340                   |
|                            | 5'- TGC ACC CTC TGC CTG CTG ACC -3' | R         | 19610987                   | 19610967                   |                |                       |
| Exon 9                     | 5'- GCA TCC TCC TCC TCC GTA GGC -3' | F         | 19610269                   | 19610249                   | 65.0           | 446                   |
|                            | 5'- AAG CTG GAA GGG GGC TGG TGA -3' | R         | 19609844                   | 19609824                   |                |                       |

<sup>a</sup>Reference sequence: NC\_000017.10 GRCh37.p9 primary assembly

TABLE S1-b (continued)

| Location              | Primer (5' to 3')                   | Direction | Position <sup>a</sup> (5') | Position <sup>a</sup> (3') | Annealing (°C) | Amplified length (bp) |
|-----------------------|-------------------------------------|-----------|----------------------------|----------------------------|----------------|-----------------------|
| Exon 9<br>(818, RFLP) | 5'- AGG AAT GAG GTG GGC AAG CAG -3' | F         | 19610130                   | 19610110                   | 63.3           | 168                   |
|                       | 5'- ATG AGG AAG CTC CCG ATC TCA -3' | R         | 19609983                   | 19609963                   |                |                       |
| Exon 10               | 5'- TGA GTC CCC AAA GCA AAG CAG -3' | F         | 19608905                   | 19608885                   | 65.0           | 224                   |
|                       | 5'- CCC CTC CTA TGA CAC CTC CAG -3' | R         | 19608702                   | 19608682                   |                |                       |
| Exon 11               | 5'- GCC CAG GCT GGC TCA GGA CTT -3' | F         | 19607564                   | 19607544                   | 55.7           | 313                   |
|                       | 5'- CCA GCA GGC TTG GAA GAT AAA -3' | R         | 19607272                   | 19607252                   |                |                       |
| Exon 12               | 5'- ACT GTC TAG CCC AAA TGA ACG -3' | F         | 19606659                   | 19606639                   | 55.7           | 341                   |
|                       | 5'- TGA GCC AGG AAT GTG ATA AAT -3' | R         | 19606339                   | 19606319                   |                |                       |
| Exon 13               | 5'- GGT GGG GTG TGG AAT AGA AGG -3' | F         | 19606068                   | 19606048                   | 55.7           | 347                   |
|                       | 5'- TGC AGA AGA AGA GGG AAG TCA -3' | R         | 19605742                   | 19605722                   |                |                       |
| Exon 14, 15           | 5'- AGG GAA GAA AGG GAG ATA AGG -3' | F         | 19585134                   | 19585114                   | 62.3           | 537                   |
|                       | 5'- GGC ATT TCT GGC TGA GTA GTC -3' | R         | 19584618                   | 19584598                   |                |                       |
| Exon 16               | 5'- GCC CCA TGA CTA TGA ATA CAT -3' | F         | 19583487                   | 19583467                   | 55.7           | 387                   |
|                       | 5'- TGT TGT CTT CCT GGT GCT TAG -3' | R         | 19583121                   | 19583101                   |                |                       |
| Exon 17-1             | 5'- CTA GGT TTC CCG ATT CCA AGG -3' | F         | 19582297                   | 19582277                   | 55.7           | 466                   |
|                       | 5'- GAC CCC TCT GAG TGT CAC CAC -3' | R         | 19581852                   | 19581832                   |                |                       |
| Exon 17-2             | 5'- ACA CTG ATG GTG GGG CTC ACG -3' | F         | 19582046                   | 19582026                   | 65.0           | 505                   |
|                       | 5'- GAG CAC ACG GGT TGT CTG GAC -3' | R         | 19581562                   | 19581542                   |                |                       |

TABLE S1-c

Oligonucleotide primers for cloning of the *SLC47A2 isoform 2* (MATE2-K) gene

| Task                                       | Primer (5' to 3')  | Direction                          | Length (mer) |
|--|--|------------------------------------|--------------|
| Cloning                                    | 5'- AGG <b>GTA</b> CCC AGT GCC CCG GCC AGG AAT GGA -3'   | Sense (KpnI site) <sup>a</sup>     | 30           |
|  | 5'- CTG <b>TCT AGA</b> CCC CTC TGA GTG TCA CCA CAA -3'   | Antisense (XbaI site) <sup>a</sup> | 30           |
| Site-directed<br>mutagenesis               | 345A>C<br>5'- CTG CAG CGG GGC GCG CTG GTC CT -3'   | Sense <sup>b</sup>                 | 23           |
|  | 5'- AGG ACC AGC GCG CCC CGC TGC AG -3'   | Antisense <sup>b</sup>             | 23           |
| mutagenesis                                | 885T>C<br>5'- TGC CCA GGC TGT CAT CTA <b>CGA</b> GGT GGC CA -3'  | Sense <sup>b</sup>                 | 29           |
|  | 5'- TGG CCA CCT <b>CGT</b> AGA TGA CAG CCT GGG CA -3'  | Antisense <sup>b</sup>             | 29           |
| MATE2 to MATE2-K<br>(Deletion mutagenesis) | 5'- GGT GAT TTT TCT TTA CAA TCT GCT GGC AAA ATA TTT GCA AAA TCA GAA<br>GAT CAC CTG GCC CCA AGT CCT CAG TGG TGT G -3' | Sense                              | 79           |
|  | 5'- CAC ACC ACT GAG GAC TTG GGG CCA GGT GAT CTT CTG ATT TTG CAA ATA<br>TTT TGC CAG CAG ATT GTA AAG AAA AAT CAC C -3' | Antisense                          | 79           |
| FLAG tag <sup>c</sup>                      | 5'- <i><b>CGA TGA CTA CAA AGA CGA TGA CGA CAA G</b></i> -3'  | Sense (ClaI site) <sup>a</sup>     | 28           |
|  | 5'- <i><b>GGC CCT TGT CGT CAT CGT CTT TGT AGT CAT</b></i> -3'  | Antisense (NotI site) <sup>a</sup> | 30           |
| FLAG tag fusion                            | 5'- CCA <b>TCG ATC</b> ATT CCT GGC CGG -3'   | Antisense (ClaI site) <sup>a</sup> | 21           |
| (Inverse PCR)                              | 5'- ATA AGA ATG <b>CGG CCG CGA</b> CAG CCT CCA GG-3'   | Sense (NotI site) <sup>a</sup>     | 29           |

<sup>a</sup>The restriction endonuclease site is marked in bold letters.<sup>b</sup>The SNP is marked in a bold letter.<sup>c</sup>The FLAG sequences are marked in italic letters.

TABLE S1-d

Oligonucleotide primers for site-directed mutagenesis of the *SLC47A2* (MATE2-K) gene

| SNPs<br>(Amino Acid substitution) | Primer (5' to 3')<br>The SNP is marked in a bold letter.   | Direction          | Length (mer) |
|-----------------------------------|--|--------------------|--------------|
| 207G>A<br>(Syn, S69S)             | 5'- GGA GCT GGC ATC <b>AGT</b> GAC CCT CGC G -3'<br>5'- CGC GAG GGT CAC <b>TGA</b> TGC CAG CTC C -3'   | Sense<br>Antisense | 25<br>25     |
| 308C>G<br>(P103R)                 | 5'- GAG CTT CGG CAG <b>CCG</b> CAA CAA GAA GCA CG -3'<br>5'- CGT GCT TCT TGT TGC <b>GGC</b> TGC CGA AGC TC -3'   | Sense<br>Antisense | 29<br>29     |
| 345C>A<br>(Syn, G115G)            | 5'- CTG CAG CGG GGA <b>GCG</b> CTG GTC CT -3'<br>5'- AGG ACC AGC GCT <b>CCC</b> CGC TGC AG -3'   | Sense<br>Antisense | 23<br>23     |
| 485C>T<br>(P162L)                 | 5'- AAT GAT TTT CAT TCC AGG ACT <b>TCT</b> GGT GAT TTT TCT TTA CAA TCT GC -3'<br>5'- GCA GAT TGT AAA GAA AAA TCA <b>CCA</b> GAA GTC CTG GAA TGA AAA TCA TT -3' | Sense<br>Antisense | 47<br>47     |
| 632_633GC>TT<br>(G211V)           | 5'- CCT GGG GGT CAG <b>GGT</b> TTC CGC CTA TGC CAA -3'<br>5'- TTG GCA TAG GCG GAA <b>ACC</b> CTG ACC CCC AGG -3'   | Sense<br>Antisense | 30<br>30     |
| 673G>A<br>(V225I)                 | 5'- CCC AGT TTG CAC AGA CCA TCT TCC TCC TTC TCT AC -3'<br>5'- GTA GAG AAG GAG GAA GAT <b>GGT</b> CTG TGC AAA CTG GG -3'  | Sense<br>Antisense | 35<br>35     |
| 818A>G<br>(Y273C)                 | 5'- TTG AGT GGT GGG CCT <b>GTG</b> AGA TCG GGA GC -3'<br>5'- GCT CCC GAT CTC <b>ACA</b> GGC CCA CCA CTC AA -3'   | Sense<br>Antisense | 29<br>29     |
| 885C>T<br>(Syn, Y295Y)            | 5'- TGC CCA GGC TGT CAT CTA <b>TGA</b> GG -3'<br>5'- CCT CAT AGA TGA CAG CCT GGG CA -3'  | Sense<br>Antisense | 23<br>23     |
| 969G>A<br>(Syn, A323A)            | 5'- CTC TGG GGG CTG <b>CAG</b> ATA CTG TGC AGG -3'<br>5'- CCT GCA CAG TAT <b>CTG</b> CAG CCC CCA GAG -3'   | Sense<br>Antisense | 27<br>27     |
| 1320C>G<br>(Syn, A440A)           | 5'- TGG GCA TGC TGG <b>CGT</b> GTG TCT TCC TGG -3'<br>5'- CCA GGA AGA CAC <b>ACG</b> CCA GCA TGC CCA -3'   | Sense<br>Antisense | 27<br>27     |



TABLE S1-e

Oligonucleotide primers for the sequence of the *SLC47A2* (MATE2-K) gene coding region

| Name  | Location <sup>a</sup> | Primer (5' to 3')                               | Direction | Length (mer) |
|-------|-----------------------|---|-----------|--------------|
| T7    | Plasmid <sup>b</sup>  | 5'- TAA TAC GAC TCA CTA TAG GG -3'              | Sense     | 20           |
| 478F  | 478 ~ 495             | 5'- CAG CCC CAA CAA GAA GCA -3'                 | Sense     | 18           |
| 846F  | 846 ~ 863             | 5'- CCG TCT TCC TCC TTC TCT -3'                 | Sense     | 18           |
| 1074F | 1074 ~ 1094           | 5'- TGA CCT ACA TGA TTC CCT TGG -3'             | Sense     | 21           |
| 1512F | 1512 ~ 1529           | 5'- CTG CTG CCT TTG TTG CTT -3'                 | Sense     | 18           |
| 363R  | 380 ~ 363             | 5'- ATG CCA GCT CCA CCT TGC -3'                 | Antisense | 18           |
| 1719R | 1739 ~ 1719           | 5'- CCT CTG GAG TCC TGA AGA AGT -3'             | Antisense | 21           |
| 2002R | 2031 ~ 2002           | 5'- TGT CAC CAC AAG GAA TCA GCC AAA GTT CTT -3' | Antisense | 30           |
| BGH   | Plasmid <sup>b</sup>  | 5'- TAG AAG GCA CAG TCG AGG -3'                 | Antisense | 18           |

<sup>a</sup>Number refers to the position from the MATE2-K transcriptional start site (reference sequence: NM\_001099646.1)

<sup>b</sup>pcDNA3.1(+)

TABLE S2

Polymorphism in the *SLC47A2* gene in 3 ethnic populations ( $n=96$ , each)

| Feature          | Genomic position <sup>a</sup> | CDS position <sup>b</sup> | Nucleotide substitution | dbSNPs ID   | PMT ID <sup>c</sup> | Population | Genotype |     |     | Frequency (%) | <i>P</i> |
|------------------|-------------------------------|---------------------------|-------------------------|-------------|---------------------|------------|----------|-----|-----|---------------|----------|
|                  |                               |                           |                         |             |                     |            | R/R      | R/V | V/V |               |          |
| Promoter         | 19621929                      | -2061                     | G>A                     | rs74786588  | N.A.                | Japanese   | 73       | 23  | 0   | 12.0%         | -        |
|                  |                               |                           |                         |             |                     | Caucasian  | 94       | 2   | 0   | 1.0%          |          |
|                  |                               |                           |                         |             |                     | African    | 93       | 3   | 0   | 1.6%          |          |
|                  | 19621055                      | -1187                     | A>G                     | rs146859478 | N.A.                | Japanese   | 96       | 0   | 0   | 0.0%          | -        |
|                  |                               |                           |                         |             |                     | Caucasian  | 94       | 2   | 0   | 1.0%          |          |
|                  |                               |                           |                         |             |                     | African    | 93       | 3   | 0   | 1.6%          |          |
|                  | 19620624                      | -756                      | T>A                     | rs758426    | N.A.                | Japanese   | 43       | 43  | 10  | 32.8%         | 0.986    |
|                  |                               |                           |                         |             |                     | Caucasian  | 47       | 40  | 9   | 30.2%         |          |
|                  |                               |                           |                         |             |                     | African    | 45       | 41  | 10  | 31.8%         |          |
|                  | 19620477                      | -609                      | T>C                     | rs758427    | N.A.                | Japanese   | 15       | 51  | 30  | 57.8%         | < 0.001  |
|                  |                               |                           |                         |             |                     | Caucasian  | 14       | 45  | 37  | 62.0%         |          |
|                  |                               |                           |                         |             |                     | African    | 4        | 16  | 76  | 87.5%         |          |
| Exon 1<br>5'-UTR | 19619998                      | -130                      | C>T                     | rs12943590  | 5597                | Japanese   | 41       | 42  | 13  | 35.4%         | 0.294    |
|                  |                               |                           |                         |             |                     | Caucasian  | 46       | 43  | 7   | 29.7%         |          |
|                  |                               |                           |                         |             |                     | African    | 53       | 36  | 7   | 26.0%         |          |

<sup>a</sup>Reference sequences: NC\_000017.10 GRCh37.p9 primary assembly (genome) , NM\_001099646.1 (mRNA)<sup>b</sup>5' region: number refers to the position from the start codon<sup>c</sup>N.A. : Not Available

SNPs of rs12943590 are also described as g.-130G&gt;A

TABLE S2 (continued)

| Feature | Genomic position <sup>a</sup> | CDS position <sup>d</sup> | Nucleotide substitution | Amino acid substitution     | dbSNPs ID <sup>c</sup> | PMT ID <sup>c</sup> | Population | Genotype |     |     | Frequency (%) | <i>P</i> |
|---------|-------------------------------|---------------------------|-------------------------|-----------------------------|------------------------|---------------------|------------|----------|-----|-----|---------------|----------|
|         |                               |                           |                         |                             |                        |                     |            | R/R      | R/V | V/V |               |          |
| Exon 2  | 19618447                      | 207                       | G>A                     | Syn <sup>e</sup><br>(S69S)  | rs149511988            | 5599                | Japanese   | 89       | 7   | 0   | 3.6%          | -        |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|         |                               |                           |                         |                             |                        |                     | African    | 96       | 0   | 0   | 0.0%          |          |
| IVS 3   | 19617393                      | c.295-107                 | C>A                     | -                           | rs9900497              | 5684                | Japanese   | 36       | 47  | 13  | 38.0%         | 0.945    |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 36       | 48  | 12  | 37.5%         |          |
|         |                               |                           |                         |                             |                        |                     | African    | 35       | 45  | 16  | 40.1%         |          |
| Exon 4  | 19617273                      | 308                       | C>G                     | P103R                       | N.A.                   | N.A.                | Japanese   | 95       | 1   | 0   | 0.5%          | -        |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|         |                               |                           |                         |                             |                        |                     | African    | 96       | 0   | 0   | 0.0%          |          |
| Exon 4  | 19617236                      | 345                       | C>A                     | Syn <sup>e</sup><br>(G115G) | rs4924792              | 5688                | Japanese   | 40       | 43  | 13  | 35.9%         | 0.873    |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 39       | 45  | 12  | 35.9%         |          |
|         |                               |                           |                         |                             |                        |                     | African    | 37       | 42  | 17  | 39.6%         |          |
| IVS 4   | 19616153                      | c.444-95                  | C>T                     | -                           | rs118148051            | 5636                | Japanese   | 88       | 8   | 0   | 4.2%          | -        |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|         |                               |                           |                         |                             |                        |                     | African    | 95       | 1   | 0   | 0.5%          |          |
| IVS 4   | 19616102                      | c.444-44                  | G>C                     | -                           | rs138948843            | 5635                | Japanese   | 88       | 8   | 0   | 4.2%          | -        |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|         |                               |                           |                         |                             |                        |                     | African    | 95       | 1   | 0   | 0.5%          |          |

<sup>d</sup>Coding region, number refers to the position from the start codon; Non-coding region, number refers to the position from the nearest CDS

<sup>e</sup>Syn, synonymous

TABLE S2 (continued)

| Feature | Genomic position <sup>a</sup> | CDS position <sup>d</sup> | Nucleotide substitution | Amino acid substitution | dbSNPs ID <sup>c</sup> | PMT ID <sup>c</sup> | Population | Genotype |     |     | Frequency (%) | <i>P</i> |
|---------|-------------------------------|---------------------------|-------------------------|-------------------------|------------------------|---------------------|------------|----------|-----|-----|---------------|----------|
|         |                               |                           |                         |                         |                        |                     |            | R/R      | R/V | V/V |               |          |
| Exon 5  | 19616017                      | 485                       | C>T                     | P162L                   | rs146901447            | 5634                | Japanese   | 96       | 0   | 0   | 0.0%          | -        |
|         |                               |                           |                         |                         |                        |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|         |                               |                           |                         |                         |                        |                     | African    | 95       | 1   | 0   | 0.5%          |          |
| IVS 5   | 19612080                      | c.487-8                   | C>T                     | -                       | N.A.                   | N.A.                | Japanese   | 96       | 0   | 0   | 0.0%          | -        |
|         |                               |                           |                         |                         |                        |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|         |                               |                           |                         |                         |                        |                     | African    | 95       | 1   | 0   | 0.5%          |          |
|         | 19611984                      | c.531+45                  | G>A                     | -                       | rs117788366            | N.A.                | Japanese   | 86       | 10  | 0   | 5.2%          | -        |
|         |                               |                           |                         |                         |                        |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|         |                               |                           |                         |                         |                        |                     | African    | 96       | 0   | 0   | 0.0%          |          |
| IVS 6   | 19611823                      | c.532-111                 | C>T                     | -                       | rs144454382            | 5691                | Japanese   | 96       | 0   | 0   | 0.0%          | -        |
|         |                               |                           |                         |                         |                        |                     | Caucasian  | 95       | 1   | 0   | 0.5%          |          |
|         |                               |                           |                         |                         |                        |                     | African    | 88       | 8   | 0   | 4.2%          |          |
|         | 19611776                      | c.532-64                  | G>A                     | -                       | rs138969135            | N.A.                | Japanese   | 96       | 0   | 0   | 0.0%          | -        |
|         |                               |                           |                         |                         |                        |                     | Caucasian  | 94       | 2   | 0   | 1.0%          |          |
|         |                               |                           |                         |                         |                        |                     | African    | 96       | 0   | 0   | 0.0%          |          |
| IVS 7   | 19611226                      | c.630-70                  | C>T                     | -                       | rs74371840             | 5642                | Japanese   | 95       | 1   | 0   | 0.5%          | -        |
|         |                               |                           |                         |                         |                        |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|         |                               |                           |                         |                         |                        |                     | African    | 96       | 0   | 0   | 0.0%          |          |

TABLE S2 (continued)

| Feature | Genomic position <sup>a</sup> | CDS position <sup>d</sup> | Nucleotide substitution | Amino acid substitution     | dbSNPs ID <sup>c</sup>       | PMT ID <sup>c</sup> | Population | Genotype  |     |     | Frequency (%) | <i>P</i> |   |
|---------|-------------------------------|---------------------------|-------------------------|-----------------------------|------------------------------|---------------------|------------|-----------|-----|-----|---------------|----------|---|
|         |                               |                           |                         |                             |                              |                     |            | R/R       | R/V | V/V |               |          |   |
| Exon 8  | 19611154                      | 632                       | G>T                     | G211V                       | rs111060532<br>(ss104806862) | N.A.                | Japanese   | 92        | 4   | 0   | 2.1%          | -        |   |
|         |                               |                           |                         |                             |                              |                     | Caucasian  | 96        | 0   | 0   | 0.0%          |          |   |
|         |                               |                           |                         |                             |                              |                     | African    | 96        | 0   | 0   | 0.0%          |          |   |
|         |                               |                           |                         |                             |                              |                     | Japanese   | 92        | 4   | 0   | 2.1%          |          |   |
|         |                               |                           |                         |                             |                              |                     | Caucasian  | 96        | 0   | 0   | 0.0%          |          |   |
|         |                               |                           |                         |                             |                              |                     | African    | 96        | 0   | 0   | 0.0%          |          |   |
|         | 19611153                      | 633                       | C>T                     | -                           | -                            | -                   | -          | Japanese  | 95  | 1   | 0             | 0.5%     | - |
|         |                               |                           |                         |                             |                              |                     |            | Caucasian | 96  | 0   | 0             | 0.0%     |   |
|         |                               |                           |                         |                             |                              |                     |            | African   | 96  | 0   | 0             | 0.0%     |   |
|         |                               |                           |                         |                             |                              |                     |            | Japanese  | 96  | 0   | 0             | 0.0%     |   |
|         |                               |                           |                         |                             |                              |                     |            | Caucasian | 96  | 0   | 0             | 0.0%     |   |
|         |                               |                           |                         |                             |                              |                     |            | African   | 96  | 0   | 0             | 0.0%     |   |
| IVS 8   | 19610990                      | c.727+69                  | G>C                     | -                           | rs145977756                  | 5639                | Japanese   | 94        | 1   | 1   | 1.6%          | -        |   |
|         |                               |                           |                         |                             |                              |                     | Caucasian  | 96        | 0   | 0   | 0.0%          |          |   |
|         |                               |                           |                         |                             |                              |                     | African    | 93        | 3   | 0   | 1.6%          |          |   |
|         |                               |                           |                         |                             |                              |                     | Japanese   | 94        | 1   | 1   | 1.6%          |          |   |
| Exon 9  | 19609984                      | 818                       | A>G                     | Y273C                       | N.A.                         | N.A.                | Caucasian  | 96        | 0   | 0   | 0.0%          | 0.554    |   |
|         |                               |                           |                         |                             |                              |                     | African    | 95        | 1   | 0   | 0.5%          |          |   |
| Exon 10 | 19608773                      | 885                       | C>T                     | Syn <sup>e</sup><br>(Y295Y) | rs4925042                    | 5647                | Japanese   | 47        | 34  | 15  | 33.3%         | 0.055    |   |
|         |                               |                           |                         |                             |                              |                     | Caucasian  | 45        | 42  | 9   | 31.3%         |          |   |
|         |                               |                           |                         |                             |                              |                     | African    | 39        | 33  | 24  | 42.2%         |          |   |

TABLE S2 (continued)

| Feature | Genomic position <sup>a</sup> | CDS position <sup>d</sup> | Nucleotide substitution | Amino acid substitution     | dbSNPs ID <sup>c</sup> | PMT ID <sup>c</sup> | Population | Genotype |     |     | Frequency (%) | <i>P</i> |
|---------|-------------------------------|---------------------------|-------------------------|-----------------------------|------------------------|---------------------|------------|----------|-----|-----|---------------|----------|
|         |                               |                           |                         |                             |                        |                     |            | R/R      | R/V | V/V |               |          |
| IVS 10  | 19608713                      | c.909+36                  | C>T                     | -                           | rs140619422            | 5646                | Japanese   | 96       | 0   | 0   | 0.0%          | < 0.001  |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 94       | 2   | 0   | 1.0%          |          |
|         |                               |                           |                         |                             |                        |                     | African    | 84       | 11  | 1   | 6.8%          |          |
| Exon 11 | 19607432                      | 969                       | G>A                     | Syn <sup>e</sup><br>(A323A) | rs34169093             | 5601                | Japanese   | 96       | 0   | 0   | 0.0%          | -        |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 85       | 11  | 0   | 5.7%          |          |
|         |                               |                           |                         |                             |                        |                     | African    | 65       | 31  | 0   | 16.1%         |          |
| IVS 11  | 19607369                      | c.1018+14                 | T>C                     | -                           | N.A.                   | N.A.                | Japanese   | 96       | 0   | 0   | 0.0%          | -        |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|         |                               |                           |                         |                             |                        |                     | African    | 95       | 1   | 0   | 0.5%          |          |
| IVS 13  | 19605884                      | c.1164+34                 | T>C                     | -                           | rs116896332            | N.A.                | Japanese   | 88       | 8   | 0   | 4.2%          | -        |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|         |                               |                           |                         |                             |                        |                     | African    | 96       | 0   | 0   | 0.0%          |          |
| Exon 15 | 19584752                      | 1320                      | C>G                     | Syn <sup>e</sup><br>(A440A) | rs34416664             | 5614                | Japanese   | 96       | 0   | 0   | 0.0%          | -        |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 93       | 3   | 0   | 1.6%          |          |
|         |                               |                           |                         |                             |                        |                     | African    | 96       | 0   | 0   | 0.0%          |          |
| IVS 16  | 19583177                      | c.1480+88                 | T>C                     | -                           | rs60425436             | 5651                | Japanese   | 96       | 0   | 0   | 0.0%          | -        |
|         |                               |                           |                         |                             |                        |                     | Caucasian  | 95       | 1   | 0   | 0.5%          |          |
|         |                               |                           |                         |                             |                        |                     | African    | 87       | 9   | 0   | 4.7%          |          |

TABLE S2 (continued)

| Feature           | Genomic position <sup>a</sup> | CDS position <sup>d</sup> | Nucleotide substitution | Amino acid substitution | dbSNPs ID   | PMT ID <sup>c</sup> | Population | Genotype |     |     | Frequency (%) | <i>P</i> |
|-------------------|-------------------------------|---------------------------|-------------------------|-------------------------|-------------|---------------------|------------|----------|-----|-----|---------------|----------|
|                   |                               |                           |                         |                         |             |                     |            | R/R      | R/V | V/V |               |          |
| IVS 16            | 19582233                      | c.1481-14                 | G>A                     | -                       | rs147093603 | 5609                | Japanese   | 95       | 1   | 0   | 0.5%          | -        |
|                   |                               |                           |                         |                         |             |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|                   |                               |                           |                         |                         |             |                     | African    | 96       | 0   | 0   | 0.0%          |          |
| Exon 17<br>3'-UTR | 19581766                      | c.*233                    | C>T                     | -                       | rs112727278 | N.A.                | Japanese   | 93       | 3   | 0   | 1.6%          | -        |
|                   |                               |                           |                         |                         |             |                     | Caucasian  | 96       | 0   | 0   | 0.0%          |          |
|                   |                               |                           |                         |                         |             |                     | African    | 92       | 4   | 0   | 2.1%          |          |

<sup>d</sup>Non-coding region, number refers to the position from the nearest CDS; \* number refers to the position from the stop codon