**Table 2.** Frequencies of FC27 and 3D7-like *msp2* in *P. falciparum* isolates from 277 malaria patients in Thailand with mild (M), severe (S) or cerebral (C) disease.

| Msp2 family | Mild (M) N=115 (%) | Severe (S) N=84 (%) | Cerebral (C) N=78 (%) | Total N=277 (%) | M vs S P-value | M vs C P-value | S vs C P-value |
|-------------|---------------------|---------------------|-----------------------|----------------|----------------|----------------|----------------|
| FC27        | 54 (47.0)           | 28 (33.3)           | 32 (41.0)             | 114 (41.2)     | *P* = 0.054    | *P* = 0.416    | *P* = 0.311    |
| 3D7         | 61 (53.0)           | 56 (66.7)           | 46 (59.0)             | 163 (58.8)     | *OR* = 0.56    | *OR* = 0.79    | *OR* = 1.39    |
| Region | Polymorphic position | Nucleotide | Codon (aa.) | Mild (%) | Severe (%) | Cerebral (%) | Total (%) | M vs S\textsuperscript{a} P-value, OR | M vs C P-value, OR | S vs C P-value, OR |
|--------|----------------------|------------|-------------|----------|------------|-------------|----------|--------------------------------|-------------------|------------------|
| Block 2 | 23 A/C\textsuperscript{b} | 8 AAG (K) | · · T (N) | 19 (35.2) | 7 (25.0) | 13 (40.6) | 39 (34.2) | 0.347, 0.61 | 0.614, 1.26 | 0.200, 2.05 |
|         | 24 G/T | · CT (T) | | 13 (24.1) | 8 (28.6) | 12 (37.5) | 42 (36.8) | 0.039, 2.73 | 0.816, 0.88 | 0.044, 0.32 |
|         | 27 T/G | 9 AGT (S) | · · G (R) | 45 (83.3) | 18 (64.3) | 26 (81.3) | 89 (78.1) | 0.053, 2.78 | 0.806, 1.15 | 0.138, 0.42 |
|         |         | 32 G/A | ·A · (D) | 51 (94.4) | 25 (89.3) | 31 (96.9) | 107 (93.9) | NA | NA | NA |
|         | 37 A/G | 13 AAT (N) | · · A (K) | 50 (92.6) | 25 (89.3) | 31 (96.9) | 106 (93.0) | NA | NA | NA |
|         | 39 T/A | · G (D) | | 1 (1.9) | 0 (0) | 0 (0) | 1 (0.9) | NA | NA | NA |
|         | 48 A/T | 16 AAA (K) | · · T (N) | 33 (61.1) | 18 (64.3) | 21 (65.6) | 72 (63.2) | 0.779, 0.87 | 0.676, 0.82 | 0.914, 0.94 |
|         | 49_57indel | 17.19 ins GCT CCA AAA | (APK) | 53 (98.1) | 26 (92.9) | 32 (100.0) | 111 (97.4) | NA | NA | NA |
|         | | 17.19 ins GCT CCA AAT | (APN) | 1 (1.9) | 0 (0) | 0 (0) | 1 (0.9) | NA | NA | NA |
| Block 3\textsuperscript{c} | (R1)(R2)\textsubscript{m} | (R1)(R2)(R2) | | 1 (1.9) | 2 (7.1) | 0 (0) | 3 (2.6) | NA | NA | NA |
|         | (R1)(R2)(R2)(R2) | | | 39 (72.2) | 22 (78.6) | 21 (65.6) | 82 (71.9) | 0.532, 1.41 | 0.520, 0.73 | 0.267, 0.52 |
|         | (R1)(R2)(R2)(R2)(R2) | | | 7 (13.0) | 3 (10.7) | 9 (28.1) | 19 (16.7) | 0.768, 0.81 | 0.081, 2.63 | 0.093, 3.26 |
|         | (R1)(R1)(R1)(R2)(R2) | | | 5 (9.3) | 1 (3.6) | 1 (3.1) | 7 (6.1) | NA | NA | NA |
|         | (R1)(R1)(R1)(R1)| | | 2 (3.7) | 0 (0) | 1 (3.1) | 3 (2.6) | NA | NA | NA |
|         | R1xR2 | A 12 | | 1 (1.9) | 0 (0) | 1 (0.9) | NA | 0.151, 1.96 | 0.804, 0.89 | 0.134, 0.45 |
|         | | A 122 | | 20 (37.0) | 15 (53.6) | 11 (34.4) | 46 (40.3) | NA | NA | NA |
|         | | A 1222 | | 6 (11.1) | 0 (0) | 7 (21.9) | 13 (11.4) | 0.066 | 0.178, 2.24 | 0.009 |
|         | | A 132 | | 2 (3.7) | 1 (3.6) | 0 (0) | 3 (2.6) | NA | NA | NA |
|         | | A 1333 | | 3 (5.6) | 0 (0) | 0 (0) | 1 (0.9) | NA | NA | NA |
|         | | A 222 | | 14 (25.9) | 9 (28.1) | 20 (60.2) | 63 (55.4) | 0.653, 0.78 | 0.595, 1.30 | 0.391, 1.67 |
|         | | A 3333 | | 5 (9.3) | 1 (3.6) | 7 (21.9) | 13 (11.4) | 0.066 | 0.178, 2.24 | 0.009 |
|         | | B 22 | | 2 (3.7) | 0 (0) | 1 (3.1) | 3 (2.6) | NA | NA | NA |
|         | | B 2222 | | 0 (0) | 1 (3.6) | 0 (0) | 1 (0.9) | NA | NA | NA |
|         | | C 2111 | | 1 (1.9) | 0 (0) | 1 (0.9) | NA | NA | NA | NA |
|         | | ADD 2 | | 2 (3.7) | 0 (0) | 1 (3.1) | 3 (2.6) | NA | NA | NA |
| Block 4 | 58 G/A | 20 GAA (E) | · · (K) | 43 (79.6) | 24 (85.7) | 30 (93.8) | 97 (85.1) | 0.499, 0.65 | 0.077, 0.26 | 0.301, 0.4 |
|         | | 64 C/A | · · (Q) | 44 (81.5) | 24 (85.7) | 30 (93.8) | 98 (86.0) | 0.629, 0.73 | 0.113, 0.29 | 0.301, 0.4 |

Table 3. Allele frequencies of polymorphisms in FC27-like msp2 of *P. falciparum* isolates from mild, severe and cerebral malaria patients in Thailand.

\textsuperscript{a} Polymorphic positions include synonymous and non-synonymous polymorphisms.

\textsuperscript{b} Nucleotide position in *P. falciparum*.

\textsuperscript{c} Block 3 includes Repeat Regions 1 and 2.
a Position relative to the first nucleotide / aa. of each block (Fig 2).

b In case of SNPs, alleles found in the msp2 sequence of K1 (FC27-liked) (M59766.1) / another found in our data set was shown and amino acid (aa.) changes were indicated.

c Variation in number of repeat 1 and 2 [(R1)\textsubscript{n}(R2)\textsubscript{n}] generated 5 distinct alleles in block 3, while 13 alleles were detected when sequence variation in repeat units were considered [R1xR2].

d Allele frequencies were compared between mild (M) and severe (S), mild and cerebral (C), as well as severe and cerebral. For bi-allelic polymorphisms, the odds ratio (OR) of a minor-frequency allele for risk to severe and cerebral malaria by comparing to a major allele was analyzed. For polymorphisms with more than 2 alleles, the presence or absence of individual alleles were compared. OR and P-values are shown, with significant values in red bold. NA. (not applicable) indicates bi-allelic polymorphisms with minor allele frequency <10% and individual alleles having frequencies <10% or >90%, in which their associations with malaria severity were not analyzed. OR was undefined in cases of zero cell count.
Table 4. Haplotype frequencies of *P. falciparum* FC27-like msp2 of from mild, severe and cerebral malaria patients in Thailand, comprising polymorphisms in block 2, 3 and 4.

| FC27 haplotype | Amino acid changesa | Mild (%) | Severe (%) | Cerebral (%) | Total (%) | M vs Sb P-value, OR | M vs C P-value, OR | S vs C P-value, OR |
|----------------|---------------------|----------|------------|-------------|-----------|---------------------|-------------------|-------------------|
| Bl.2 - Bl.3 - Bl.4 Haplotype 1b | 8 - 9 -11 -13 -16 -indel - R1R2 - 20 - 22 | A3333 - - del - del - del - E Q | 14 (25.9) | 6 (21.4) | 10 (31.3) | 30 (26.3) | 0.653, 0.78 | 0.595, 1.30 | 0.39, 1.67 |
| 2 | K S G N K del A3333 - - | 0 (0) | 0 (0) | 2 (6.3) | 2 (1.8) | NA. | NA. | NA. |
| 3 | - del - del A3333 - - | 5 (9.3) | 1 (3.6) | 1 (3.1) | 7 (6.1) | NA. | NA. | NA. |
| 4 | T - - - del A122 - - | 3 (5.6) | 0 (0) | 2 (6.3) | 5 (4.4) | NA. | NA. | NA. |
| 5 | T - - - N del A122 - - | 1 (1.9) | 3 (10.7) | 1 (3.1) | 5 (4.4) | NA. | NA. | NA. |
| 6b | T - - - N del A1222 - - | 5 (8.3) | 0 (0) | 7 (21.9) | 12 (10.5) | 0.097 | 0.103, 2.75 | 0.009 |
| 7 | T - - - N del A132 - - | 2 (3.7) | 1 (3.6) | 0 (0) | 3 (2.6) | NA. | NA. | NA. |
| 8 | T - - - N del A1222 K - | 1 (1.9) | 0 (0) | 0 (0) | 1 (0.9) | NA. | NA. | NA. |
| 9 | T - - - N del A12 K K | 1 (1.9) | 0 (0) | 0 (0) | 1 (0.9) | NA. | NA. | NA. |
| 10b | T - - - N del A122 K K | 8 (14.8) | 4 (14.3) | 2 (6.3) | 14 (12.3) | 0.949, 0.96 | 0.231, 0.38 | 0.301, 0.4 |
| 11 | T R - - N del A122 - - | 1 (1.9) | 0 (0) | 0 (0) | 1 (0.9) | NA. | NA. | NA. |
| 12 | N - - - N APN A222 K K | 1 (1.9) | 0 (0) | 0 (0) | 1 (0.9) | NA. | NA. | NA. |
| 13 | N - - - D del C2111 - - | 1 (1.9) | 0 (0) | 0 (0) | 1 (0.9) | NA. | NA. | NA. |
| 14 | N - D K - del ADD2 - - | 1 (1.9) | 0 (0) | 0 (0) | 1 (0.9) | NA. | NA. | NA. |
| 15 | N - D K - del B22 - - | 0 (0) | 2 (7.1) | 0 (0) | 2 (1.8) | NA. | NA. | NA. |
| 16 | N - D K - del A222 - - | 1 (1.9) | 0 (0) | 0 (0) | 1 (0.9) | NA. | NA. | NA. |
| 17 | N - D K - del B2222 - - | 0 (0) | 1 (3.6) | 0 (0) | 1 (0.9) | NA. | NA. | NA. |
| 18 | N - D K N del ADD2 - - | 1 (1.9) | 0 (0) | 1 (3.1) | 2 (1.8) | NA. | NA. | NA. |
| 19b | N R - - - del A122 - - | 7 (13.0) | 8 (28.6) | 6 (18.8) | 21 (18.4) | 0.083, 2.69 | 0.469, 1.55 | 0.370, 0.58 |
| 20 | N R - - - del A222 - - | 1 (1.9) | 0 (0) | 0 (0) | 1 (0.9) | NA. | NA. | NA. |
| 21 | N R - - - N APN A1333 - - | 0 (0) | 2 (7.1) | 0 (0) | 2 (1.8) | NA. | NA. | NA. |

a Position relative to the first aa. of each block (Fig 2). Blocks are shaded using different colors.

b Major haplotypes (frequency ≥ 10%) observed in the parasite population that were analyzed for association with malaria severity.

c Haplotype frequencies were compared between mild (M) and severe (S), mild and cerebral (C), and severe and cerebral. *P*-value and Odds ratios (OR) are shown, with statistically significant differences in red bold. NA. (not applicable) indicates haplotypes with frequencies >10% whose association with malaria severity was not analyzed. OR was undefined in cases of zero cell count.
Table 5. Allele frequencies of polymorphisms in the 3D7-like *msp2* sequences of *P. falciparum* isolates from mild, severe and cerebral malaria patients in Thailand.

| Region | Polymorphic position* | Mild (%) | Severe (%) | Cerebral (%) | Total (%) | M vs S | M vs C | S vs C |
|--------|-----------------------|----------|------------|--------------|-----------|--------|--------|--------|
|        | Nucleotide | Codon (aa.) |          |             |            |         |        |        |
| Block 2 | 12 G/T | 4 AAG (K) | 26 (43.3) | 24 (45.3) | 16 (37.2) | 66 (42.3) | 0.835, 1.08 | 0.533, 0.77 | 0.425, 0.72 |
|        | A · · T | (N) | 34 (56.7) | 29 (54.7) | 27 (62.8) | 90 (57.7) |          |        |        |
|        | 13 C/A | 5 CCT (P) | 48 (78.7) | 47 (83.9) | 36 (83.7) | 131 (81.9) | 0.469, 1.41 | 0.521, 1.39 | 0.978, 0.98 |
|        | 14 C/T | A · · (T) | 11 (18.0) | 8 (14.3) | 7 (16.3) | 26 (16.3) | 0.583, 0.76 | 0.816, 0.88 | 0.784, 1.17 |
|        | · · (L) | | 2 (3.3) | 1 (1.8) | 0 (0) | 3 (1.9) | NA | NA | NA |
|        | 16 T/C | 6 TCT (S) | 7 (11.5) | 7 (12.5) | 7 (16.3) | 21 (13.1) | 0.865, 1.10 | 0.480, 1.50 | 0.593, 1.36 |
|        | C · · (P) | | 54 (88.5) | 49 (87.5) | 36 (83.7) | 139 (86.9) |          |        |        |
| R1 region c | 162 | : GAVAGS | 14 (23.0) | 11 (19.6) | 11 (23.9) | 36 (22.1) | 0.663, 0.82 | 0.907, 1.06 | 0.602, 1.29 |
|        | 185 | : GASGSA | 10 (16.4) | 8 (14.3) | 8 (14.3) | 26 (16.0) | 0.752, 0.85 | 0.891, 1.07 | 0.668, 1.26 |
|        | 1852 | : GASGSAGS | 7 (11.5) | 13 (23.2) | 5 (10.9) | 25 (15.3) | 0.092, 2.33 | 0.922, 0.94 | 0.104, 0.40 |
|        | 18585 | : GASGASGSA | 6 (9.8) | 6 (10.7) | 6 (13.0) | 18 (11.0) | 0.876, 1.11 | 0.603, 1.38 | 0.716, 1.25 |
|        | 2165 | : GSGA VASA | 6 (9.8) | 3 (5.4) | 2 (4.3) | 11 (6.7) | NA | NA | NA |
|        | 27165 | : GSRDGA VASA | 6 (9.8) | 6 (10.7) | 2 (4.3) | 14 (8.6) | NA | NA | NA |
|        | 35 | : GGSA | 5 (8.2) | 2 (3.6) | 4 (8.7) | 11 (6.7) | NA | NA | NA |
|        | 385 | : GGSGSA | 6 (9.8) | 7 (12.5) | 8 (17.4) | 21 (12.9) | 0.647, 1.31 | 0.251, 1.93 | 0.488, 1.47 |
|        | 385_35: GGSGSA GGSA | 1 (1.6) | 0 (0) | 0 (0) | 1 (0.6) | NA | NA | NA |
| NR region | 1_30 indel | 1_10 ins GNGANPGADA | 18 (29.5) | 12 (21.4) | 13 (28.3) | 43 (26.4) | 0.317, 0.65 | 0.888, 0.94 | 0.425, 1.44 |
|        | 1_10 ins R N G A N P G AD A | 13 (21.3) | 19 (33.9) | 7 (15.2) | 39 (23.9) | 0.126, 1.90 | 0.423, 0.66 | 0.031, 0.35 |
|        | 3: 6 del GN - - - - G A D A | 14 (23.0) | 11 (19.6) | 11 (23.9) | 36 (22.1) | 0.663, 0.82 | 0.907, 0.96 | 0.602, 1.29 |
|        | 1_8 del - - - - - - - - DA | 9 (14.8) | 6 (10.7) | 9 (19.6) | 24 (14.7) | 0.514, 0.69 | 0.510, 1.41 | 0.209, 2.03 |
|        | 1_10 del - - - - - - - - | 7 (11.5) | 8 (14.3) | 6 (13.0) | 21 (12.9) | 0.650, 1.29 | 0.806, 1.16 | 0.856, 0.90 |
| Block 3 | 31 G/A | 11 GAG (E) | 46 (75.4) | 44 (78.6) | 33 (71.7) | 23 (75.5) | 0.685, 0.84 | 0.669, 1.21 | 0.425, 1.44 |
|        | A · · (K) | | 15 (24.6) | 12 (21.4) | 13 (28.3) | 40 (24.5) |          |        |        |
|        | 34 A/G | 12 AGA (R) | 35 (57.4) | 30 (53.6) | 31 (67.4) | 96 (58.9) | 0.679, 1.17 | 0.292, 0.65 | 0.157, 0.56 |
|        | G · · (G) | | 26 (42.6) | 26 (46.4) | 15 (32.6) | 67 (41.1) |          |        |        |
|        | 40 C/T | 14 CCA (P) | 41 (67.2) | 35 (62.5) | 37 (80.4) | 113 (69.3) | 0.594, 1.23 | 0.128, 0.50 | 0.048, 0.41 |
|        | T · · (S) | | 20 (32.8) | 21 (37.5) | 9 (19.6) | 50 (30.7) |          |        |        |
|        | 50 G/C | 17 CCC (P) | 60 (98.4) | 56 (100.0) | 44 (95.7) | 160 (98.2) | 0.471, 1.4 | 0.859, 0.76 | 0.557, 1.85 |
|        | · · G (R) | | 1 (1.6) | 0 (0) | 2 (4.3) | 3 (1.8) | NA | NA | NA |
|        | 52 G/A | 18 GCT (A) | 61 (100) | 56 (100) | 45 (97.8) | 162 (99.4) | NA | NA | NA |
|        | A · · (T) | | 0 (0) | 0 (0) | 1 (2.2) | 0 (0.6) |          |        |        |
| R2 region d | (ACT ACC ACA)₂ | (T)₈ | 42 (68.9) | 37 (66.1) | 35 (76.1) | 114 (69.9) | 0.748, 0.88 | 0.410, 1.44 | 0.269, 1.63 |
|        | (ACT ACC ACA)₃ | (T)₉ | 8 (13.1) | 4 (7.1) | 7 (15.2) | 19 (11.7) | 0.288, 0.51 | 0.757, 1.19 | 0.191, 1.33 |
|        | (ACT ACC ACA)₄ | (T)₄ | 11 (18.0) | 15 (26.8) | 4 (8.7) | 30 (18.7) | 0.255, 1.66 | 0.168, 0.43 | 0.020, 0.26 |

* denotes the number of bases in the polymorphism.
Table 5. (continued)

| Region | Polymorphic position<sup>a</sup> | Nucleotide | Codon (aa.) | Mild (%) | Severe (%) | Cerebral (%) | Total (%) | M vs S<sup>e</sup> P-value, OR | M vs C P-value, OR | S vs C P-value, OR |
|--------|---------------------------------|------------|-------------|----------|------------|-------------|----------|-------------------------------|-------------------|-------------------|
|        |                                 |            |             |          |            |             |          |                               |                   |                   |
|        |                                 |            |             |          |            |             |          |                               | NA.               | NA.               |
| 40 C/T | 14 CCA (P)                      | T · · (S)  | 55 (90.2)   | 6 (9.8)  | 50 (89.3)  | 6 (10.7)    | 44 (95.7)| 2 (4.3)                        | 149 (91.4)        | 14 (8.6)          |
|        |                                 |            |             |          |            |             |          |                               | NA.               | NA.               |
| 51 A/T | 17 AAA (K)                      | · · T (N)  | 5 (8.2)     | 56 (91.8)| 7 (12.5)   | 49 (87.5)   | 11 (23.9)| 35 (76.1)                      | 23 (14.1)         | 140 (85.9)        |
|        |                                 |            |             |          |            |             |          |                               | 0.443, 1.60       | 0.024, 3.52       |
|        |                                 |            |             |          |            |             |          |                               | 0.132, 2.20       |                   |
| 58 G/A | 20 GAA (E)                      | A · · (K)  | 38 (62.3)   | 23 (37.7)| 39 (69.6)  | 17 (30.4)   | 31 (67.4)| 15 (32.6)                      | 108 (66.3)        | 55 (33.7)         |
|        |                                 |            |             |          |            |             |          |                               | 0.403, 0.72       | 0.586, 0.80       |
|        |                                 |            |             |          |            |             |          |                               | 0.807, 1.11       |                   |
| 78 A/T | 26 AAA (K)                      | · · T (N)  | 30 (53.6)   | 26 (46.4)| 35 (64.8)  | 19 (35.2)   | 28 (68.3)| 13 (31.7)                      | 93 (61.6)         | 58 (38.4)         |
|        |                                 |            |             |          |            |             |          |                               | 0.231, 0.62       | 0.144, 0.54       |
|        |                                 |            |             |          |            |             |          |                               | 0.722, 0.86       |                   |
| 82 G/C/A | 28 GAA (E)                      | · · T (N)  | 29 (51.8)   | 17 (30.4)| 12 (22.2)  | 4 (7.4)     | 27 (65.9)| 2 (4.9)                        | 90 (59.6)         | 59 (40.4)         |
|        |                                 |            |             |          |            |             |          |                               | 0.236, 1.58       | 0.333, 0.66       |
|        |                                 |            |             |          |            |             |          |                               | 0.166, 1.80       | 0.517, 0.74       |
| 83 A/G | 26 AAT (K)                      | · · T (N)  | 30 (53.6)   | 26 (46.4)| 35 (64.8)  | 19 (35.2)   | 28 (68.3)| 13 (31.7)                      | 93 (61.6)         | 58 (38.4)         |
|        |                                 |            |             |          |            |             |          |                               | 0.231, 0.62       | 0.144, 0.54       |
|        |                                 |            |             |          |            |             |          |                               | 0.722, 0.86       |                   |
| 91_93 indel | 31 ins GAA (E)                  | ins AAA (K)| 26 (46.4)   | 24 (42.9)| 24 (44.4)  | 3 (5.6)     | 15 (36.6)| 4 (9.8)                        | 68 (45.0)         | 10 (6.6)          |
|        |                                 | del        | 6 (10.7)    | 3 (5.6)  | 25 (61.0)  | 1 (2.4)     | 2 (4.9) | 6 (10.7)                       | 3 (5.6)           | 10 (6.6)          |
|        |                                 |            |             |          |            |             |          |                               | 0.867, 1.07       | 0.837, 1.08       |
|        |                                 |            |             |          |            |             |          |                               | 0.078, 2.08       | 0.332, 0.67       |
|        |                                 |            |             |          |            |             |          |                               |                   | 0.110, 1.95       |
|        |                                 |            |             |          |            |             |          |                               |                   |                   |
| 95 C/A | 32 CCA (P)                      | · · A (Q)  | 51 (91.1)   | 5 (8.9)  | 43 (79.6)  | 11 (20.4)   | 37 (90.2)| 4 (9.8)                        | 131 (86.8)        | 20 (13.2)         |
|        |                                 | del        | 5 (8.2)     | 2 (3.6)  | 54 (96.4)  | 2 (3.6)     | 41 (89.1)| 5 (10.9)                       | 151 (92.6)        | 12 (7.4)          |
|        |                                 |            |             |          |            |             |          |                               | NA.               | NA.               |
| 67_99 indel | 23_33 insert                    | 23_33 deletion | 56 (91.8)   | 5 (8.2)  | 54 (96.4)  | 2 (3.6)     | 41 (89.1)| 5 (10.9)                       | 151 (92.6)        | 12 (7.4)          |
|        |                                 |            |             |          |            |             |          |                               | NA.               | NA.               |
|        |                                 |            |             |          |            |             |          |                               | NA.               | NA.               |

<sup>a</sup> Position relative to the first nucleotide / aa. of each block (Fig 3)

<sup>b</sup> In case of SNPs, alleles found in the *msp2* sequence of 3D7 (PFB0300c) / another allele found in our data set was shown, and amino acid (aa.) changes are indicated.

<sup>c</sup> For The R1 region in block 3, sequences can be grouped into nine types according to the presence of different types of numerically coded dipeptide motifs (Table S1).

<sup>d</sup> For the R2 region, there were 8, 11, and 14 Threonine repeats encoded by 2-4 copies of nanomer (ACT ACC ACA) followed by ACT ACT.

<sup>e</sup> Allele frequencies were compared between mild (M) and severe (S), mild and cerebral (C), and severe and cerebral. For bi-allelic polymorphisms, the odds ratios (OR) of minor-frequency alleles compared to major alleles associated with severe and cerebral malaria were analyzed. For
polymorphisms with more than 2 alleles, the presence/absence of individual alleles were compared. OR and \( P \)-values are shown, with significant differences in red bold. NA. (not applicable) indicates bi-allelic polymorphisms with a minor allele frequency <10\% and individual alleles with frequencies <10\% or >90\%, in which their association with malaria severity were not analyzed.
Table 6. Haplotype frequencies of 3D7 like msp2 of *P. falciparum* from mild, severe and cerebral malaria patients in Thailand, with each block analyzed separately.

| 3D7 haplotype | Amino acid changesa | Mild (%) | Severe (%) | Cerebral (%) | Total (%) | M vs Sb P-value, OR | M vs C P-value, OR | S vs C P-value, OR |
|---------------|---------------------|----------|------------|--------------|-----------|---------------------|---------------------|---------------------|
| **Block 2**   |                     |          |            |              |           |                     |                     |                     |
| Haplotype 1b  |                     |          |            |              |           |                     |                     |                     |
| 4 – 5 – 6     |                     | 27 (45.0)| 22 (41.5)  | 20 (46.5)    | 69 (44.2) | 0.709, 0.87         | 0.879, 1.06         | 0.623, 1.23         |
| N P P        |                     |          |            |              |           |                     |                     |                     |
| 2b           |                     | 7 (11.7) | 7 (13.2)   | 7 (16.3)     | 21 (13.5) | 0.804, 1.15         | 0.501, 1.47         | 0.672, 1.28         |
| 3b           |                     | 13 (21.7)| 17 (32.1)  | 9 (20.9)     | 39 (25.0) | 0.211, 1.71         | 0.928, 0.96         | 0.222, 0.56         |
| 4b           |                     | 11 (18.3)| 6 (11.3)   | 7 (16.3)     | 24 (15.4) | 0.298, 0.57         | 0.787, 0.87         | 0.480, 1.52         |
| 5 K L        |                     | 2 (3.3)  | 1 (1.9)    | 0 (0)        | 3 (1.9)   | NA                  | NA                  | NA                  |
| **Block 3** NR-R2 |                 |          |            |              |           |                     |                     |                     |
| Haplotype 1b  |                     |          |            |              |           |                     |                     |                     |
| 1_10indel -11 - 12 - 14 - 17 - 18 - [T] | | 11 (18.0)| 8 (14.3)  | 10 (21.7)    | 29 (17.8) | 0.583, 0.76         | 0.633, 1.26         | 0.326, 1.67         |
| 2 Ins G · G S · · 14 | | 4 (6.6)  | 3 (5.4)   | 0 (0)       | 7 (4.3)   | NA                  | NA                  | NA                  |
| 3 Ins G · G S · · 11 | | 1 (1.6)  | 0 (0)     | 0 (0)       | 1 (0.6)   | NA                  | NA                  | NA                  |
| 4 Ins G · G S R · 11 | | 1 (1.6)  | 0 (0)     | 2 (4.3)     | 3 (1.8)   | NA                  | NA                  | NA                  |
| 5 Ins G K · · · · 8 | | 1 (1.6)  | 1 (1.8)   | 0 (0)       | 1 (0.6)   | NA                  | NA                  | NA                  |
| 6 Ins R · · · · 11 | | 0 (0)    | 1 (1.8)   | 0 (0)       | 1 (0.6)   | NA                  | NA                  | NA                  |
| 7 Ins R · G S · · 8 | | 6 (9.8)  | 6 (10.7)  | 2 (4.3)     | 14 (8.6)  | NA                  | NA                  | NA                  |
| 8b Ins R · G S · · 16 | | 6 (9.8)  | 12 (21.4) | 4 (8.7)     | 22 (13.5) | 0.083, 2.50         | 0.841, 0.87         | 0.079, 0.35         |
| 9 Ins R · G S · · 11 | | 1 (1.6)  | 0 (0)     | 7 (2.2)     | 2 (1.2)   | NA                  | NA                  | NA                  |
| 10b Del3_6 K · · · · 8 | | 14 (23.0)| 11 (19.6) | 11 (23.9)   | 36 (22.1) | 0.663, 0.82         | 0.907, 1.06         | 0.602, 1.29         |
| 11 Del1_8 · · · · 8 | | 4 (6.6)  | 6 (10.7)  | 4 (8.7)     | 14 (8.6)  | NA                  | NA                  | NA                  |
| 12 Del1_8 · · · · 11 | | 5 (8.2)  | 3 (5.4)   | 4 (8.7)     | 12 (7.4)  | NA                  | NA                  | NA                  |
| 13 Del1_8 · G S · · 14 | | 1 (1.6)  | 0 (0)     | 0 (0)       | 1 (0.6)   | NA                  | NA                  | NA                  |
| 14 Del1_8 K · · · T 8 | | 0 (0)    | 0 (0)     | 1 (2.2)     | 1 (0.6)   | NA                  | NA                  | NA                  |
| 15b Del1_10 · G · · · 8 | | 6 (9.8)  | 5 (8.9)   | 5 (10.9)    | 16 (9.8)  | NA                  | NA                  | NA                  |
| **Block 4**   |                     |          |            |              |           |                     |                     |                     |
| Haplotype 1b  |                     |          |            |              |           |                     |                     |                     |
| 14 – 17 – 20 – 26 – 28 – 31 – 32 | | 7 (11.5)| 8 (14.3)  | 6 (13.0)    | 21 (12.9) | 0.650, 1.29         | 0.806, 1.16         | 0.856, 0.90         |
| P N E K E K P | | 5 (8.2)  | 11 (19.6) | 4 (8.7)     | 20 (12.3) | 0.072, 2.74         | 0.927, 1.07         | 0.120, 0.39         |
| 2a           |                     | 7 (11.5)| 4 (7.1)   | 2 (4.3)     | 13 (8.0)  | NA                  | NA                  | NA                  |
| 3 · · · · Q E · | | 1 (1.6)  | 0 (0)     | 0 (0)       | 1 (0.6)   | NA                  | NA                  | NA                  |
| 4 · · · · N K · · | | 2 (3.3)  | 1 (1.8)   | 0 (0)       | 2 (0.6)   | NA                  | NA                  | NA                  |
| 5 · · · · N K E · | | 6 (9.8)  | 5 (8.9)   | 5 (10.9)    | 16 (9.8)  | NA                  | NA                  | NA                  |
| 6 · · · · K N G · | | 5 (8.2)  | 4 (7.1)   | 3 (6.5)     | 12 (7.4)  | NA                  | NA                  | NA                  |
| 7 · · · · K N G E | | 12 (19.7)| 8 (14.3)  | 7 (15.2)    | 27 (16.6) | 0.439, 0.68         | 0.551, 0.73         | 0.895, 1.08         |
| 8b · · K N G E | | 5 (8.2)  | 7 (12.5)  | 11 (23.9)   | 23 (14.1) | 0.443, 1.60         | 0.024, 3.52         | 0.132, 2.20         |
| 9b · · K N G E | | 6 (9.8)  | 3 (5.4)   | 1 (2.2)     | 10 (6.1)  | NA                  | NA                  | NA                  |
| 10 S · · N · del | | 0 (0)    | 3 (5.4)   | 1 (2.2)     | 4 (2.5)   | NA                  | NA                  | NA                  |
| 11 S · · N K · | | 5 (8.2)  | 2 (3.6)   | 5 (10.9)    | 12 (7.4)  | NA                  | NA                  | NA                  |
| 12 · · · · 23_33 del · · | | 6 (9.8)  | 3 (5.4)   | 1 (2.2)     | 4 (2.5)   | NA                  | NA                  | NA                  |
a Position relative to the first aa. of each block (Fig 3).

b Major haplotypes (frequency ≥ 10%) observed in the parasite population that were analyzed for association with malaria severity.

c Haplotype frequencies were compared between mild (M) and severe (S), mild and cerebral (C), as well as severe and cerebral. *P*-values and odds ratios (OR) are shown, with significant differences in red bold. NA. (not applicable) indicates haplotypes with frequencies >10% whose associations with malaria severity were not analyzed.