

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Table of contents

Authors' full names, academic degrees and affiliations.....	4
Contributors' full names, academic degrees and affiliations	9
Geospatial mapping methodology, details	13
Figure S1.....	14
Figure S2.....	15
Figure S3.....	17
Figure S4.....	18
Figure S5.....	19
Figure S6.....	20
Figure S7.....	21
Figure S8.....	23
Figure S9.....	24
Figure S10.....	32
Figure S11	34
Figure S12.....	35
Figure S13	37
Figure S14.....	38
Table S1	42
Table S2	56
Table S3	57
Table S4	60
Table S5	75

Table S6	78
Table S7	79
Table S8	90
Table S9	100
Table S10	117

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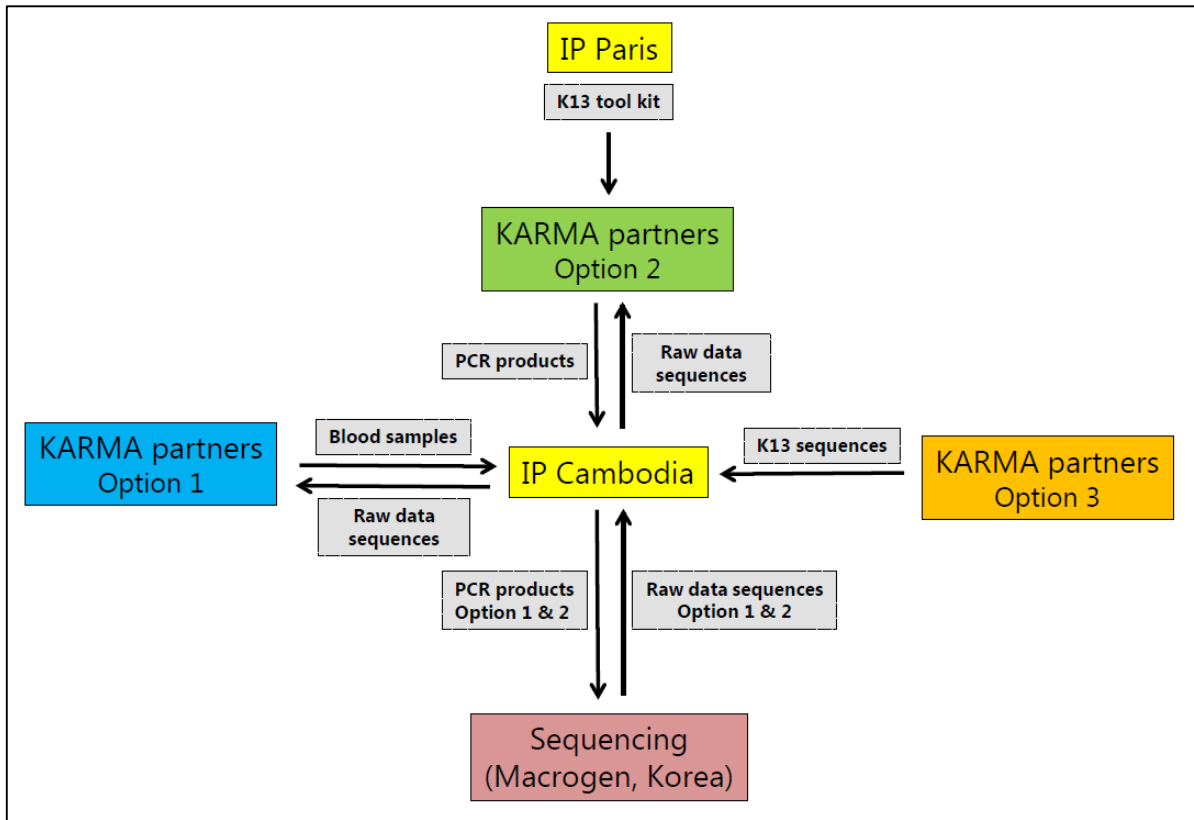
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Geospatial mapping methodology.

Vectorial maps were downloaded from world map using the raster package (<http://cran.r-project.org/web/packages/raster/>) from the open access DIVA-GIS system (<http://www.diva-gis.org>).¹ R packages sp (R package for Spatial Data - <http://cran.r-project.org/web/packages/sp/index.html>) and rgeos (R package for Geometry Engine Open Source - <http://cran.r-project.org/web/packages/rgeos/index.html>) were used for dealing with spatial data. The geographic distribution of malaria endemicity areas was downloaded from malaria map (http://www.map.ox.ac.uk/browse-resources/endemicity/Pf_mean/). The proportion of wild type K13 in each country was calculated (details in Table S5) and only sites where >5 samples were collected were included in the mapping. Data were interpolated using two different approaches and the map censored for regions with very low to nil reported malaria prevalence. To generate the Asia map (Figure 2A), we used the well-established spatial statistical interpolation of ordinary kriging² using a 50 km radius for the area surrounding the coordinate sampling site(s). To generate the world map (Figure 2B), we used an inverse distance weighted interpolation method with the Gstat package,³ where the inverse distance weighting power was arbitrarily set to 5. A 100 km radius surrounding the coordinate sampling site(s) was used.

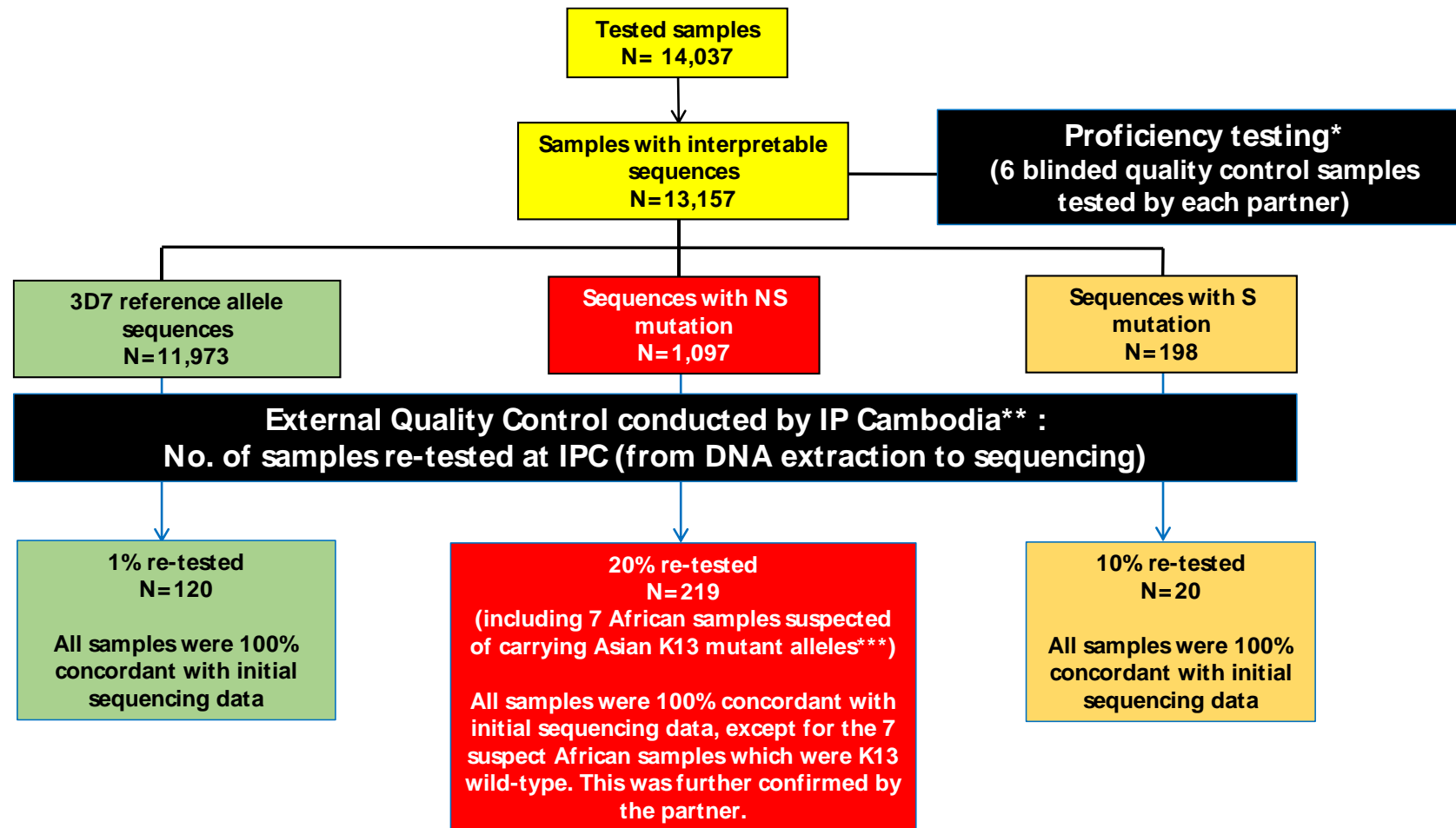
1. Hijmans RJ, Guarino L, Cruz M, Rojas E. Computer tools for spatial analysis of plant genetic resources data: 1. DIVA-GIS. *Plant Genetic Resources* 2001; Newsletter: 15-9.
2. Matheron G. Principles of geostatistics. *Econ Geol* 1963; 58: 1246–66.
3. Pebesma EJ. Multivariable geostatistics in S: the gstat package. *Computers & Geosciences* 2004; 30:683-91

Figure S1. Options proposed to partners involved in the KARMA study: reagents, samples and data flow chart, KARMA study 2014.



For details see Tables S3 and S4.

Figure S2. Detailed information regarding the sequencing pipeline and the quality control assessment conducted at IP Cambodia, KARMA study 2014

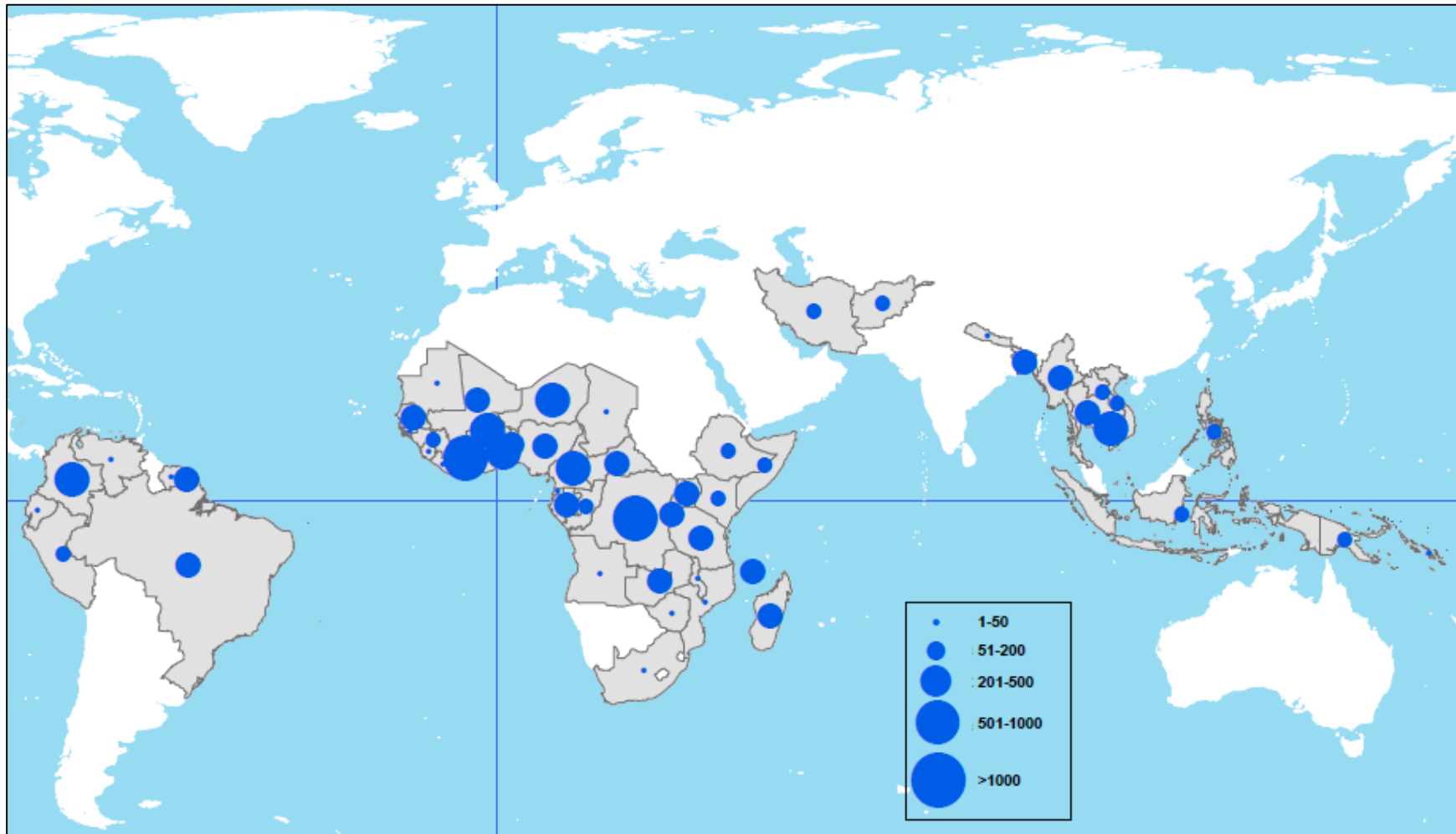


* For the proficiency testing, among the 162 96-well plates used for PCR/sequencing the 14037 samples, only 6 plates gave discordant results with respect to the expected results of the 6 blinded quality control samples. All samples contained in these 6 plates were re-tested (from DNA extraction to sequencing) and validated by the second testing, as all 6 blinded quality control samples were found 100% concordant with their respective sequence.

** For the external quality control, 359 samples were re-tested: 1% of the K13 wild-type isolates (n=120), 10% of the samples with synonymous mutations (n=20) and 20% of the samples with non-synonymous mutations (n=219). The latter batch included in particular all 7 African samples suspected of carrying an Asian K13 mutant allele. Results from the re-testing at IP-Cambodia showed that 352/359 samples were 100% concordant with the initial testing, except for the 7 suspect African samples, which were all 7 unambiguously found K13 wild-type. For these 7 cases, we strongly suspected a lab contamination from the blinded quality control samples sent to each partner. We asked the partner to re-test all samples from the 96-well plate containing the suspect case. The partner confirmed the presence of a K13 wild type in the suspected mutant sample, and all other samples were 100% concordant with the initial sequencing results. Therefore these 7 samples were classified wild-type.

*** Angola (R539T and I543T), Comoros (R539T), Burkina Faso (I543T and I543T), Niger (C580Y) and Zambia (C580Y).

Figure S3. Location of sampling sites and sample sizes, KARMA study 2014



Blue circles show numbers of isolates in each country. For details see Table S3.

Figure S4. Assessment of the detection of minority alleles in artificially mixed DNA samples, containing various proportions of K13 wild-type and C580Y or R539T alleles, KARMA study 2014

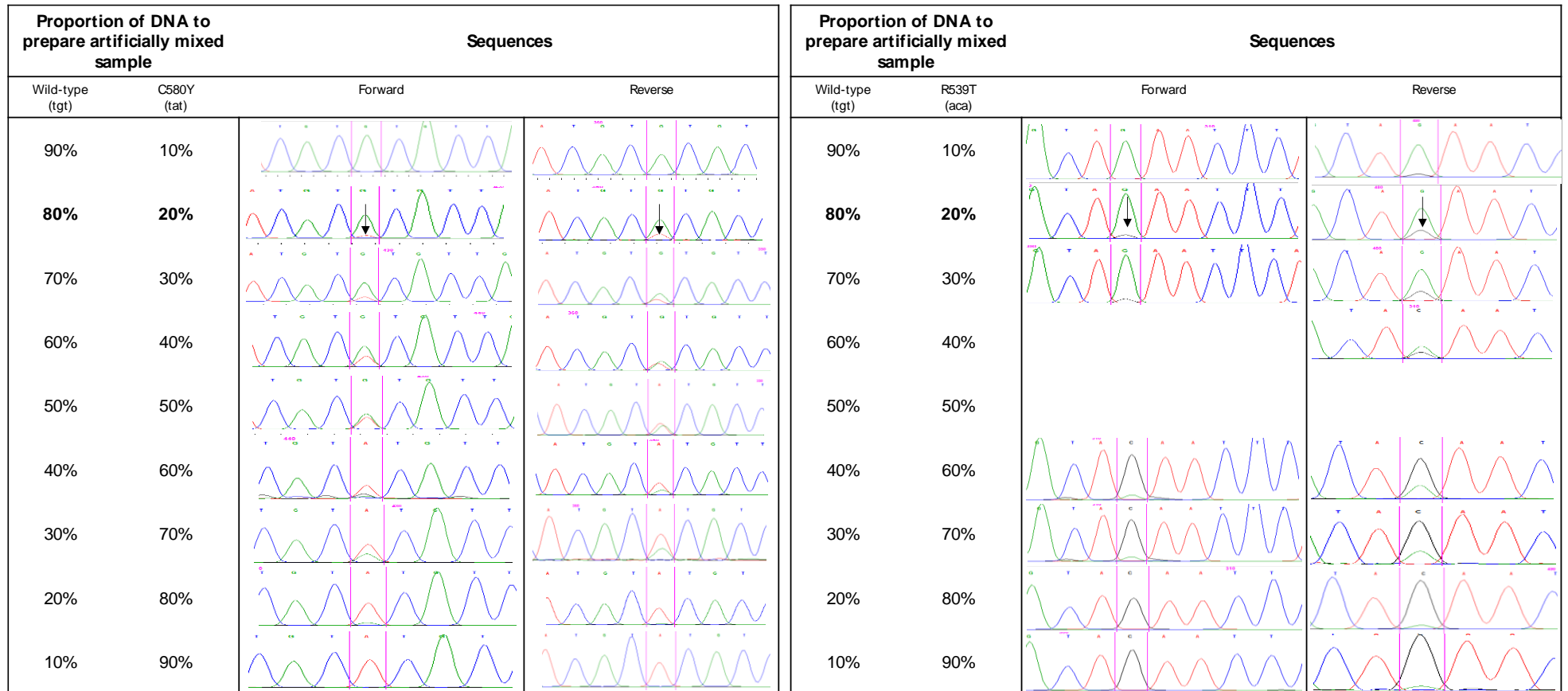


Figure S5. Flow chart describing the number of tested samples, the number of interpretable sequences, the number of 3D7-reference and mutant alleles sequences and the number of sequences with non-synonymous (NS) or synonymous (S) mutations observed in the KARMA study 2014.

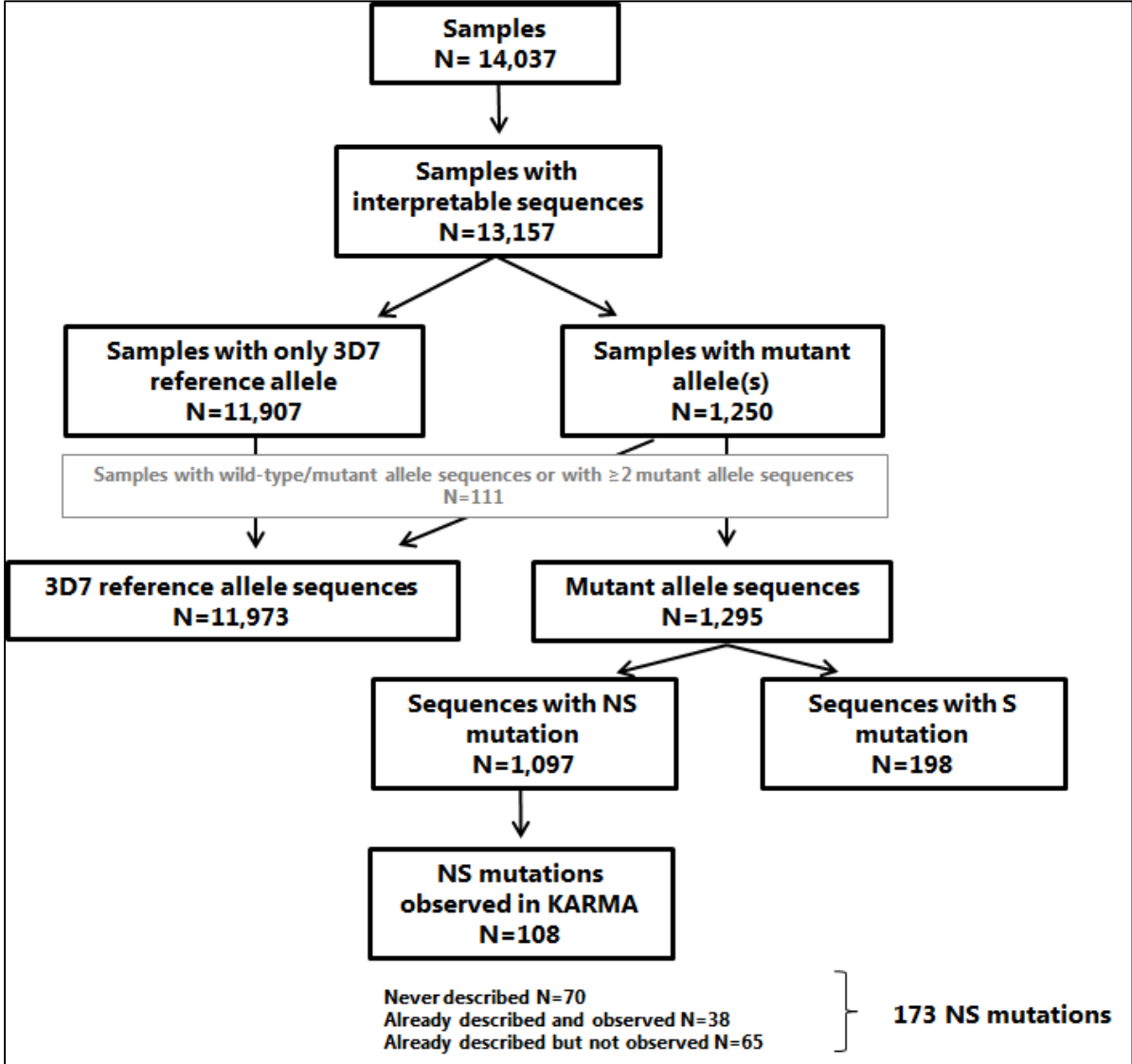
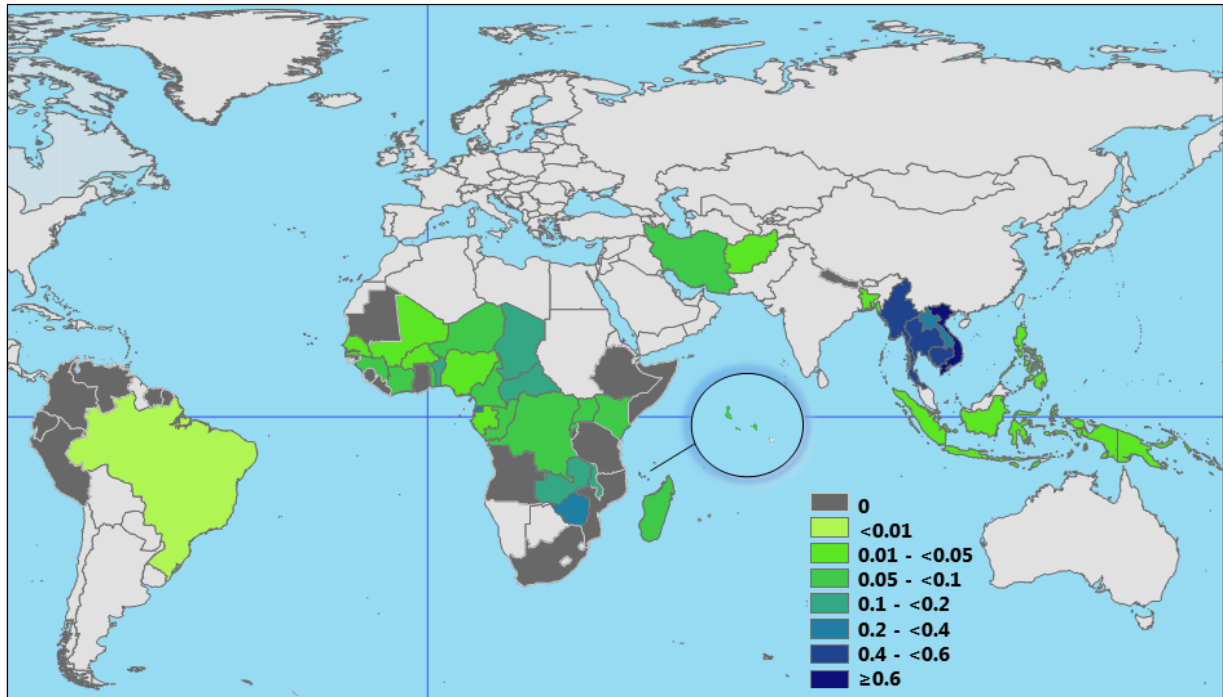
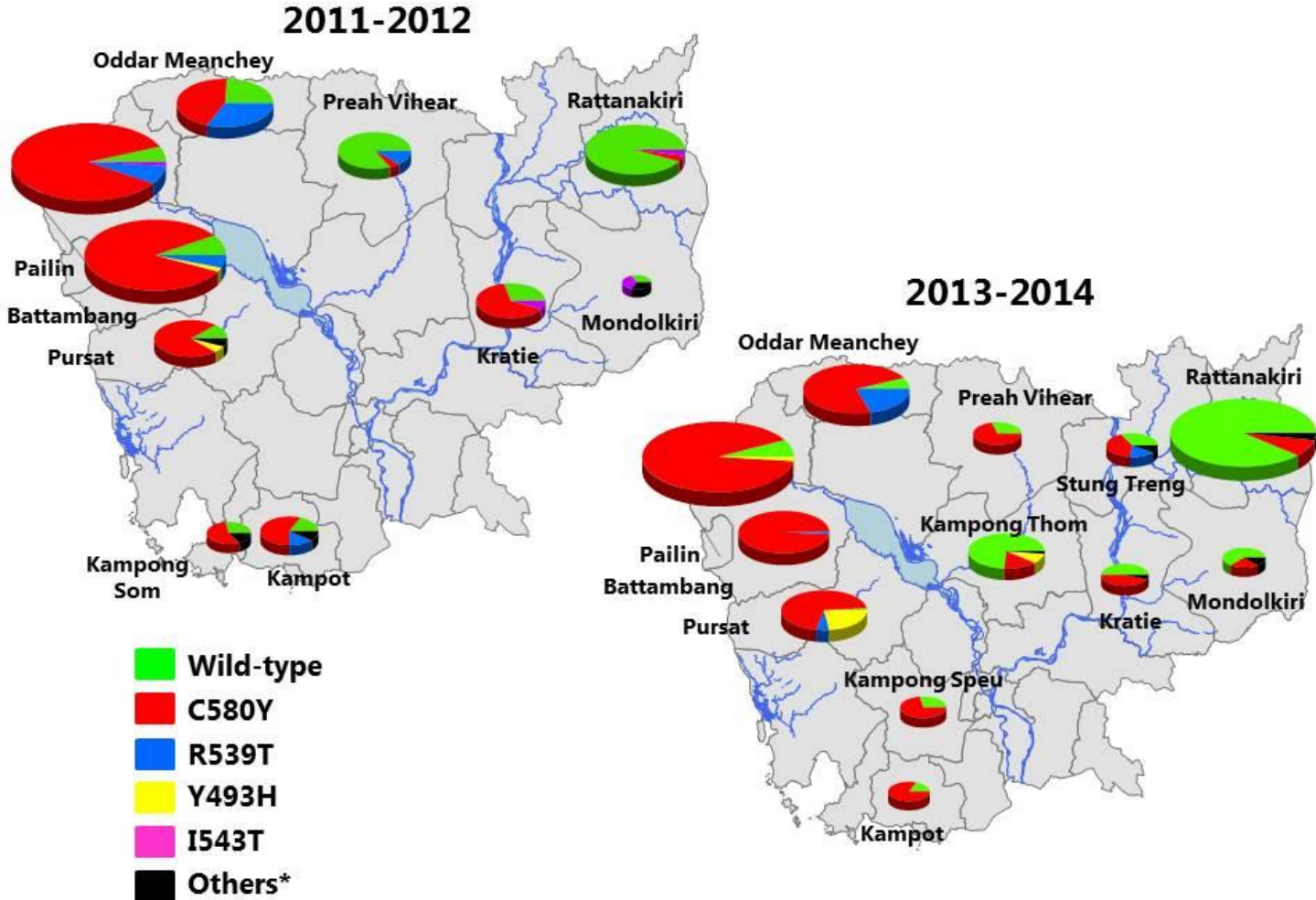


Figure S6. Worldwide distribution of haplotype diversity in the KARMA sampling sites, KARMA study 2014



Details are provided in Table S5. Haplotype diversity (H_d) was calculated using DnaSP (Nei 1987).

Figure S7. Geographic distribution of K13-propeller alleles in Cambodia in 2011–2012 and in 2013–2014, respectively, KARMA study 2014.



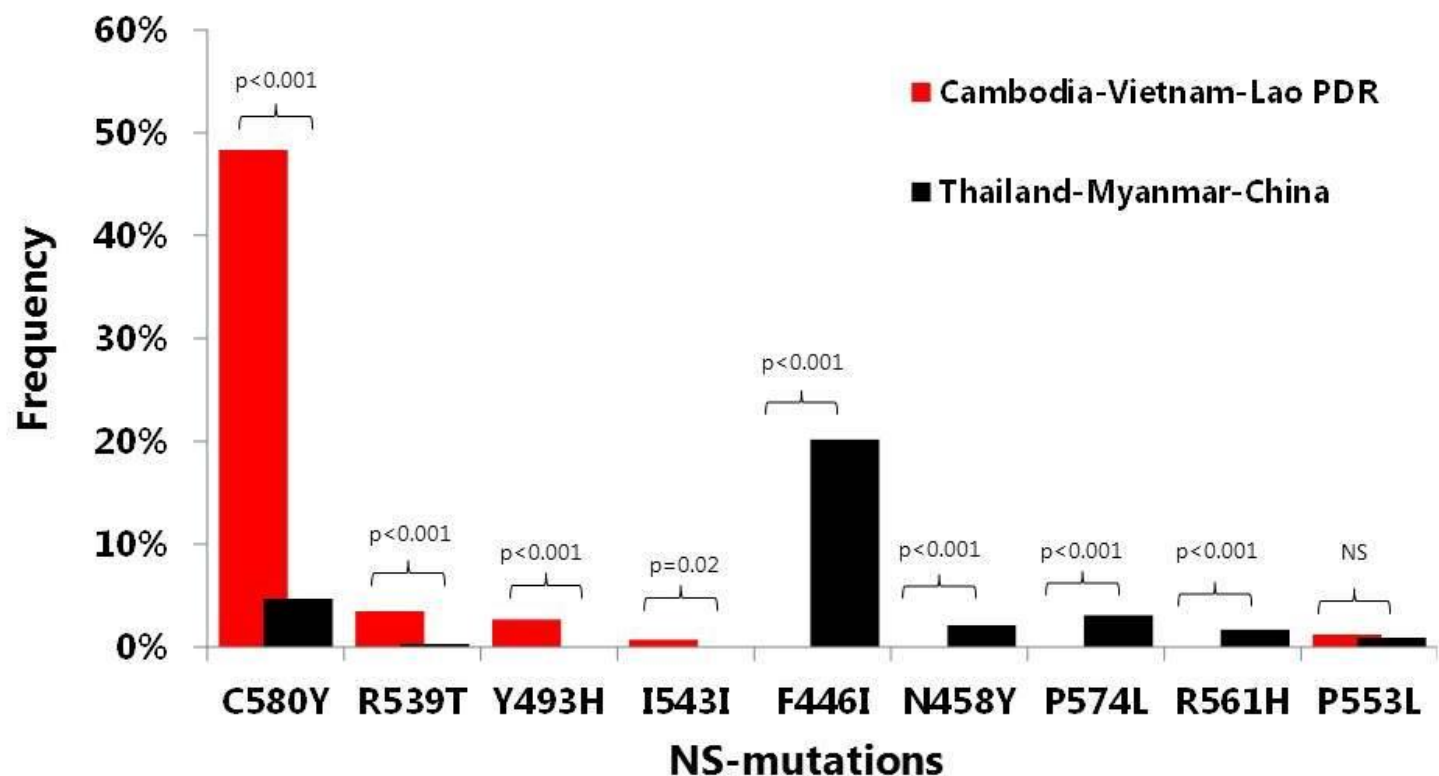
* N458Y, C469F, S485N, A486V, P553L, V568G, D584V, E556D, I646L, N664S

Pie charts of K13-propeller allele frequency among 300 parasite isolates collected in ten Cambodian provinces in 2011-2012 ¹ and 642 isolates collected in twelve provinces in 2013-2014 (KARMA study 2014). Pie sizes are proportional to the number of isolates and the different alleles are color-coded as indicated.

The frequencies of mutant K13-propeller alleles are as follows: West Cambodia: Pailin (2011-2012: 95%, n=84 vs. 2013-2014: 94%, n=164, P=0.97), Battambang (2011-2012: 93%, n=71 vs. 2013-2014: 100%, n=81, P=0.04), Pursat (2011-2012: 89%, n=19 vs. 2013-2014: 98%, n=52, P=0.32); Southwest Cambodia: Kampot (2011-2012: 83%, n=12 vs. 2013-2014: 83%, n=12, P=0.58), Kampong Som (2011-2012: 71%, n=74), Kampong Speu (2013-2014: 71%, n=15); Central Cambodia: Kampong Thom (2013-2014: 26%, n=42); Northwest Cambodia: Oddar Meanchey (2011-2012: 76%, n=33 vs. 2013-2014: 95%, n=81, P=0.008), Preah Vihear (2011-2012: 16%, n=19 vs. 2013-2014: 70%, n=17, P=0.003); East Cambodia: Kratie (2011-2012: 71%, n=17 vs. 2013-2014: 50%, n=16, P=0.38), Mondulkiri (2011-2012: 67%, n=3 vs. 2013-2014: 39%, n=13, P=0.81), Stung Treng (2013-2014: 65%, n=19), Ratanakiri (2011-2012: 6%, n=35 vs. 2013-2014: 11%, n=152, P=0.56).

¹ Ariey F, Witkowski B, Amaratunga C, et al. A molecular marker of artemisinin-resistant *Plasmodium falciparum* malaria. *Nature* 2014; 505:50-5.

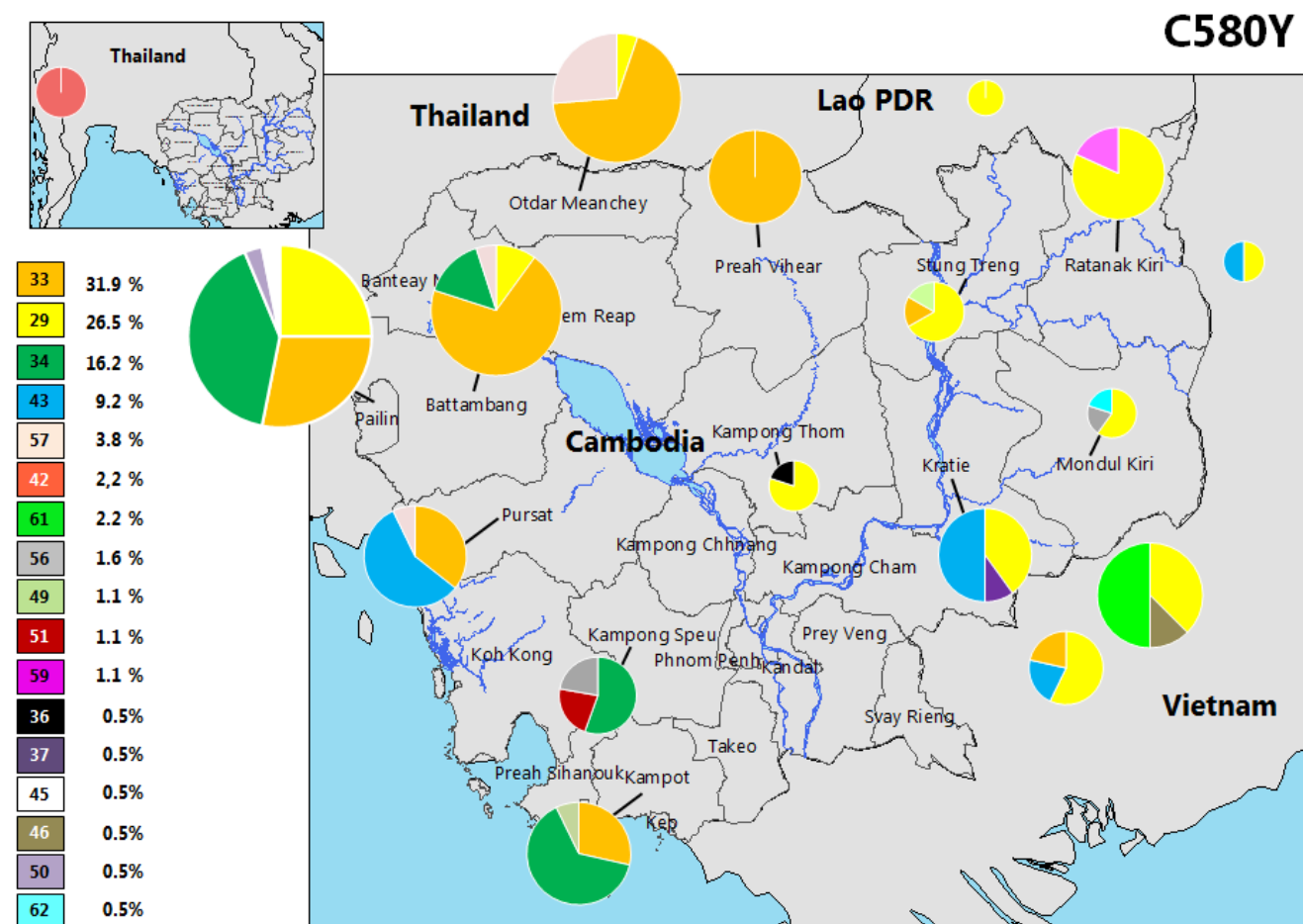
Figure S8. Frequency distribution of the most prevalent NS-mutations in Cambodia-Vietnam-Lao PDR and Thailand-Myanmar-China areas, KARMA study 2014.



C580Y: 48.3% Cambodia-Vietnam-Lao PDR vs. 4.7% Thailand-Myanmar-China; R539T: 3.5% Cambodia-Vietnam-Lao PDR vs. 0.3% Thailand-Myanmar-China; Y493H: 2.7% Cambodia-Vietnam-Lao PDR vs. 0% Thailand-Myanmar-China; I543I: 0.7% Cambodia-Vietnam-Lao PDR vs. 0% Thailand-Myanmar-China; F446I: 0% Cambodia-Vietnam-Lao PDR vs. 20.2% Thailand-Myanmar-China; N458Y: 0% Cambodia-Vietnam-Lao PDR vs. 2.1% Thailand-Myanmar-China; P574L: 0% Cambodia-Vietnam-Lao PDR vs. 3.1% Thailand-Myanmar-China; R561H: 0% Cambodia-Vietnam-Lao PDR vs. 1.7% Thailand-Myanmar-China; P553L: 1.2% Cambodia-Vietnam-Lao PDR vs. 0.9% Thailand-Myanmar-China (NS= not significant).

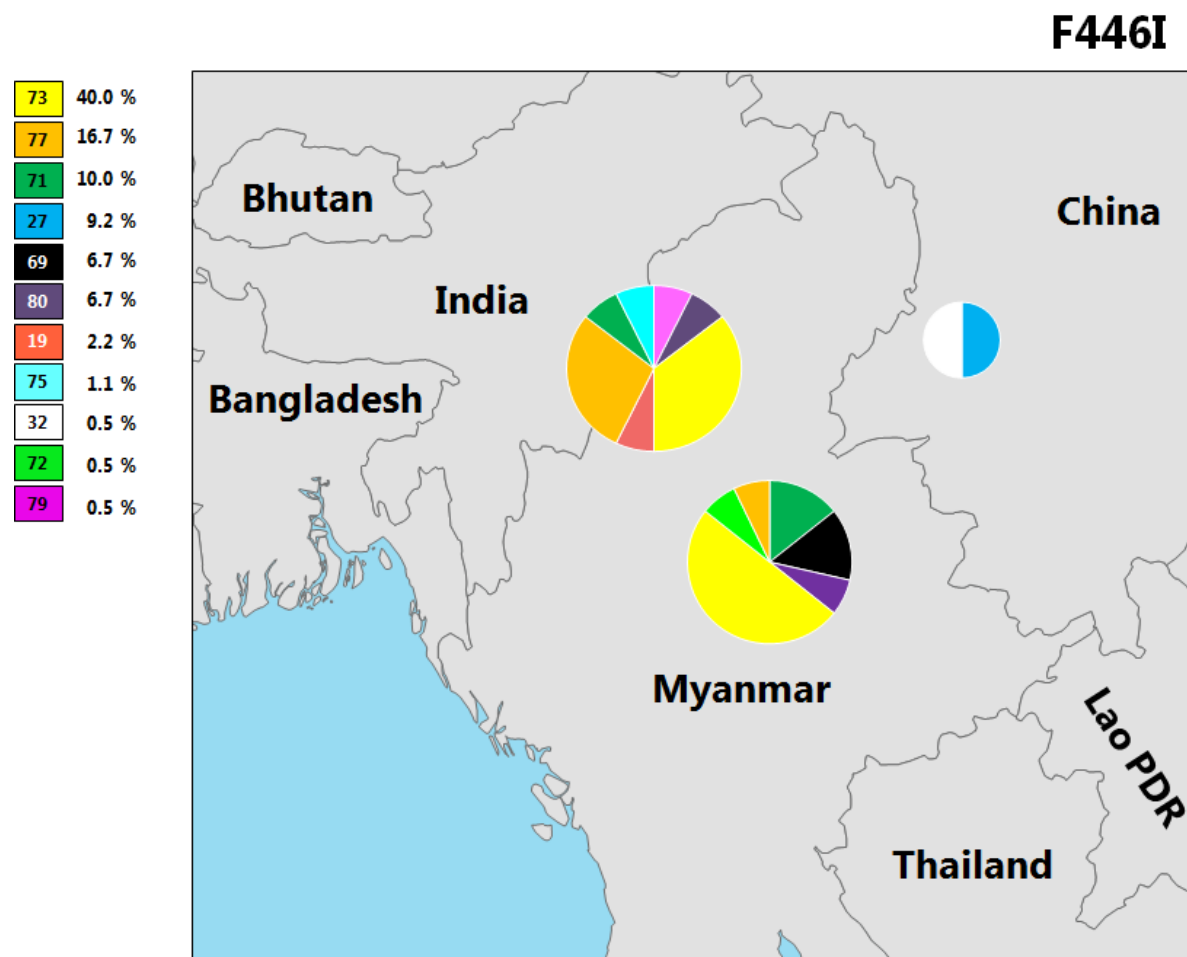
Figure S9. Regional distribution of the three-loci haplotypes of (A) the C580Y NS-mutant alleles in Cambodia, Lao PDR and Vietnam, (B) the F446I NS-mutant alleles in Myanmar and China, (C) the Y493H, R539T and I543T NS-mutant alleles in Cambodia and Vietnam and (D) the P553L, P574L, E605K, N458Y, R561H NS-mutant alleles in Cambodia, Vietnam, Thailand, Myanmar and China, KARMA study 2014.

A. C580Y haplotype distribution.



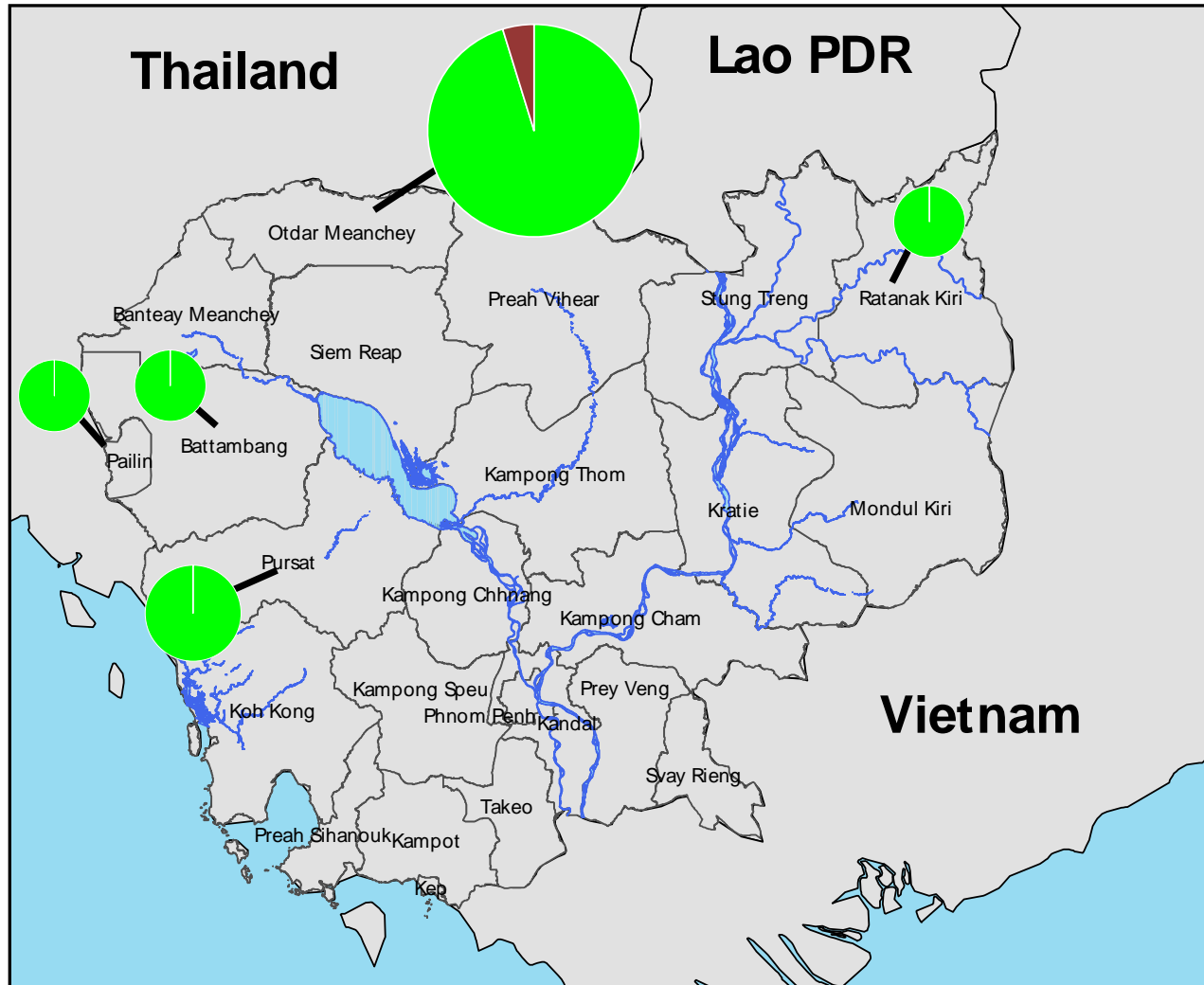
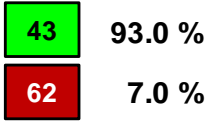
Colored-pies represent the proportion of C580Y-haplotypes observed by site. Numbers inside the colored-squares (left side) refer to the flanking haplotype ID (for haplotype numbering see Table S9) and the percentage indicated refers to the relative frequency of each C580Y haplotype. 182, 24, 2 and 4 isolates were studied from Cambodia, Vietnam, Lao PDR and Thailand, respectively. Details are provided in Table S9.

B. F446I haplotype distribution



Colored-pies represent the proportion of F446-haplotypes observed by site. Numbers inside the colored-squares refer to the flanking haplotype ID (for haplotype numbering see Table S9) and percentages indicate the relative frequency of each F446I haplotype. 28 and 2 isolates were studied from Myanmar and China PR, respectively. Details are provided in Table S9.

R539T



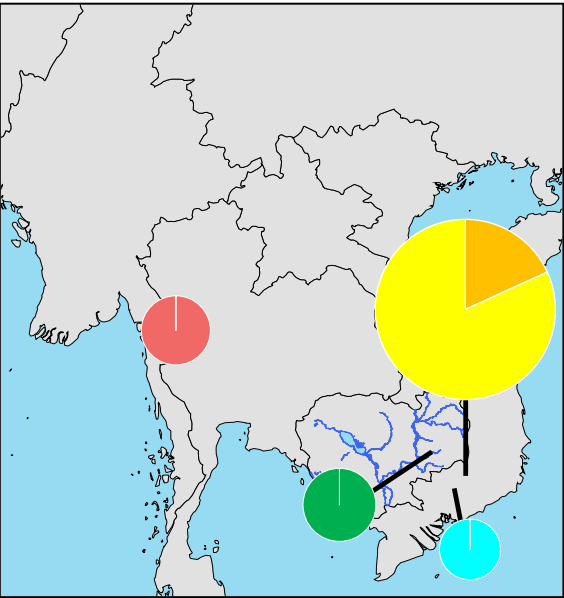


Colored-pies represent the proportion of Y493H-, R539T- and I543T-haplotypes observed by site. Numbers refer (left side) to the flanking haplotype ID (see Table S9) and percentages indicate the relative frequency of each three-loci haplotype in the set of samples harboring the same mutation (for full details, see Table S9).

D. P553L, P574L, E605K, N458Y, R561H three-loci haplotype distribution.

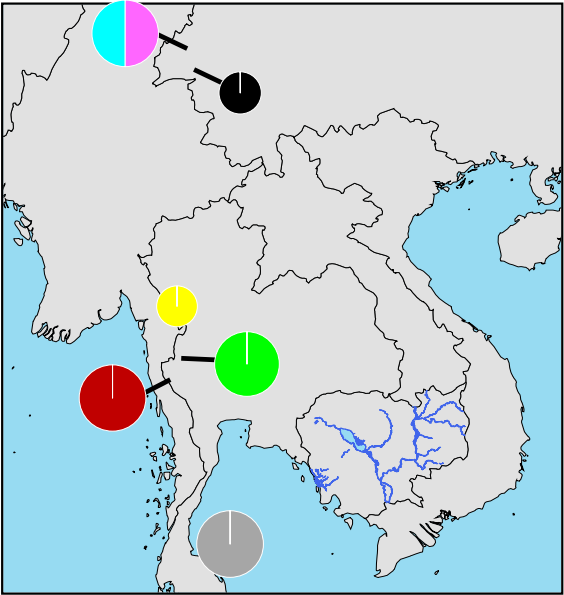
P553L

38	64.0 %
32	14.0 %
1	7.0 %
3	7.0 %
66	7.0 %



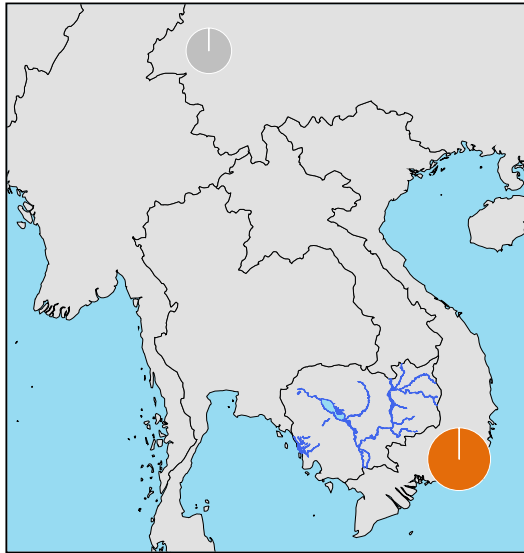
P574L

31	20.0 %
50	20.0 %
60	20.0 %
40	10.0 %
55	10.0 %
64	10.0 %
30	10.0 %



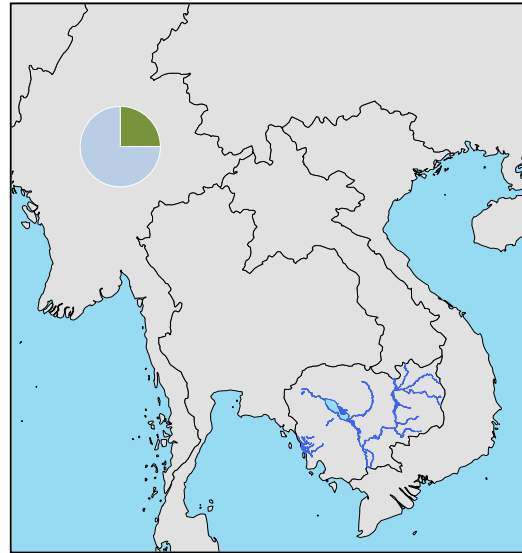
E605K

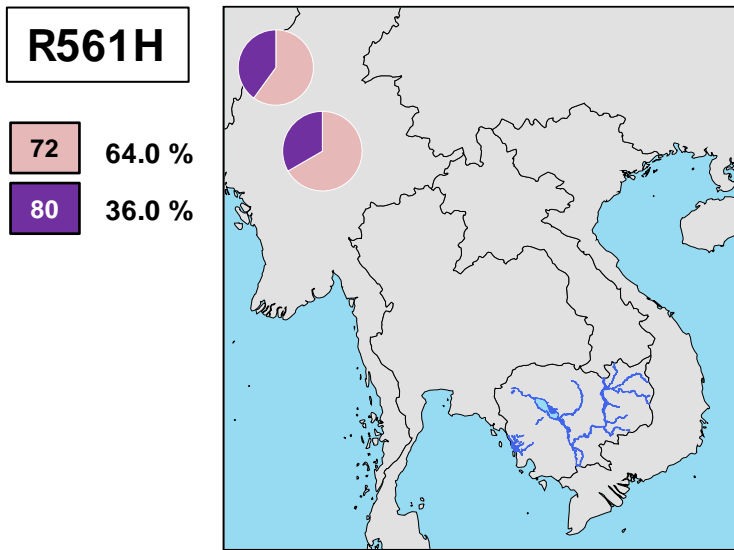
53	66.0 %
54	34.0 %



N458Y

78	75.0 %
76	25.0 %



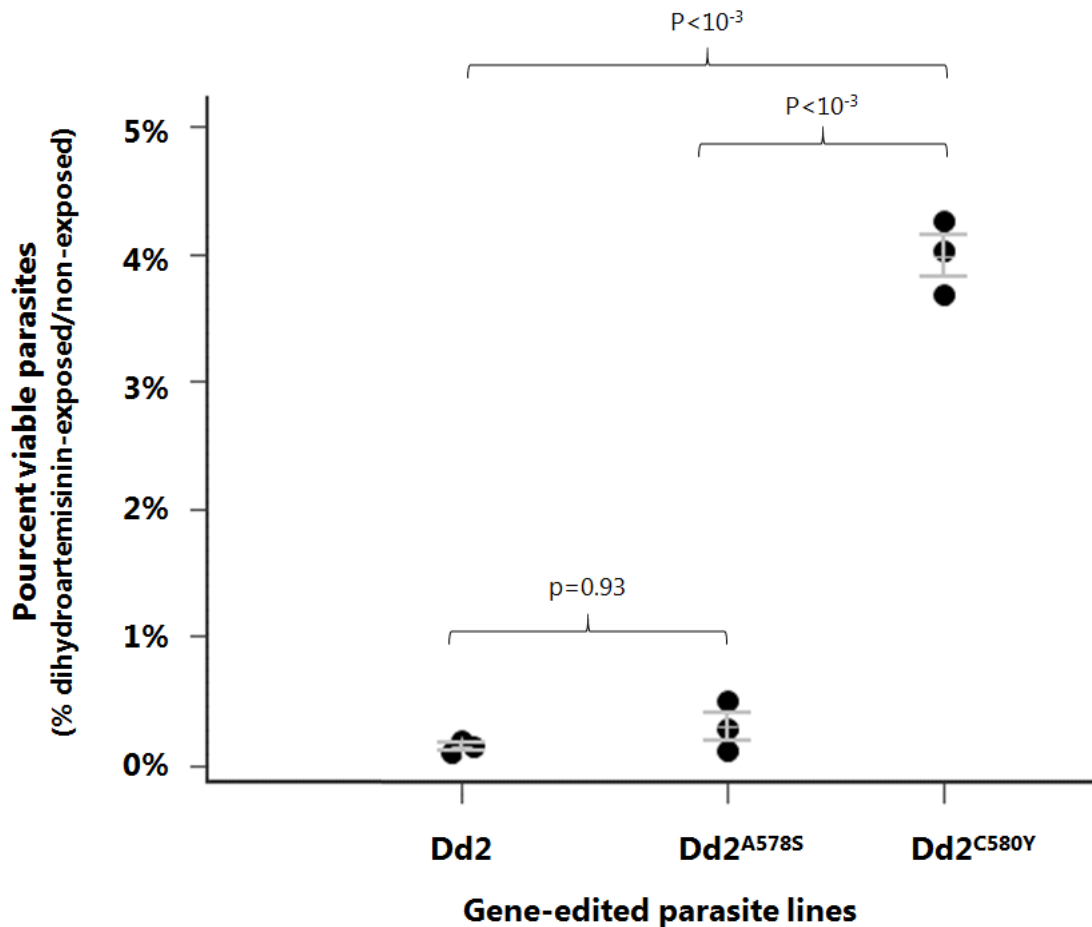


Colored-pies represent the proportion of P553L-, P574L-, E605K-, N458Y- and R561H-haplotypes observed by site. Numbers refer (left side) to the flanking haplotype ID (see Table S9) and percentages indicate the relative frequency of each three-loci haplotype in the set of samples harboring the same mutation (for full details see Table S9)

Haplotype distribution of A578S in 35 isolates (32 from Africa and 3 from Asia, 2 samples from Bangladesh ¹ were included for this analysis) .The colored-squares represent one isolate and number inside the colored-square, the flanking haplotype ID. Haplotype numbering is indicated in Table S9 and sequence of individual PF3D7_1337500 (K13_151) and PF3D7_1339700 (K13_159) alleles is shown in Table S8. The squares with heavy lines indicate the 4 haplotypes observed in 2 samples (H5, H15, H19 and H22). For details about the samples, see Table S9.

¹ Mohon AN, Alam MS, Bayih AG, et al. Mutations in *Plasmodium falciparum* K13 propeller gene from Bangladesh (2009-2013). Malar J 2014;13:431.

Figure S11. Mean survival rates (expressed as percent of viable parasites) of the Dd2, Dd2^{A578S} and Dd2^{C580Y} gene-edited lines in the RSA^{0-3h}, KARMA study 2014.

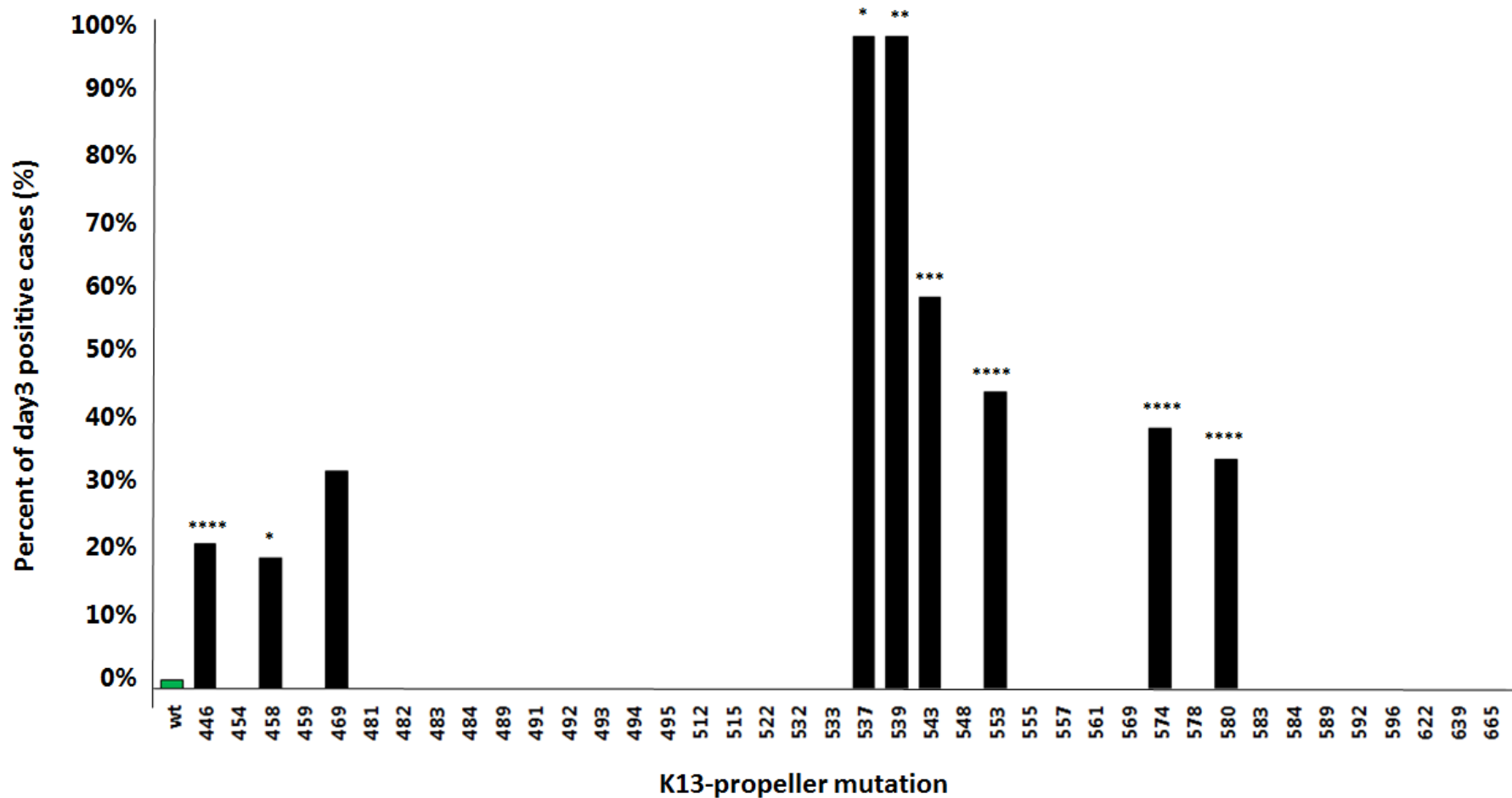


RSA survival rates (% of viable parasites) were as follows: for Dd2 (N=3 independent assays, mean=0.14 ± Standard Error of the Mean=0.03); for Dd2^{A578S} (N=3 independent assays, mean=0.29 ± Standard Error of the Mean=0.11) and for Dd2^{C580Y} (N=3 independent assays, mean=4.01 ± Standard Error of the Mean=0.16).

Two-sample t tests with unequal variances were used to assess for statistically significant differences between K13-edited clones and their comparator lines. No statistical difference between Dd2 and Dd2^{A578S} survival rates (adjusted p-value in multiple comparisons = 0.93) were found, while survival rates of Dd2^{C580Y} significantly differed from Dd2 (adjusted p-value in multiple comparisons <10⁻³) or from Dd2^{A578S} (adjusted p-value in multiple comparisons <10⁻³). The test of differences in proportions (one-way analysis of variance) shows that the mean survival rates of Dd2^{A578S} and the Dd2^{C580Y} positive control were statistically different (p<10⁻²).

The horizontal lines represent the means and whiskers, the 95% confidence levels. The limit of detection of viable parasites was estimated 0.06% parasitemia (number of red blood cells counted in each assay = 30,000).

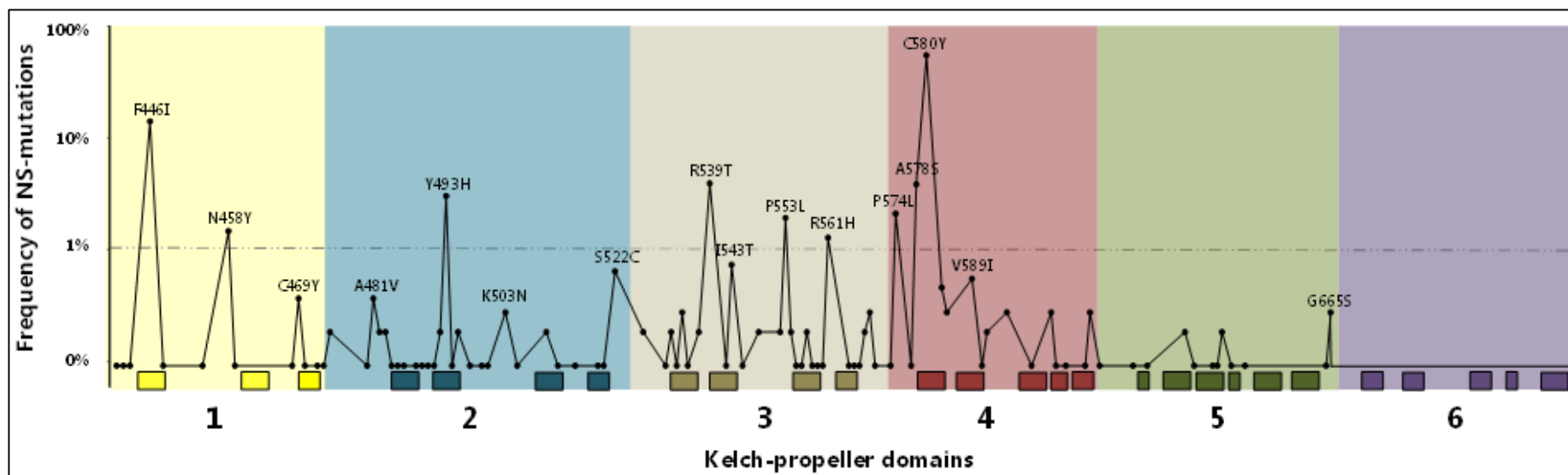
Figure S12. Distribution of the day3 positivity cases according to the K13 NS mutation detected in the day0 isolate in 2450 patients receiving a 7-day artesunate monotherapy or standard 3-day course of ACT#, KARMA study 2014.



#ACT treatments were: artemether/lumefantrine, artesunate/amodiaquine, artesunate/sulfadoxine-pyrimethamine or dihydroartemisinin/piperaquine.

The graph shows the percent of day3 positive cases for each mutation observed in the group of 2450 patients enrolled in therapeutic efficacy studies : wild-type (1.4%, 30/2105); F446I (22.3%, 25/112, $P < 0.0001$, Fisher exact test, compared to the percent of day3 positive case observed in patients harboring wild-type allele), N458Y (20.0%, 2/10, $P < 0.05$), C469Y (33%, 1/3, $P > 0.05$), N537D (100%, 1/1, $P < 0.05$), R539T (100%, 2/2, $P < 0.01$), I543T (60%, 3/5, $P < 0.001$), P553L (45.5%, 10/22, $P < 0.0001$), P574L (40%, 4/10, $P < 0.0001$) and C580Y (35.2%, 43/122 $P < 0.0001$). For the others mutations (V454A, N=3; S459L, N=2; A481V, N=2; Y482S, N=1; F483S, N=2; G484R, N= 1; N489S, N=1; F491S, N=1; L492S, N=1; Y493C, N=1; V494L, N=1; F495L, N=1; D512N, N=1; R515K, N=1; S522C, N=3; C532S, N=1; G533S, N=1; G548D, N=1; V555A, N=1; A557S, N=1; R561H, N=13; A569T, N=1; A578S, N=9, F583L, N=1; D584V, N=1; V589I, N=1; G592R, N=1; E596K, N=1; R622I, N=1; G639S, N=1; G655S, N=1), no day3 positive case was recorded. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ and **** $P < 0.0001$

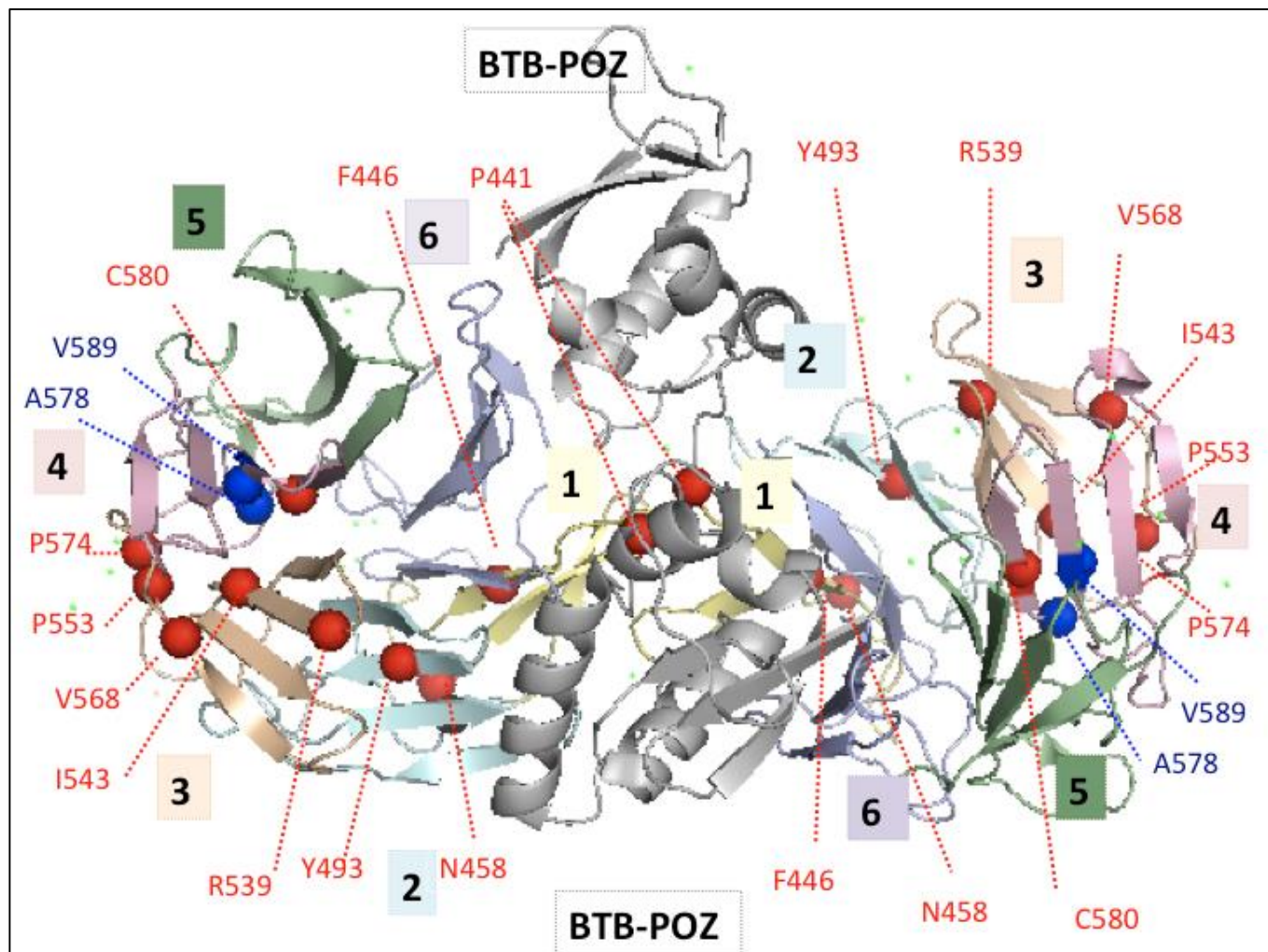
Figure S13. Schematic representation of the frequency of NS-mutants mapped to the individual K13 kelch domains, KARMA study 2014.

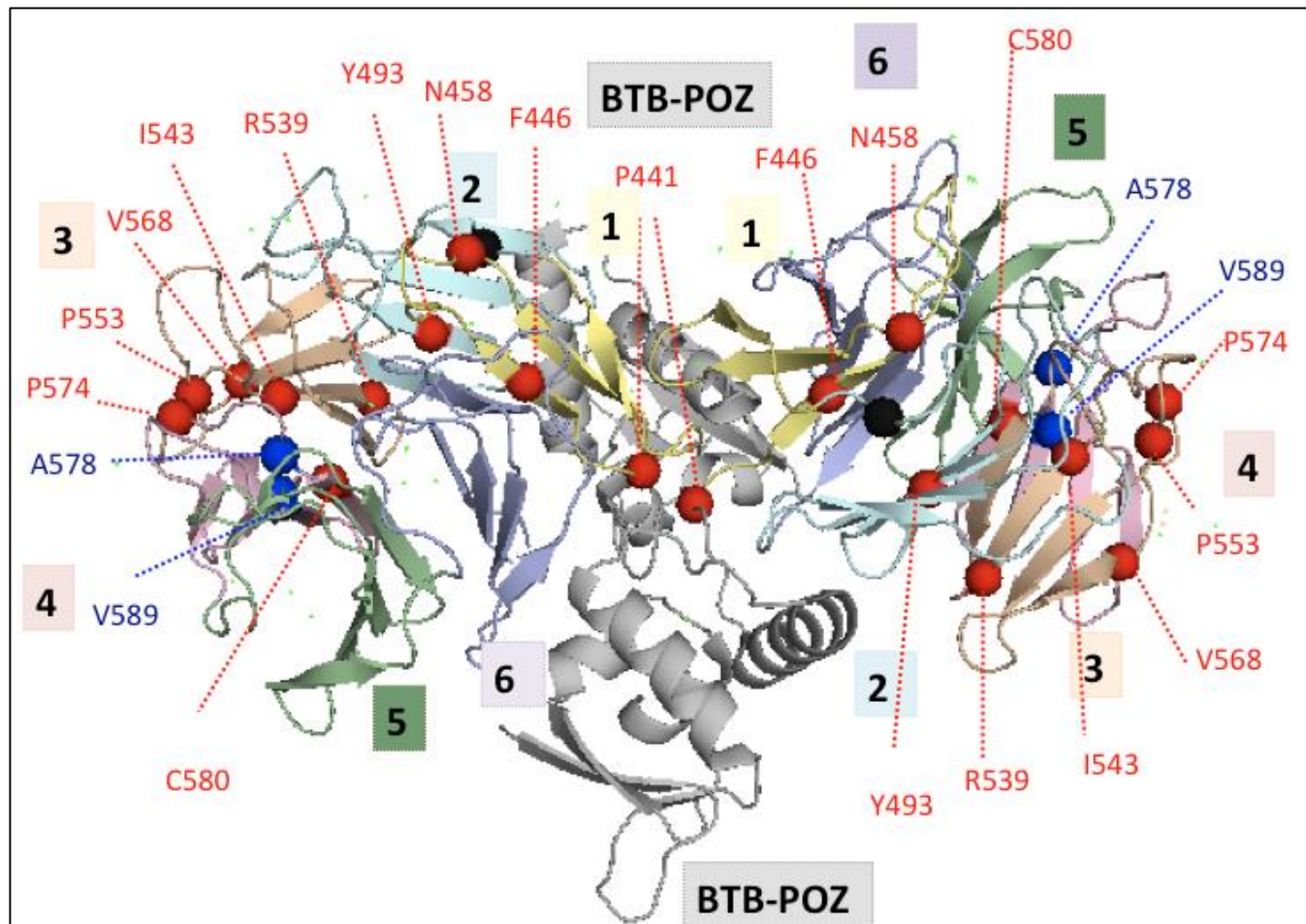


Individual Kelch domains are colored in yellow (domain 1), blue (domain 2), brown (domain 3), red (domain 4), green (domain 5) and purple (domain 6). Colored-rectangles underneath correspond to the positions of the β -sheets in each kelch-propeller domain in the crystal structure of the wild type BTB-POZ propeller domain (PDB AYY8).

Figure S14. Mapping of K13 mutations on the crystal structure of *P. falciparum* K13 BTB-POZ propeller domain (PDB 4YY8), KARMA study 2014.

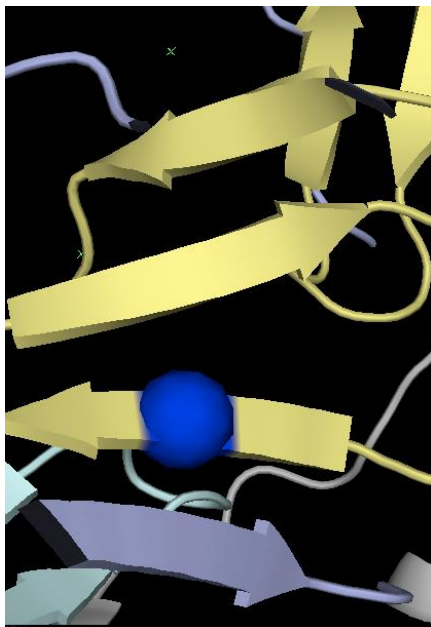
A. Two views of the K13 BTB-POZ-Kelch propeller dimer.



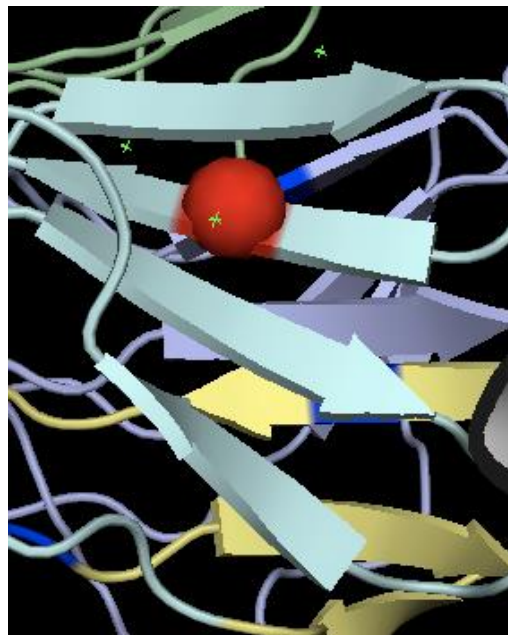


Localization of the mutants was prepared using PyMOL Molecular Graphics System version 1.5.0.4 (<http://www.pymol.org>). Grey: BTB-POZ ; individual kelch domains are color-coded as yellow, pale cyan, wheat, pale pink, pale green and pale blue for kelch domain 1, 2, 3, 4, 5 and 6 respectively. Red colored spheres correspond to the resistance-associated mutations (validated and associated). A578 and V589 are indicated in blue.

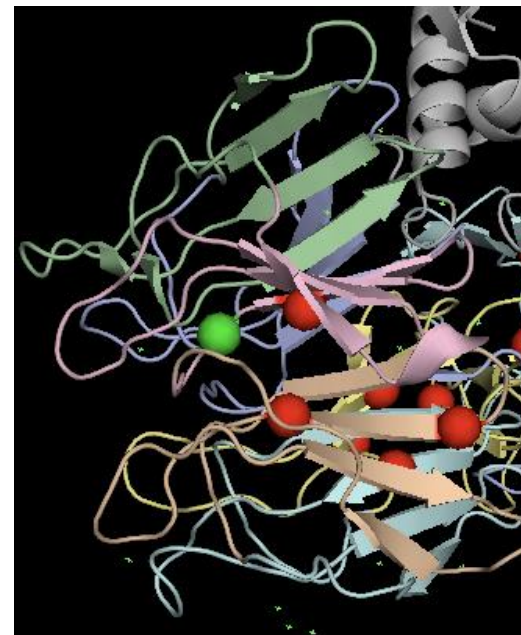
B. Localization and environment of some mutations.



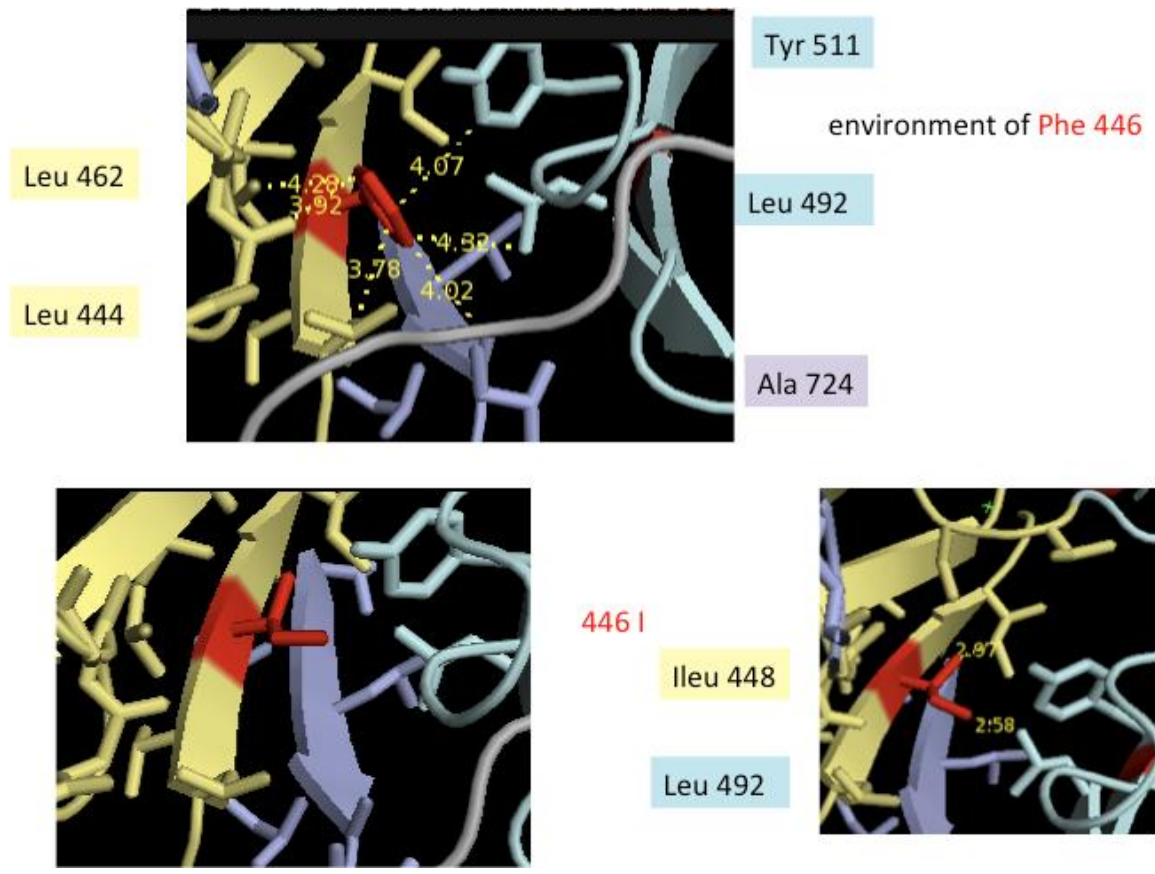
F446I (blue sphere) in the context of the 4th β -sheeted blade 1 F446 is located in the 2nd β -sheet, the first one being provided by the C-terminal sequence of K13



Position of Y493 (red sphere) in the 2nd β -sheet of kelch domain



A578S (green) is located within the blade3-blade4 junction region. Resistance-associated mutations of kelch domains 3 and 4 are shown as red spheres



Distances (in Å) between atoms are indicated in yellow

The structure (X-Ray diffraction with resolution of 1.81 Angström) has been solved by Jiang DQ, Tempel W, Loppnau P, Graslund S, He H, Ravichandran M, Seitova A, Arrowsmith CH, Edwards AM, Bountra C, Ei Bakkouri M, Senisterra G, Osman KT, Lovato DV, Hui R, Hutchinson A, Lin YH, Structural Genomics Consortium and released in April 2015.

Table S1. The K13-toolbox: reagents, quality controls and detailed standard operating procedures provided to partners involved in the KARMA consortium, KARMA study 2014.

List of needed equipments, consumables & reagents

Equipments

- Thermocycler
- 2 Heating blocks for 1.5 ml tubes (or 1 heating block and 1 incubator)
- Centrifuge for 1.5 ml tubes
- Scissors and tweezers
- (Bunsen burner)
- P1000/ P200/ P20/ P10 pipets
- Weighting scale (for preparation Saponin solution and agarose gel)
- All equipments to perform agarose gel electrophoresis: microwave, generator, gel tank, UV illuminator

Consumables

- PCR plates & seal
- 1.5 ml tubes

Reagents

- RNase/DNase free water
- Agarose
- Ethidium bromide
- TBE 1X buffer
- Loading dye
- MW Marker

K13 tool box

Reagents

- QiaAmp DNA mini kit (250 tests/kit) – Qiagen # 51306
- 5x HOT FIREPol blend Master mix with 12.5 mM MgCl₂ (tubes of 1 ml) – Solis Biodyne # 04-27-00125
- Set of Primers: 4 tubes of primers (K13_PCR_F&R; K13_N1_F&R) – Sigma
- PBS tablets (Sigma – P4417)
- Saponin (Sigma – 84510-500G)

Quality Controls

Dried Blood spots K13_1, K13_2, K13_3, K13_4, K13_5, and K13_6

KARMA project - Qiagen DNA Purification from Dried Blood Spot

1. Object

This procedure describes the method used for parasite DNA extraction from Dried Blood Spots using the spin protocol of the QIAamp Mini kit.

2. Introduction

The QIAamp DNA Mini Kit is used for DNA isolation from Dried Blood Spots with fast spin-column procedures. DNA binds specifically to the QIAamp silica-gel membrane while contaminants pass through. QIAamp DNA technology yields parasite DNA from Dried Blood Spots ready to use in PCR procedures. Yield expected with this method from a 3mm blood spot: 75-150 ng.

3. Associated documents and files

QIAamp DNA Mini and Blood Mini Handbook 04/2010

4. Hygiene and security

Universal safety precautions should be taken when handling chemicals and potentially infectious specimens. PPE (lab coat and gloves) are to be worn at all time. **DO NOT add bleach or acidic solutions directly to the sample-preparation waste.** The sample-preparation waste contains guanidine hydrochloride from Buffers AL and AW1, which can form highly reactive compounds when combined with bleach.

If liquid containing these buffers is spilt, clean with suitable laboratory detergent and water. If the spilt liquid contains potentially infectious agents, clean the affected area first with laboratory detergent and water, and then with 1% (v/v) sodium hypochlorite.

For more information, please consult the laboratory biosafety manual and the QIAamp DNA Mini Kit MSDS.

5. Reagents and consumables

5.1. Reagents

Reagent name	Producer	Reference	Technical data
QIAamp DNA Mini Kit (250)	Qiagen	51306	Qiagen DNA Mini and Blood Mini Handbook
Saponine	SIGMA	84510-500G	MSDS
PBS tablet	SIGMA	P4417	MSDS
Alcohol 70%			
Bleach 10%			

5.2. Consumables

Consumable name	Producer	Reference	Technical data
Kit consumables (spin columns; tubes)	Qiagen	51306	
Tips 10, 20, 200 & 1000 µl			
1.5 ml tubes			
Stericup			

6. Equipment needed

- Heating block for 1.5ml and one incubator (or 2 heating blocks)
- Centrifuge for 1.5ml
- Bunsen burner
- Scissors and twisters
- PH meter
- Vortex
- P1000, P200, P20 pipets

7. Procedures

7.1. Preparation of reagents

QIAGEN reagents (when starting a new kit)

QIAGEN Protease stock solution (stable up to 2 months at 2–8°C or longer at –20°C)

Before using it for the first time, pipet 5.5 ml protease solvent into the vial containing lyophilized QIAGEN Protease, as indicated on the label. Date the vial.

Buffer AL (stable up to 1 year at room temperature, 15–25°C)

Mix Buffer AL thoroughly by shaking or vortexing before use.

Buffer AW1 (stable up to 1 year at room temperature, 15–25°C)

Before using it for the first time, add the appropriate amount of ethanol (96–100%) to Buffer AW1 concentrate as indicated on the bottle. Label the bottle: date, name and tick inside the square on the top of the bottle

Buffer AW2 (stable up to 1 year at room temperature, 15–25°C)

Before using for the first time, add the appropriate amount of ethanol (96–100%) to Buffer AW2 concentrate as indicated on the bottle. Label the bottle: date, name and tick inside the square on the top of the bottle.

Cell lysis reagents preparation

Saponine 10%

- Weight 1g of saponine in a 10ml flask"
- Add 10 ml of distilled water
- Filtration using a stericup
- Store at 4C

PBS 1X

Dissolve one tablet in 200 ml of distilled water.

Store at ambient temperature

7.2. Sample preparation

1. Prepare the bench to work under **sterile condition** for sample preparation:

- prepare a 15ml/50ml tube of absolute ethanol
- Place a piece of aluminium foil on the bench
- Light the Bunsen burner

2. Disinfect scissors and tweezers by soaking them in absolute ethanol and passing them through the Bunsen flame.

3. Hold the DBS filter with the sterile tweezers. Cut the dried blood spot with sterile scissors, then cut it in small pieces (few mm squares).

4. Transfer the DBS pieces in 1.5 ml labeled tube.

Note 1: sterilize scissors and tweezers between each samples

Note 2: Always extract quality controls at the same time as the samples

7.3. Cell lysis

1. Add 1 ml of PBS 1X/ Saponine 0.5% per tube (950 μ l PBS 1X + 50 μ l saponine 10%), mix gently

2. Incubate at 4°C for at least 1h30min (or overnight)

3. Remove the liquid

4. Wash filters with 1 ml PBS 1X per tube

5. Incubate 5 min at 4°C

6. Repeat the last 3 steps (Second wash)

7.4. Procedure for DNA purification

Notes: All centrifugation steps are carried out at room temperature (15–25°C).

Things to do before starting

- Prepare one heating block at 85°C for use in step 2, and one heating block (or incubator) at 56°C for use step 3

- Equilibrate Buffer AE to room temperature for elution in step.16.

- Ensure that Buffer AW1 and Buffer AW2 have been prepared according to the instructions on section 7.1.1.

- If a precipitate has formed in Buffer AL or Buffer ATL, dissolve by incubating at 56°C.

- Clean bench and pipettes with bleach 10%

Qiagen kit procedure:

1. Add **180 μ l of Buffer ATL per tube**

2. Incubate at **85°C for 30 min**. Briefly centrifuge to remove drops from inside the lid.

3. Add **20 μ l proteinase K** QIAGEN stock solution. Mix by vortexing, and incubate at **56°C for 1 h**. Briefly centrifuge to remove drops from inside the lid.

Note: Set up the incubator at 70°C for next step.

4. Add **200 μ l Buffer AL** to the sample. Mix thoroughly by vortexing, and incubate at **70°C for 30 min**. Briefly centrifuge to remove drops from inside the lid. In order to ensure efficient lysis, it is essential that the sample and Buffer AL are mixed immediately and thoroughly.

Note: Do not add proteinase K directly to Buffer AL.

5. Add **200 µl ethanol (96–100%)** to the sample, and mix again by pulse vortexing for 15 s. After mixing, briefly centrifuge the 1.5 ml microcentrifuge tube to remove drops from the inside of the lid.
6. Carefully transfer the mixture from step 5 to the **QIAamp Mini spin column** (place in a clean 2 ml collection tube) without wetting the rim. Close the cap of spin column in order to avoid aerosol formation during centrifugation.
7. **Centrifuge** at 8,000 rpm for 1 min.
Note: If the lysate has not completely passed through the column after centrifugation, centrifuge again at higher speed (10,000 rpm) until the QIAamp Mini spin column is empty.
8. Place the QIAamp Mini spin column in a **new clean 2 ml collection tube** and discard the old collection tube containing the filtrate.
9. Carefully open the QIAamp Mini spin column and add **500 µl Buffer AW1** without wetting the rim. Close the cap.
10. **Centrifuge** at 8,000 rpm for 1 min.
11. Place the QIAamp Mini spin column in a new clean 2 ml collection tube and discard the old collection tube containing the filtrate.
12. Carefully open the QIAamp Mini spin column and add **500 µl Buffer AW2** without wetting the rim. Close the cap.
13. **Centrifuge** at 13,000 rpm for 3 min.
14. Discard the filtrate from the 2 ml collection tube. Replace the QIAamp Mini spin column in the 2 ml collection tube and **centrifuge** at full speed for 3 min. This step helps to eliminate the chance of possible Buffer AW2 carryover.
15. Place the QIAamp Mini spin column in a **new clean 1.5 ml microcentrifuge tube** (not provided), and discard the 2 ml collection tube containing the filtrate. Allow the column to **dry for 1 to 5 min**.
16. Carefully open the QIAamp Mini spin column and add **100 µl Buffer AE**. **Incubate at room temperature** (15–25°C) for **5 min**, and then **centrifuge** at 10,000 rpm for 1 min.
17. Storage DNA at 4°C for short-term storage (DNA will be use for PCR in the following days). For long-term storage of DNA, store DNA at –20°C or – 80°C. Avoid freezing / thawing samples.

KARMA project - Qiagen DNA Purification from whole blood

1. Object

This procedure describes the method used for DNA purification (genomic, mitochondrial, and viral) from whole blood using the spin protocol of the QIAamp Mini kit.

2. Introduction

The QIAamp DNA Mini Kit is used for DNA isolation from whole blood with fast spin-column procedures. DNA binds specifically to the QIAamp silica-gel membrane while contaminants pass through. QIAamp DNA technology yields parasite DNA from whole blood ready to use in PCR.

Yields with the QIAamp DNA Mini Kit

Sample	Yield	
	Total nucleic acids (µg)*	DNA
Blood (200 µl)	4–12	4–12 µg

3. Associated documents and files

QIAamp DNA Mini and Blood Mini Handbook 04/2010

4. Hygiene and security

Universal safety precautions should be taken when handling chemicals and potentially infectious specimens. PPE (lab coat and gloves) are to be worn at all time. **DO NOT add bleach or acidic solutions directly to the sample-preparation waste.** The sample-preparation waste contains guanidine hydrochloride from Buffers AL and AW1, which can form highly reactive compounds when combined with bleach.

If liquid containing these buffers is spilt, clean with suitable laboratory detergent and water. If the spilt liquid contains potentially infectious agents, clean the affected area first with laboratory detergent and water, and then with 1% (v/v) sodium hypochlorite.

For more information, please consult the laboratory biosafety manual and the QIAamp DNA Mini Kit MSDS.

5. Reagents and consumables

5.1. Reagents

Reagent name	Producer	Reference	Technical data
QIAamp DNA Mini Kit (250)	Qiagen	51306	Qiagen DNA Mini and Blood Mini Handbook
PBS			

5.2. Consumables

Consumable name	Producer	Reference	Technical data
Kit consumables (spin columns; tubes) Tips 10, 20, 200 & 1000 µl 1.5 ml tubes	Qiagen	51306	

6. Equipment needed

- Heating block for 1.5 ml tubes or incubator
- Centrifuge for 1.5 ml tubes
- Vortex
- P1000, P200, P20 pipets

7. Procedures

7.1. Preparation of reagents (when starting a new kit)

QIAGEN Protease stock solution (stable up to 2 months at 2–8°C or longer at –20°C)
Before first use, pipet 5.5 ml protease solvent into the vial containing lyophilized QIAGEN Protease, as indicated on the label. Date the vial.

Buffer AL (stable up to 1 year at room temperature, 15–25°C)
Mix Buffer AL thoroughly by shaking or vortexing before use.

Buffer AW1 (stable up to 1 year at room temperature, 15–25°C)
Before first use, add the appropriate amount of ethanol (96–100%) to Buffer AW1 concentrate as indicated on the bottle. Label the bottle: date, name and tick · inside the square on the top of the bottle

Buffer AW2 (stable up to 1 year at room temperature, 15–25°C)
Before first use, add the appropriate amount of ethanol (96–100%) to Buffer AW2 concentrate as indicated on the bottle. Label the bottle: date, name and tick · inside the square on the top of the bottle.

7.2 DNA purification

Notes:

- All centrifugation steps are carried out at room temperature (15–25°C).
- 200 µl of whole blood yields 3–12 µg of DNA.

Things to do before starting

- Equilibrate samples to room temperature.
- Set up the heating block (or incubator) at 56°C.
- Equilibrate Buffer AE or distilled water to room temperature for elution in step 17.
- Ensure that Buffer AW1, Buffer AW2, and QIAGEN Protease have been prepared according to the instructions in section 7.1.
- if a precipitate has formed in Buffer AL, dissolve by incubating at 56°C.
- Clean bench with bleach 10%.

Procedure

1. Pipet **20 µl QIAGEN Protease K** into the bottom of a 1.5 ml microcentrifuge tube.
2. Add **200 µl sample** to the microcentrifuge tube:
 - 200 µl of whole blood or
 - 100 µl of red blood cells pellet + 100 µl PBSNote: If the amount of blood is less than 200µl, add sufficient PBS to reach 200µl. If the whole blood is too viscous, add PBS.
3. Add **200 µl Buffer AL** to the sample. Mix by pulse-vortexing for 15 s.
In order to ensure efficient lysis, it is essential that the sample and **Buffer AL** are mixed thoroughly to yield a homogeneous solution.
Note: Do not add QIAGEN Protease or proteinase K directly to Buffer AL.
4. Incubate at **56°C for 20 min** (prepare spin column for step 7 to save time).
5. Briefly **centrifuge** the 1.5 ml microcentrifuge tube to remove drops from the inside of the lid.
6. Add **200 µl ethanol (96–100%)** to the sample, and mix again by pulse vortexing for 15 s. After mixing, briefly centrifuge the 1.5 ml microcentrifuge tube to remove drops from the inside of the lid.
7. Carefully transfer the mixture from step 6 to the QIAamp Mini spin column (place in a clean 2 ml collection tube) without wetting the rim. Close the cap of spin column in order to avoid aerosol formation during centrifugation
8. **Centrifuge** at 8,000 rpm for 1 min..
Note: If the lysate has not completely passed through the column after centrifugation, centrifuge again at higher speed (10,000 rpm) until the QIAamp Mini spin column is empty.
9. Place the QIAamp Mini spin column in a new clean 2 ml collection tube and discard the old collection tube containing the filtrate.

10. Carefully open the QIAamp Mini spin column and add **500 µl Buffer AW1** without wetting the rim. Close the cap.
11. Centrifuge at 8,000 rpm for 1 min.
12. Place the QIAamp Mini spin column in a new clean 2 ml collection tube and discard the old collection tube containing the filtrate.
13. Carefully open the QIAamp Mini spin column and add **500 µl Buffer AW2** without wetting the rim. Close the cap.
14. **Centrifuge** at 13,000 rpm for 3 min.
15. Discard the filtrate from the 2 ml collection tube. Replace the QIAamp Mini spin column in the 2 ml collection tube and **centrifuge** at full speed for 3 min. This step helps to eliminate the chance of possible Buffer AW2 carryover.
16. Place the QIAamp Mini spin column in a clean 1.5 ml microcentrifuge tube (not provided), and discard the 2 ml collection tube containing the filtrate.
17. Carefully open the QIAamp Mini spin column and add **200 µl Buffer AE**. Incubate at room temperature (15–25°C) for **5 min**, and then centrifuge at 10,000 rpm for 1 min.
18. Storage DNA at 4°C for short-term storage (DNA will be use for PCR in the following days). For long-term storage of DNA, store DNA at –20°C or – 80°C. Avoid freezing / thawing samples.

KARMA Project - K13 PCR assay

1. Purpose

This procedure is designed to genotype point mutations on chromosome 13 (PF3D7_1343700) in Kelch protein propeller domain of Plasmodium falciparum. Presence of mutations in this gene was demonstrated to strongly correlate with artemisinin resistance (Ariey et al, 2014).

2. Scope

This procedure is intended for use in molecular studies of DNA extracted from dried blood spots or whole blood samples for genotyping of P. falciparum infections. It describes the genotyping procedure for SNPs (Single Nucleotide Polymorphism) detection in Kelch protein propeller domain of Plasmodium falciparum (PF3D7_1343700).

Full gene sequences are given in Appendix A and SNPs already observed are given in Appendix B. This procedure is applicable for well-equipped laboratories with staff familiar with PCR and sequencing.

3. Hygiene and security

- Always wear gloves and lab coat when handling samples.
- Wear a dedicated lab coat when working in the electrophoresis room.
- Wear Nitrile gloves when working with 10X TBE, Ethidium Bromide, or when working with a 1X TBE solution that contains Ethidium Bromide.

Ethidium Bromide is a **mutagen** and should be handled with extreme caution.

4. Materials and Equipment

4.1. Materials

- General
 - Micropipets and tips (10 μ L, 200 μ L and 1000 μ L)
 - 1.5 mL centrifuge tubes
 - PCR tubes with caps
 - Disposable gloves
 - Fine tip marker pens
 - Nuclease-free water
- PCR
 - 5x HOT FIREPol Blend Master mix with 12.5 mM MgCl₂, (Solis Biodyne #04-27-00125)
 - Primers for PCR and nested PCR (see Table 1)
 - IPC_K13 DNA Controls
- Agarose gel electrophoresis
 - Loading dye
 - Ethidium bromide (10 mg/mL)
 - Agarose
 - 1X TBE (Tris/Borate/EDTA) buffer
 - 50 bp or 100 bp or 200 bp size standard with xylene cyanol dye added or ready-to-use MW marker
 - Parafilm

Table 1. Primary and secondary forward (F) and reverse (R) PCR primers

Primer name	PCR	Sequence (5' – 3')
K13_PCR_F	PCR	CGGAGTGACCAAATCTGGGA
K13_PCR_R		GGGAATCTGGTGGTAACAGC
K13_N1_F	Nested 1	GCCAAGCTGCCATTCATTTG
K13_N1_R		GCCTTGTTGAAAGAAGCAGA

4.2. Equipment

- Thermocycler
- Gel electrophoresis apparatus including chamber and power pack
- Microwave to melt agarose
- Vortex, mini-centrifuge

– P1000, P200, P20, P10 pipettman

5. Procedure

5.1. PCR

1. Prepare Primary PCR Master Mixes in a 1.5 mL centrifuge tube according to the volumes calculated using Table 2. Include enough reactions for DNA controls (section 6) and negative (no template) controls, as shown in section 6.

Table 2. Master Mix calculation for Primary and Secondary PCR for PF3D7_1343700

Reagent	Stock Conc.	Final Conc.	Vol. X 1 sample	Vol. X N samples
1.	Nuclease-free water		13.75 µl	
2.	Primer - K13_PCR_F	10 µM	0.625 µl	
3.	Primer - K13_PCR_R	10 µM	0.625 µl	
4.	5x HOT FirePol Master Mix	5X	5 µl	
	Total (without DNA)		20 µl	

2. Label PCR 96-well plate and add 20 µl Primary Master Mix to each well.

3. Add 5 µl of template DNA to each well. Seal the plate and run PCR in thermocycler according to the conditions listed in Table 3.

Table 3. PCR thermocycling conditions for Primary PCR for PF3D7_1343700

Step no.	Cycle	Temperature (°C)	Time (min)	No. of cycles
1.	Initial Denaturation	95	15:00	1
2.	Denaturation	95	0:30	30
3.	Annealing	58	2:00	
4.	Extension	72	2:00	
5.	Final extension	72	10:00	1

5.2. Nested N1 PCR

1. Prepare nested N1 PCR Master Mixes in a 1.5 mL centrifuge tube according to the volumes calculated using Table 4.

Table 4. Master Mix calculation for Secondary N1 PCR for PF3D7_1343700

	Reagent	Stock Conc.	Final Conc.	Vol. X 1 sample	Vol. X N samples
1.	Nuclease-free water			32.5 μ l	
2.	Primer - K13_N1_F	10 μ M	0.25 μ M	1.25 μ l	
3.	Primer - K13_N1_R	10 μ M	0.25 μ M	1.25 μ l	
4.	5x HOT FirePol Master Mix	5X	1X	10 μ l	
	Total			45 μl	

2. Label PCR 96-well plate and add 45 μ l Secondary Master Mix to each well.
3. Add 5 μ l of Primary PCR product to each well. Seal the plate and run PCR in thermocycler according to the conditions listed in Table 5.

Table 5. PCR thermocycling conditions for Secondary N1 PCR for PF3D7_1343700

Step no.	Cycle	Temperature ($^{\circ}$ C)	Time (min)	No. of cycles
1.	Initial Denaturation	95	15:00	1
2.	Denaturation	95	0:30	40
3.	Annealing	60	1:00	
4.	Extension	72	1:00	
5.	Final extension	72	10:00	1

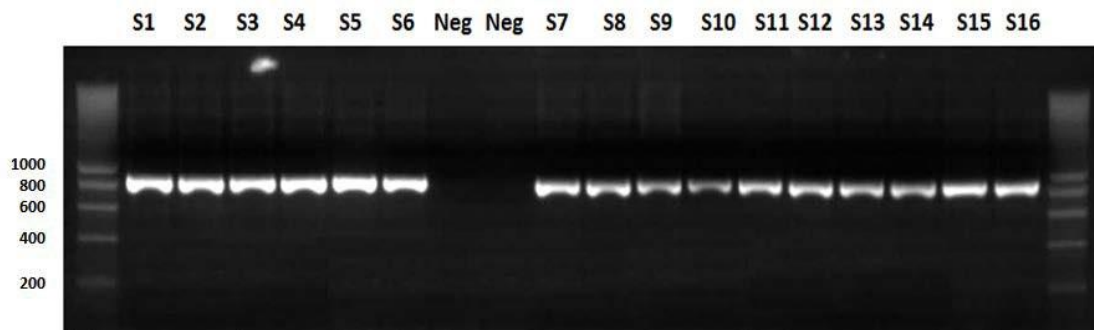
4. Run an agarose gel of Secondary N1 PCR product to ensure amplification has been successful (See Section 5.3).

NOTE: PCR products may be stored at 4 $^{\circ}$ C for up to 1 week or at – 20 $^{\circ}$ C or -80 $^{\circ}$ C for long-term storage.

5.3 Agarose gel electrophoresis

1. Make a 2% agarose gel:
 - Dissolve 2 grams of agarose and 100 mL of 1X TBE in the microwave.
 - Cool, then add 4 μ L Ethidium bromide and gently swirl to mix.
 - Pour into assembled gel tray with comb(s) and leave at room temperature for 30 minutes to set.
2. Load the gel:
 - Place the gel in gel apparatus and fill to line with 1X TBE.
 - Place 2 μ L dots of xylene cyanol per sample on Parafilm.
 - Carefully pipet 10 μ L secondary N1 PCR product to each dot of dye.
 - Add 4-5 μ L of size standard.
3. Run gel at 100-150 volts for 60 minutes and view using a UV trans-illuminator.

Figure 1. PCR products for Secondary N1 PCR for PF3D7_1343700. S1: 3D7, S2-S16: tested samples, Neg: PCR negative controls (Image source: Didier Ménard, Institut Pasteur du Cambodge).



Expected size: 849 bp

5.4. Sequencing

- Send 20-40 µl of N1 PCR products for sequencing in 96-wells plate using a sealed box to:

Malaria Molecular Epidemiology Unit
Institut Pasteur in Cambodia
5 Boulevard Monivong - PO Box 983
Phnom Penh - Cambodia
Tel +855 23 426 009 poste 219
Cell-phone: +855 17 666 442
Fax +855 23 725 606

6. Quality Controls

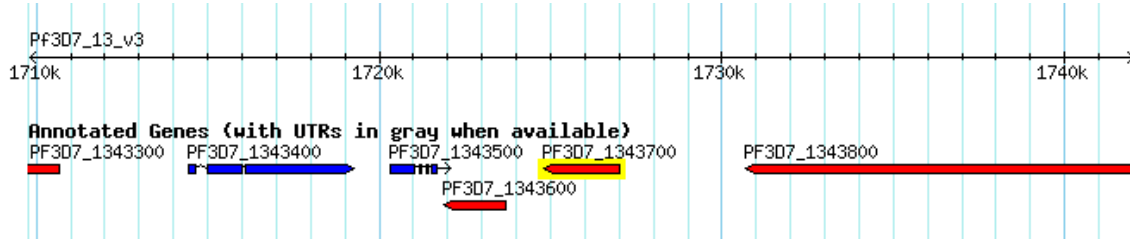
Six *P. falciparum* strains with a known K13 allele were cultured at Institut Pasteur du Cambodge and spotted on filter paper to be used as quality controls for the K13 molecular assays: K13_1, K13_2, K13_3, K13_4, K13_5, K13_6.

The six K13 quality controls have to be processed at the same time as studied samples, from the extraction step (on set of 6 QC per batch of sample analysed). At least one negative control (no template control) has to be added per PCR run.

Results will be considered valid only if K13 allele from each strain match with expected results. If results are not valid, all samples have to be repeated from the DNA extraction step.

8. Appendix A. 3D7 sequences of PF3D7_1343700 Kelch protein propeller domain

P. falciparum 3D7 protein coding gene on Pf3D7_13_v3 from 1,724,817 to 1,726,997 (Chromosome: 13)



2181 bp sequences flanking candidate marker SNPs from 3D7 complete genome are given. Positions of primary primers (yellow) and secondary primer (in green) are shown.

>gi|124513603|ref|XM_001350122.1| Plasmodium falciparum 3D7 kelch protein, putative (PF13_0238) mRNA, complete cds

```

ATGGAAGGAGAAAAAGTAAAAACAAAAGCAAATAGTATCTCGAATTTTTCTATGACGTATGATAGGGAAT
CTGGTGGTAACAGCAATAGTGATGATAAAAAGCGGAAGTAGTAGCGAGAATGATTCTAATTCATTTATGAA
TCTAACTAGTGATAAAAATGAGAAAACGGAAAAATAATAGTTTCCTTTTAAATAATAGTAGTTATGGAAAT
GTTAAAGATAGCCTATTAGAATCCATTGATATGAGTGTATTAGATTCGAACTTTGATAGTAAAAAAGATT
TTTTACCAAGTAATTTATCAAGAACATTTAATAATATGTCTAAAGATAATATAGGAAATAAATATTTAAA
TAAATTGTTAAATAAAAAAAGATACTATTACAAATGAAAAATAAATAATTAATCATAATAATAATAAT
AATAATCTGACAGCAAATAATAACTAATAATCTTATTAATAATAATATGAATTCATCAATTATGA
ATACCAACAAAAAAGAGAATTTTTTAGATGCAGCAAATCTTATAAATGATGATTCTGGATTAAACAATTT
AAAAAATTTTCAACTGTAAATAATGTAATGATACTTATGAAAAGAAAATTATTGAAACGGAATTAAGT
GATGCTAGTGATTTTGAAAATATGGTAGGTGATTTAAGAATTACATTTATTAATTGGTTAAAAAAGACAC
AAATGAATTTTATTCGAGAAAAAGATAAATTTATTTAAAGATAAGAAAGAACTAGAAATGGAAAGAGTACG
ATTGTACAAAGAATTAGAAAACCGTAAAAATATTGAAGAACAGAAATTACATGATGAAAGAAAGAAATTA
GATATTGATATATCTAATGGTTATAAACAATAAAAAAAGAAAAAGAAGAACATAGGAAACGATTTGATG
AAGAAAGATTAAGATTTTACAAGAAATCGATAAAATTAATTAGTATTATTTAGAAAAAGAAAAATA
TTATCAAGAATATAAAAATTTTGAGAATGATAAAAAAATTTGTTGATGCAAATATTGCTACTGAACT
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CATTTATAGAGAAATTAATAAGTGAAGACATCATGTAACCAGAGATAAACAAGGAAGAATATTCTTAGA
TAGGGATAGTGAGTTATTTAGAATTATACTTAACTTCTTAAGAAATCCGTTAACTATACCCATACCAAAA
GATTTAAGTGAAAGTGAAGCCTTGTTGAAAGAAGCAGAATTTTATGGTATTAAATTTTTACCATTCCCAT
TAGTATTTTGTATAGGTGGATTTGATGGTGTAGAATATTTAAATTCGATGGAATTATTAGATATTAGTCA
ACAATGCTGGCGTATGTGTACACCTATGTCTACCAAAAAAGCTTATTTTGGAAAGTGTGATTGAATAAT
TTCTTATACGTTTTTGGTGGTAATAACTATGATTATAAGGCTTTATTTGAAACTGAGGTGTATGATCGTT
TAAGAGATGTATGGTATGTTTCAAGTAATTTAAATATACCTAGAAGAAATAATTGTGGTGTACGTCAAA
TGGTAGAATTTATTGTATTGGGGGATATGATGGCTCTTCTATTATACCGAATGTAGAAGCATATGATCAT
CGTATGAAAGCATGGGTAGAGGTGGCACCTTTGAATACCCCTAGATCATCAGCTATGTGTGTTGCTTTTG
ATAATAAAATTTATGTCATTGGTGAACATAATGGTGAGAGATTAATTTCTATTGAAGTATATGAAGAAAA
AATGAATAAATGGGAACAATTTCCATATGCCTTATTAGAAGCTAGAAGTTCAGGAGCAGCTTTTAATTAC
CTTAATCAAATATATGTTGTTGGAGGTATTGATAATGAACATAACATATTAGATTCCGTTGAACAATATC
AACCATTTAATAAAAAGATGGCAATTTCTAAATGGTGTACCAGAGAAAAAATGAATTTTGGAGCTGCCAC
ATTGTCAGATTCTTATATAATTACAGGAGGAGAAAAATGGCGAAGTCTAAATTCATGTCATTTCTTTTCA
CCAGATACAATGAATGGCAGCTTGGCCCATCTTTATTAGTTCCAGATTTGGTCACTCCGTTTTAATAG
CAAATATATA
    
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Table S2. Sequence of primers and PCR conditions used to amplify PF3D7_1337500 (1509589...1519593, K13_151) and PF3D7_1339700 (1590510...1596320, K13_159) genes in *Plasmodium falciparum* isolates harboring a K13 mutant allele, KARMA study 2014.

Target gene	PCR	Primer name	Sequence (5'-3')	Hybridization T°	Size of PCR product
PF3D7_1337500 (K13_151)	Primary	PfK13_151_PCR_F	TTTTCGTTTGTCTACTCATATCAT	54°C	994 bp
		PfK13_151_PCR_R	TAATCTCTCAAATGAATCAAAAA		
	Secondary	PfK13_151_Nested_F	ACCATAAGGAAATTGGTTCATCA	60°C	866 bp
		PfK13_151_Nested_R	TCGAGAGCATAAATGAGCAATC		
PF3D7_1339700 (K13_159)	Primary	PfK13_159_PCR_F	TTGTCATCTTGATCATTTGTTG	57°C	1287 bp
		PfK13_159_PCR_R	AACTCTTTGTGAGGAAAAGAAA		
	Secondary	PfK13_159_Nested_F	CATATTTTCATTTTCAATGTGATGA	60°C	866 bp
		PfK13_159_Nested_R	GAATCTTACGAGAGACGACTGGA		

Primary PCR amplifications were performed in 25 µL reaction mixture containing 0.5 µL DNA, 0.25 µM each primer, 200 µM each dNTP, 2.5 mM MgCl₂ and 1.25 U HotFirePol DNA Polymerase® (Solis Biodyne®, Tartu, Estonia). Secondary, internal amplifications were done in 55 µL reaction buffer with 5 µL of PCR products, 0.5 µM each primer, 200 µM each dNTP, 2.5 mM MgCl₂ and 2.5 U HotFirePol DNA polymerase. PCR amplifications were performed under the following conditions: for PF3D7_1337500 (K13_151) primary amplification, heating at 95°C for 15 min, followed by 30 cycles of heating at 95°C for 30 s, 54°C for 60 s, 72°C for 60 s and a final extension at 72°C for 10 min; secondary reaction: heating at 95°C for 15 min, followed by 40 cycles of heating at 95°C for 20 s, 60°C for 60 s, 72°C for 60 s and a final extension at 72°C for 10 min and for PF3D7_1339700 (K13_159) primary amplification, heating at 95°C for 15 min, followed by 30 cycles of heating at 95°C for 30 s, 57°C for 90 s, 72°C for 120 s and a final extension at 72°C for 10 min; secondary reaction: heating at 95°C for 15 min, followed by 40 cycles of heating at 95°C for 30 s, 60°C for 90 s, 72°C for 120 s and a final extension at 72°C for 10 min.

Table S3. Number of samples collected from residents and travelers, day3 positivity rates and proportion of sequences with a non-synonymous mutation of K13-propeller domain by continent, region and country, KARMA study 2014.

Continent	Region	Country	No. collection sites (for residents only)	No. samples		Travelers	Total	No. interpretable sequences	Proportion of sequences with non-synonymous propeller mutations (95%CI) ¹	No. samples with D3 clinical phenotype	D3 positivity rate ² (95%CI) following artesunate monotherapy or ACT treatment ³	Proportion of D3 positive case with K13 mutations (95%CI) ⁴
				Residents symptomatic	Residents asymptomatic							
Africa	Central Africa	Cameroon	2	702	140	69	911	901	1.2% (0.6-2.2%)	50	0% (0-7.4%)	NA
		Central African Republic	4	400		69	469	423	4.5% (2.7-7.0%)	72	0% (0-5.1%)	NA
		Chad	0	0		33	33	33	3.0% (0.1-16.9%)	5	0% (0-74%)	NA
		Congo	0	0		72	72	71	0% (0-5.2%)	11	0% (0-33.5%)	NA
		Democratic Republic of Congo	5	1262		26	1288	1230	1.1% (1.1-1.2%)	3	0% (0-100%)	NA
		Equatorial Guinea	0	0		7	7	7	0% (0-52.7%)	0	NA	NA
		Gabon	4	138	314	44	496	407	1.0% (0.3-2.5%)	2	0% (0-100%)	NA
	East Africa	Burundi	0	0		1	1	1	0% (0-100%)	0	NA	NA
		Ethiopia	1	146		0	146	126	0% (0-2.9%)	0	NA	NA
		Kenya	1	191		7	198	184	3.3% (1.2-7.1%)	0	NA	NA
		Rwanda	4	293		0	293	292	1.4% (0.4-3.5%)	287	0.3% (0-1.9%)	0%
		Somalia	2	186		0	186	186	0% (0-2.0%)	186	0% (0-2.0%)	NA
		Sudan	0	0		5	5	5	0% (0-74%)	1	NA	NA
		South Sudan	0	0		1	1	1	0% (0-100%)	0	NA	NA
		Tanzania	8	232		4	236	236	0% (0-1.5%)	0	NA	NA
	Uganda	1	88	191	15	294	283	1.1% (0.2-3.1%)	1	0% (0-100%)	NA	
	Southern Africa	Angola	2	31		3	34	34	0% (0-10.8%)	0	NA	NA
		Malawi	0	0		13	13	13	0% (0-28.4%)	0	NA	NA
		Mozambique	0	0		5	5	5	0% (0-74%)	0	NA	NA
		South Africa	0	0		2	2	2	0% (0-100%)	0	NA	NA
		Zambia	1	298		6	304	283	4.6% (2.4-7.8%)	277	0% (0-1.3%)	NA
		Zimbabwe	0	0		7	7	7	0% (0-53%)	0	NA	NA
	West Africa	Benin	1	232		33	265	234	0.9% (0.1-3.1%)	11	0% (0-33.5%)	NA
Burkina Faso		5	551		61	612	589	0.3% (0.1-1.2%)	4	0% (0-92%)	NA	
Gambia		0	0		12	12	12	8.3% (0.2-46%)	0	NA	NA	
Ghana		0	0		37	37	37	0% (0-10%)	1	0% (0-100%)	NA	
Guinea		0	0		87	87	86	3.5% (0.7-10.1%)	11	0% (0-33.5%)	NA	

		Guinea Bissau	0	0		3	3	3	0% (0-100%)	1	0% (0-100%)	NA
		Ivory Coast	7	1110		47	1157	1083	0.9% (0.4-1.7%)	71	0% (0-5.2%)	NA
		Liberia	0	0		1	1	1	0% (0-100%)	0	NA	NA
		Mali	2	458		9	467	465	0.4% (0.1-1.5%)	40	0% (0-9.2%)	NA
		Mauritania	0	0		1	1	1	0% (0-100%)	0	NA	NA
		Niger	2	766		10	776	521	1.3% (0.5-2.8%)	2	0% (0-100%)	NA
		Nigeria	1	161	41	97	299	273	1.1% (0.2-3.2%)	1	0% (0-100%)	NA
		Senegal	2	246		67	313	246	0% (0-1.5%)	7	0% (0-52.3%)	NA
		Sierra Leone	0	0		37	37	37	0% (0-10%)	1	0% (0-100%)	NA
		Togo	3	476		32	508	508	1.8% (0.8-3.4%)	485	1.6% (0.7-3.2%)	0%
	Indian Ocean	Comoros	4	297	39	18	354	352	3.7% (2.0-6.3%)	2	0% (0-100%)	NA
		Madagascar	23	59	216	2	277	256	0.4% (0.1-2.1%)	1	0% (0-100%)	NA
	Central Asia	Afghanistan	1	62		0	62	62	1.6% (0.1-9.0%)	0	NA	NA
		Iran	4	78		0	78	76	2.6% (0.1-9.5%)	0	NA	NA
	East Asia	China	4	216		0	216	215	25.6% (19.3-33.3%)	148	10.1% (5.7-16.7%)	93% (51-100%)
		Myanmar	4	347		0	347	343	46.9% (46.2-47.7%)	189	15.3% (10.3-22.0%)	72% (45-100%)
	South Asia	Bangladesh	9	333		0	333	318	0.9% (0.2-2.7%)	61	0% (0-6.1%)	NA
		Nepal	4	24		0	24	22	0% (0-16.8%)	18	0% (0-20.5%)	NA
	Southeast Asia	Cambodia	12	748	134	0	882	882	66.4% (61.2-72.0%)	171	22.2% (15.7-30.5%)	90% (62-100%)
		Indonesia	1	110		0	110	106	0.9% (0.1-5.2%)	0	NA	NA
		Lao PDR	3	82	40	0	122	120	20.0% (13.0-30.0%)	48	0% (0-7.7%)	NA
		Philippines	2	120		0	120	99	0% (0-3.7%)	66	0% (0-5.6%)	NA
		Thailand	4	150	57	0	207	205	26.3% (19.8-34.4%)	0	NA	NA
		Vietnam	4	177		0	177	175	39.4% (31.0-50.0%)	175	16.0% (10.6-23.1%)	79% (49-100%)
Oceania	Oceania	Papua New Guinea	12	13	42	1	56	43	0% (0-8.6%)	1	0% (0-100%)	NA
		Solomon Islands	2	44		0	44	43	2.3% (0.1-12.9%)	38	5.3% (0.1-19.0%)	0%
		Brazil	1	219	18	0	237	237	0.4% (0.1-2.3%)	2	0% (0-100%)	NA
		Colombia	3	535		0	535	523	0% (0-0.7%)	0	NA	NA
South America	South America	Ecuador	0	0		1	1	1	0% (0-100%)	0	NA	NA
		French Guiana	7	198		5	203	183	0% (0-2.0%)	0	NA	NA
		Peru	1	75		0	75	69	0% (0-5.3%)	0	NA	NA
		Venezuela	0	0		1	1	1	0% (0-100%)	0	NA	NA
			163	11854	1232	951	14037			2450		

NA: Not applicable; ¹ 95% CI (95% confidence interval) were calculated with the Wilson Test; ² D3 (Day 3) positivity rate is the proportion of patients who are parasitemic on day 3 following 7-day artesunate monotherapy or standard 3-day ACT treatment. According to the World Health Organization (<http://www.who.int/malaria/publications/atoz/arupdate042012.pdf>), this parameter is currently the best available indicator used in routine monitoring to measure *P. falciparum* sensitivity to artemisinins; ³ ACT treatments administered were artemether/lumefantrine, artesunate/amodiaquine, artesunate/sulfadoxine-pyrimethamine or dihydroartemisinin/piperaquine; ⁴ Proportion of D3 positive cases with a K13 mutation.

K13 genotypes of the 121 D3 positive cases were as follows: Rwanda: wild-type (N=1); Togo: wild-type (N=8); China: wild-type (N=1), C469Y (N=1), F446I (N=7), N458Y (N=1), N537D (N=1), P553L (N=2), P574L (N=2); Myanmar: wild-type (N=8), F446I (N=18), P574L (N=2), R539T (N=1); Cambodia: wild-type (N=4), C580Y (N=33), R539T (N=1); Vietnam: wild-type (N=6), C580Y (N=10), I543T (N=3), N458Y (N=1), P553L (N=8); Solomon Islands: wild-type (N=2).

Table S4. List of the samples tested for sequencing of the K13 gene propeller domain including detailed information on the partner institution, samples collected (number, location, individual clinical status, parasitemia, age and gender) and KARMA option chosen, KARMA study 2014.

Continent	Region	Country	Partner Institution	No. samples	Location of sample collection	Year of collection	Traveler or resident	Clinical status	Age (range, year)	Male (%)	Completeness of demographic data for the country	Parasitemia (P/ μ L, range)	Partner's option*
AFRICA	Central Africa	Cameroon	Parasitologie et mycologie, Centre Hospitalier Universitaire, Toulouse, France	66	Yaounde	2012	Resident	Symptomatic	0.7-17	56%		NA	2
AFRICA	Central Africa	Cameroon	Parasitologie et mycologie, Centre Hospitalier Universitaire, Toulouse, France	41	Yaounde	2012	Resident	Asymptomatic	NA	NA		NA	2
AFRICA	Central Africa	Cameroon	Parasitologie et mycologie, Centre Hospitalier Universitaire, Toulouse, France	311	Yaounde	2013	Resident	Symptomatic	0.4-15	47%		NA	2
AFRICA	Central Africa	Cameroon	Parasitologie et mycologie, Centre Hospitalier Universitaire, Toulouse, France	100	Yaounde	2013	Resident	Asymptomatic	6-12	NA		NA	2
AFRICA	Central Africa	Cameroon	Parasitologie et mycologie, Centre Hospitalier Universitaire, Toulouse, France	75	Douala	2013	Resident	Symptomatic	NA	NA	50%	NA	2
AFRICA	Central Africa	Cameroon	Parasitologie et mycologie, Hôpital Bichat Claude-Bernard, Paris, France	160	NA	2013	Resident	Symptomatic	1-76	NA		NA	2
AFRICA	Central Africa	Cameroon	Parasitologie et mycologie, Hôpital Bichat Claude-Bernard, Paris, France	89	NA	2014	Resident	Symptomatic	5-69	59%		NA	2
AFRICA	Central Africa	Cameroon	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	26	NA	2013	Traveler	Symptomatic	NA	NA		50-500,000	2
AFRICA	Central Africa	Cameroon	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France/Malaria Reference Laboratory, London, UK	43	NA	2014	Traveler	Symptomatic	NA	NA		50-300,000	2
AFRICA	Central Africa	Central African Republic	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	39	NA	2013	Traveler	Symptomatic	3-70	NA		NA	2
AFRICA	Central Africa	Central African Republic	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	30	NA	2014	Traveler	Symptomatic	1-68	NA		NA	2
AFRICA	Central Africa	Central African Republic	Institut Pasteur de Bangui, Bangui, Central African Republic	47	Bangassou	2009	Resident	Symptomatic	NA	NA		NA	1
AFRICA	Central Africa	Central African Republic	Institut Pasteur de Bangui, Bangui, Central African Republic	78	Bangui	2009	Resident	Symptomatic	NA	NA	5%	NA	1
AFRICA	Central Africa	Central African Republic	Institut Pasteur de Bangui, Bangui, Central African Republic	131	Bangui	2011	Resident	Symptomatic	NA	NA		NA	1
AFRICA	Central Africa	Central African Republic	Institut Pasteur de Bangui, Bangui, Central African Republic	53	Bayanga	2009	Resident	Symptomatic	NA	NA		NA	1
AFRICA	Central Africa	Central African Republic	Institut Pasteur de Bangui, Bangui, Central African Republic	91	Bria/Bouar	2009	Resident	Symptomatic	NA	NA		NA	1
AFRICA	Central Africa	Chad	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	30	NA	2013	Traveler	Symptomatic	5-64	NA		NA	2
AFRICA	Central Africa	Chad	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	3	NA	2014	Traveler	Symptomatic	33-43	NA	0%	NA	2

AFRICA	Central Africa	Congo	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	38	NA	2013	Traveler	Symptomatic	2-68	NA	NA	2	
AFRICA	Central Africa	Congo	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France/Malaria Reference Laboratory, London, UK	34	NA	2014	Traveler	Symptomatic	5-62	NA	24%	NA	2/3
AFRICA	Central Africa	Democratic Republic of Congo	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	17	NA	2013	Traveler	Symptomatic	4-59	NA	NA	2	
AFRICA	Central Africa	Democratic Republic of Congo	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	9	NA	2014	Traveler	Symptomatic	20-58	62.5%	NA	2	
AFRICA	Central Africa	Democratic Republic of Congo	University of Kinshasa, Kinshasa, Democratic Republic of Congo	673	Kinshasa	2013	Resident	Symptomatic	0.3-86	49%	594-513,382	1	
AFRICA	Central Africa	Democratic Republic of Congo	University of Kinshasa, Kinshasa, Democratic Republic of Congo	251	Kinshasa	2014	Resident	Symptomatic	0.1-64	49%	40-572,394	1	
AFRICA	Central Africa	Democratic Republic of Congo	WHO, Global Malaria Programme, Geneva, Switzerland	179	Kingasani	2013	Resident	Symptomatic	NA	NA	71%	NA	3
AFRICA	Central Africa	Democratic Republic of Congo	WHO, Global Malaria Programme, Geneva, Switzerland	54	Bolenge	2013	Resident	Symptomatic	NA	NA	NA	3	
AFRICA	Central Africa	Democratic Republic of Congo	WHO, Global Malaria Programme, Geneva, Switzerland	29	Kapolowe	2013	Resident	Symptomatic	NA	NA	NA	3	
AFRICA	Central Africa	Democratic Republic of Congo	WHO, Global Malaria Programme, Geneva, Switzerland	76	Katana	2013	Resident	Symptomatic	NA	NA	NA	3	
AFRICA	Central Africa	Equatorial Guinea	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	6	NA	2013	Traveler	Symptomatic	24-60	NA	0%	NA	2
AFRICA	Central Africa	Equatorial Guinea	Malaria Reference Laboratory, London, UK	1	NA	2014	Traveler	Symptomatic	NA	NA	NA	3	
AFRICA	Central Africa	Gabon	Centre de Recherche Médicales de Lambaréné, Libreville, Gabon	266	Lambarene	2012	Resident	Asymptomatic	NA	NA	NA	1	
AFRICA	Central Africa	Gabon	Centre de Recherche Médicales de Lambaréné, Libreville, Gabon	84	Lambarene	2013	Resident	Asymptomatic	NA	NA	NA	1	
AFRICA	Central Africa	Gabon	Centre de Recherche Médicales de Lambaréné, Libreville, Gabon	10	Lambarene	2014	Resident	Asymptomatic	NA	NA	NA	1	
AFRICA	Central Africa	Gabon	Centre de Recherche Médicales de Lambaréné, Libreville, Gabon	5	Bindo	2012	Resident	Asymptomatic	NA	NA	15%	NA	1
AFRICA	Central Africa	Gabon	Centre de Recherche Médicales de Lambaréné, Libreville, Gabon	23	Makouké	2012	Resident	Asymptomatic	NA	NA	NA	1	
AFRICA	Central Africa	Gabon	Centre de Recherche Médicales de Lambaréné, Libreville, Gabon	8	Makouké	2013	Resident	Asymptomatic	NA	NA	NA	1	
AFRICA	Central Africa	Gabon	Centre International de Recherches Médicales de Franceville, Franceville, Gabon	56	NA	2013	Resident	Symptomatic	NA	NA	70-161,480	1	

AFRICA	Central Africa	Gabon	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	34	NA	2013	Traveler	Symptomatic	9-73	NA		NA	2
AFRICA	Central Africa	Gabon	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France/Malaria Reference Laboratory, London, UK	10	NA	2014	Traveler	Symptomatic	NA	NA		NA	2
AFRICA	East Africa	Burundi	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	1	NA	2013	Traveler	Symptomatic	NA	NA	0%	NA	2
AFRICA	East Africa	Ethiopia	Medical University of Vienna, Vienna, Austria	146	NA	2012	Resident	NA	NA	NA	0%	NA	2
AFRICA	East Africa	Kenya	Epicentre Research Center, Mbarara, Uganda	46	Ahero	2011	Resident	Symptomatic	NA	NA		NA	1
AFRICA	East Africa	Kenya	Epicentre Research Center, Mbarara, Uganda	124	Ahero	2012	Resident	Symptomatic	NA	NA	0%	NA	1
AFRICA	East Africa	Kenya	Epicentre Research Center, Mbarara, Uganda	21	Ahero	2013	Resident	Symptomatic	NA	NA		NA	1
AFRICA	East Africa	Kenya	Malaria Reference Laboratory, London, UK	7	NA	2014	Traveler	Symptomatic	NA	NA		NA	3
AFRICA	East Africa	Rwanda	Rwanda BioMedical Center, Kigali, Rwanda	20	Bugarama	2012	Resident	Symptomatic	1-5	50%		3,800-92,600	2
AFRICA	East Africa	Rwanda	Rwanda BioMedical Center, Kigali, Rwanda	48	Bugarama	2013	Resident	Symptomatic	1-5	54.1%		1,520-88,600	2
AFRICA	East Africa	Rwanda	Rwanda BioMedical Center, Kigali, Rwanda	26	Kibilizi	2012	Resident	Symptomatic	15-58	61.5%		1,200-98,960	2
AFRICA	East Africa	Rwanda	Rwanda BioMedical Center, Kigali, Rwanda	52	Kibilizi	2013	Resident	Symptomatic	15-59	53.8%		1,240-91,600	2
AFRICA	East Africa	Rwanda	Rwanda BioMedical Center, Kigali, Rwanda	12	Kibilizi	2014	Resident	Symptomatic	15-56	50%	100%	1,160-91,800	2
AFRICA	East Africa	Rwanda	Rwanda BioMedical Center, Kigali, Rwanda	22	Nyarurema	2012	Resident	Symptomatic	1-5	59%		2,720-70,240	2
AFRICA	East Africa	Rwanda	Rwanda BioMedical Center, Kigali, Rwanda	38	Nyarurema	2013	Resident	Symptomatic	1-5	52.6%		1,200-688,800	2
AFRICA	East Africa	Rwanda	Rwanda BioMedical Center, Kigali, Rwanda	25	Rukara	2012	Resident	Symptomatic	11-59	68%		2,280-58,160	2
AFRICA	East Africa	Rwanda	Rwanda BioMedical Center, Kigali, Rwanda	50	Rukara	2013	Resident	Symptomatic	10-55	54%		1,080-94,160	2
AFRICA	East Africa	Somalia	WHO, Global Malaria Programme, Geneva, Switzerland	94	Janale	2013	Resident	Symptomatic	1-58	51%	100%	370-45,935	3
AFRICA	East Africa	Somalia	WHO, Global Malaria Programme, Geneva, Switzerland	92	Jowhar	2013	Resident	Symptomatic	2-36	62%		1,171-162,000	3
AFRICA	East Africa	Sudan	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	2	NA	2013	Traveler	Symptomatic	42-47	NA	0%	NA	2
AFRICA	East Africa	Sudan	Malaria Reference Laboratory, London, UK	3	NA	2014	Traveler	Symptomatic	NA	NA		NA	3
AFRICA	East Africa	South Sudan	Malaria Reference Laboratory, London, UK	1	NA	2014	Traveler	Symptomatic	NA	NA	0%	NA	3
AFRICA	East Africa	Tanzania	Malaria Reference Laboratory, London, UK	4	NA	2014	Traveler	Symptomatic	NA	NA		NA	3
AFRICA	East Africa	Tanzania	WHO, Global Malaria Programme, Geneva, Switzerland	232	NA	2014	Resident	Symptomatic	NA	NA	0%	NA	3
AFRICA	East Africa	Uganda	Epicentre Research Center, Mbarara, Uganda	201	Mbarara	2010	Resident	Asymptomatic	NA	NA		1,024-247,078	2
AFRICA	East Africa	Uganda	Epicentre Research Center, Mbarara, Uganda	7	Mbarara	2011	Resident	Symptomatic	NA	43%		95-581,556	2

AFRICA	East Africa	Uganda	Epicentre Research Center, Mbarara, Uganda	35	Mbarara	2012	Resident	Symptomatic	NA	57.1%	27%	56-472,431	2
AFRICA	East Africa	Uganda	Epicentre Research Center, Mbarara, Uganda	36	Mbarara	2013	Resident	Symptomatic	NA	57.1%		39-203,005	2
AFRICA	East Africa	Uganda	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	3	NA	2013	Traveler	Symptomatic	36-39	NA		NA	2
AFRICA	East Africa	Uganda	Malaria Reference Laboratory, London, UK	12	NA	2014	Traveler	Symptomatic	NA	NA		NA	3
AFRICA	Indian Ocean	Comoros	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	17	NA	2013	Traveler	Symptomatic	18-49	NA		NA	2
AFRICA	Indian Ocean	Comoros	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	1	NA	2014	Traveler	Symptomatic	NA	NA		NA	2
AFRICA	Indian Ocean	Comoros	Institut Pasteur de Madagascar, Antananarivo, Madagascar	42	Anjouan	2011	Resident	Symptomatic	0.8-10	46%		600-199,750	2
AFRICA	Indian Ocean	Comoros	Institut Pasteur de Madagascar, Antananarivo, Madagascar	64	Grande Comore	2011	Resident	Symptomatic	0.5-5	51%		549-192,000	2
AFRICA	Indian Ocean	Comoros	Institut Pasteur de Madagascar, Antananarivo, Madagascar	14	Grande Comore	2011	Resident	Asymptomatic	0.7-6	43%	92%	1,035-177,777	2
AFRICA	Indian Ocean	Comoros	Institut Pasteur de Madagascar, Antananarivo, Madagascar	156	Grande Comore	2013	Resident	Symptomatic	1-11	48%		468-200,000	2
AFRICA	Indian Ocean	Comoros	Institut Pasteur de Madagascar, Antananarivo, Madagascar	13	Grande Comore	2013	Resident	Asymptomatic	1-9	64%		514-131,076	2
AFRICA	Indian Ocean	Comoros	Institut Pasteur de Madagascar, Antananarivo, Madagascar	8	Moheli	2011	Resident	Symptomatic	2-9	0%		517-1,442	2
AFRICA	Indian Ocean	Comoros	Institut Pasteur de Madagascar, Antananarivo, Madagascar	12	Moheli	2011	Resident	Asymptomatic	1-12	58%		557-2,297	2
AFRICA	Indian Ocean	Comoros	Institut de Recherche Biomédicale des Armées, Marseille, France	27	Mayotte	2013	Resident	Symptomatic	0.5-70	59%		500-500,000	3
AFRICA	Indian Ocean	Madagascar	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	2	NA	2013	Traveler	Symptomatic	61-62	NA		NA	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	9	Ambato Boeny	2012	Resident	Symptomatic	3-13	44%		556-359,280	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	26	Ambato Boeny	2012	Resident	Asymptomatic	6-43	69.2%		0-2,082	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	3	Ambovombe	2012	Resident	Symptomatic	5-15	33%		48-1,067	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	2	Ambovombe	2012	Resident	Asymptomatic	11-14	50%	99%	NA	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	1	Ihosy	2012	Resident	Asymptomatic	5	100%		40	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	1	Antsirabe	2012	Resident	Asymptomatic	17	100%		40-643	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	1	Antsiranana	2012	Resident	Symptomatic	13	100%		2,088	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	4	Antsiranana	2012	Resident	Asymptomatic	11-19	50%		NA	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	3	Antsohihy	2012	Resident	Symptomatic	6-7	66%		720-17,820	2

AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	45	Antsohihy	2012	Resident	Asymptomatic	1-75	51.1%	0-6,596	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	4	Belo Tsiribihina	2012	Resident	Symptomatic	4-22	25%	3,675-8912	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	5	Belo Tsiribihina	2012	Resident	Asymptomatic	7-12	60%	NA	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	2	Ejeda	2012	Resident	Asymptomatic	11-50	0%	NA	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	1	Farafangana	2012	Resident	Symptomatic	4	100%	0	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	9	Farafangana	2012	Resident	Asymptomatic	1-38	66.6%	16-1,980	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	2	Fianarantsoa	2012	Resident	Symptomatic	11-31	50%	12,251	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	1	Ihosy	2012	Resident	Asymptomatic	5	100%	40	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	3	Maevatanana	2012	Resident	Symptomatic	7-14	66%	0-24	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	10	Maevatanana	2012	Resident	Asymptomatic	2-18	40%	0-22,272	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	5	Mahajanga	2012	Resident	Asymptomatic	3-46	60%	16-151	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	28	Maintirano	2012	Resident	Asymptomatic	1-23	61%	0-19,440	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	4	Mananjary	2012	Resident	Asymptomatic	3-14	75%	469-2,010	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	1	Mandritsara	2012	Resident	Asymptomatic	8	100%	39	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	2	Maroantsetra	2012	Resident	Asymptomatic	15-16	50%	NA	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	1	Miandrivazo	2012	Resident	Symptomatic	11	100%	4,883	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	3	Miandrivazo	2012	Resident	Asymptomatic	6-44	66%	NA	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	1	Moramanga	2012	Resident	Asymptomatic	12	0%	NA	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	2	Moramanga	2013	Resident	Asymptomatic	6-15	100%	174	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	2	Morombe	2012	Resident	Symptomatic	5-10	100%	1,530-26,271	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	13	Morombe	2012	Resident	Asymptomatic	2-35	61%	0-667,080	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	4	Morondava	2012	Resident	Symptomatic	5-10	75%	163-4,067	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	7	Morondava	2012	Resident	Asymptomatic	6-18	28.5%	95-112	2

AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	2	Nosy-be	2012	Resident	Asymptomatic	2-5	100%		23-158	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	5	Sainte Marie	2012	Resident	Asymptomatic	3-32	60%		NA	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	4	Taolagnaro	2012	Resident	Symptomatic	5-20	50%		8-2,520	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	33	Taolagnaro	2012	Resident	Asymptomatic	3-40	44.1%		0-3,492	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	3	Toamasina	2012	Resident	Symptomatic	46447	66%		27-152	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	22	Toamasina	2012	Resident	Asymptomatic	3-29	54.5%		0-2,394	2
AFRICA	Indian Ocean	Madagascar	Institut Pasteur de Madagascar, Antananarivo, Madagascar	1	Tsiroanomandidy	2012	Resident	Asymptomatic	8	100%		NA	2
AFRICA	Southern Africa	Angola	Fiocruz Fundação Oswaldo Cruz, Rio de Janeiro, Brazil	2	Lubango	2011	Resident	Symptomatic	19-28	0%		1,000-5,000	1
AFRICA	Southern Africa	Angola	Fiocruz Fundação Oswaldo Cruz, Rio de Janeiro, Brazil	29	Luanda	2012	Resident	Symptomatic	12-67	58%	91%	500-5,000	1
AFRICA	Southern Africa	Angola	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	1	NA	2014	Traveler	Symptomatic	NA	NA		50	2
AFRICA	Southern Africa	Angola	Malaria Reference Laboratory, London, UK	2	NA	2014	Traveler	Symptomatic	NA	NA		NA	3
AFRICA	Southern Africa	Malawi	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France/Malaria Reference Laboratory, London, UK	13	NA	2014	Traveler	Symptomatic	NA	NA	0%	NA	2/3
AFRICA	Southern Africa	Mozambique	Malaria Reference Laboratory, London, UK	5	NA	2014	Traveler	Symptomatic	NA	NA	0%	NA	3
AFRICA	Southern Africa	South Africa	Malaria Reference Laboratory, London, UK	2	NA	2014	Traveler	Symptomatic	NA	NA	0%	NA	3
AFRICA	Southern Africa	Zambia	Tropical Diseases Research Center, Ndola, Zambia	298	NA	2012	Resident	NA	NA	NA	0%	NA	1
AFRICA	Southern Africa	Zambia	Malaria Reference Laboratory, London, UK	6	NA	2014	Traveler	Symptomatic	NA	NA		NA	3
AFRICA	Southern Africa	Zimbabwe	Malaria Reference Laboratory, London, UK	7	NA	2014	Traveler	Symptomatic	NA	NA	0%	NA	3
AFRICA	West Africa	Benin	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	21	NA	2013	Traveler	Symptomatic	3-87	NA		NA	2
AFRICA	West Africa	Benin	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	12	NA	2014	Traveler	Symptomatic	15-69	50%	77%	NA	2
AFRICA	West Africa	Benin	Institut de Recherche pour le Développement, Cotonou, Benin	61	Cotonou	2012	Resident	Symptomatic	0.4-6	51%		300-720,000	1
AFRICA	West Africa	Benin	Institut de Recherche pour le Développement, Cotonou, Benin	171	Cotonou	2013	Resident	Symptomatic	0.8-6	59%		1280-360,000	1
AFRICA	West Africa	Burkina Faso	Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso	145	Balonghin	2012	Resident	Symptomatic	1-62	52%	90%	832-332,818	2
AFRICA	West Africa	Burkina Faso	Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso	39	Banfora	2013	Resident	Symptomatic	0,1-33	67%		NA	2

AFRICA	West Africa	Burkina Faso	Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso	103	Niangologo	2013	Resident	Symptomatic	0,6-10	52%		NA	2
AFRICA	West Africa	Burkina Faso	Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso	21	Niangologo	2012	Resident	Symptomatic	0,4-57	33%		NA	2
AFRICA	West Africa	Burkina Faso	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	50	NA	2013	Traveler	Symptomatic	8-73	NA		NA	2
AFRICA	West Africa	Burkina Faso	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	11	NA	2014	Traveler	Symptomatic	15-61	NA		NA	2
AFRICA	West Africa	Burkina Faso	Institut de Recherche Biomédicale des Armées, Marseille, France	15	NA	2014	Resident	Symptomatic	NA	100%		NA	3
AFRICA	West Africa	Burkina Faso	Institut de Recherche en Sciences de la Santé, Ouagadougou, Burkina Faso	200	Colsama	2012	Resident	Symptomatic	0.5-61	43.5%		2,039-199,250	2
AFRICA	West Africa	Burkina Faso	Institut de Recherche en Sciences de la Santé, Ouagadougou, Burkina Faso	28	Sakabi	2012	Resident	Symptomatic	1.6-20	46%		2,708-161,212	2
AFRICA	West Africa	Gambia	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	2	NA	2013	Traveler	Symptomatic	NA	NA	0%	NA	2
AFRICA	West Africa	Gambia	Malaria Reference Laboratory, London, UK	10	NA	2014	Traveler	Symptomatic	NA	NA		NA	3
AFRICA	West Africa	Ghana	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	7	NA	2013	Traveler	Symptomatic	NA	NA	0%	NA	2
AFRICA	West Africa	Ghana	Malaria Reference Laboratory, London, UK	30	NA	2014	Traveler	Symptomatic	NA	NA		NA	3
AFRICA	West Africa	Guinea	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	79	NA	2013	Traveler	Symptomatic	1-72	NA	0%	NA	2
AFRICA	West Africa	Guinea	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	8	NA	2014	Traveler	Symptomatic	NA	NA		NA	2
AFRICA	West Africa	Guinea Bissau	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	3	NA	2013	Traveler	Symptomatic	14-48	NA	0%	NA	2
AFRICA	West Africa	Ivory Coast	Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Abidjan, Ivory Coast	31	Abobodoume	2014	Resident	Symptomatic	18-57	41.9%		32-342,000	2
AFRICA	West Africa	Ivory Coast	Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Abidjan, Ivory Coast	25	Adiopodoume	2013	Resident	Symptomatic	19-62	28.0%		144-109,360	2
AFRICA	West Africa	Ivory Coast	Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Abidjan, Ivory Coast	23	Wassakara	2013	Resident	Symptomatic	18-54	34.7%		112-133,680	2
AFRICA	West Africa	Ivory Coast	Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Abidjan, Ivory Coast	67	Wassakara	2014	Resident	Symptomatic	19-81	35.8%		32-305,120	2
AFRICA	West Africa	Ivory Coast	Parasitologie et mycologie, Hôpital Bichat Claude-Bernard, Paris, France	296	NA	2013	Resident	Symptomatic	0.5-69	NA	67%	NA	2
AFRICA	West Africa	Ivory Coast	Parasitologie et mycologie, Hôpital Bichat Claude-Bernard, Paris, France	111	NA	2014	Resident	Symptomatic	2-78	58.3%		NA	2
AFRICA	West Africa	Ivory Coast	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	32	NA	2013	Traveler	Symptomatic	NA	NA		NA	2
AFRICA	West Africa	Ivory Coast	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France/Malaria Reference Laboratory, London, UK	15	NA	2014	Traveler	Symptomatic	NA	NA		NA	2/3
AFRICA	West Africa	Ivory Coast	Institut Pasteur de Côte d'Ivoire, Abidjan, Ivory Coast	176	Abidjan	2013	Resident	Symptomatic	0.8-68	45.4%		1,066-587,000	2

AFRICA	West Africa	Ivory Coast	Institut Pasteur de Côte d'Ivoire, Abidjan, Ivory Coast	133	Abidjan	2014	Resident	Symptomatic	0.7-49	43.1%		1,000-450,909	2
AFRICA	West Africa	Ivory Coast	Institut Pasteur de Côte d'Ivoire, Abidjan, Ivory Coast	62	Ayamé	2013	Resident	Symptomatic	0.1-53	55.7%		1,340-397,730	2
AFRICA	West Africa	Ivory Coast	Institut Pasteur de Côte d'Ivoire, Abidjan, Ivory Coast	78	Korhogo	2013	Resident	Symptomatic	1-70	44.1%		2,000-200,000	2
AFRICA	West Africa	Ivory Coast	Institut Pasteur de Côte d'Ivoire, Abidjan, Ivory Coast	108	Man	2013	Resident	Symptomatic	1-62	54.6%		2,005-200,000	2
AFRICA	West Africa	Liberia	Malaria Reference Laboratory, London, UK	1	NA	2014	Traveler	Symptomatic	NA	NA	0%	NA	3
AFRICA	West Africa	Mali	Parasitologie et mycologie, Hôpital Bichat Claude-Bernard, Paris, France	83	NA	2012	Resident	Symptomatic	5-78	NA		NA	2
AFRICA	West Africa	Mali	Parasitologie et mycologie, Hôpital Bichat Claude-Bernard, Paris, France	132	NA	2013	Resident	Symptomatic	0.1-73	NA		NA	2
AFRICA	West Africa	Mali	Parasitologie et mycologie, Hôpital Bichat Claude-Bernard, Paris, France	2	NA	2014	Resident	Symptomatic	32-49	NA		NA	2
AFRICA	West Africa	Mali	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	9	NA	2013	Traveler	Symptomatic	NA	NA	52%	50-345,000	2
AFRICA	West Africa	Mali	Institut de Recherche Biomédicale des Armées, Marseille, France	14	NA	2013	Resident	Symptomatic	NA	100%		50-125,000	3
AFRICA	West Africa	Mali	Malaria Research & Training Cente, Bamako Mali	227	Banambani	2013	Resident	Symptomatic	0,75-42	56%		1,000-345,789	1
AFRICA	West Africa	Mauritania	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	1	NA	2013	Traveler	Symptomatic	64	NA	0%	NA	2
AFRICA	West Africa	Niger	Centre de Recherche Médicale et Sanitaire, Niamey, Niger	602	Niamey	2013	Resident	Symptomatic	0.08-75	45.0%		NA	1
AFRICA	West Africa	Niger	Epicentre Research Center, Mbarara, Uganda	164	Maradi, Madarounfa	2013	Resident	Symptomatic	NA	NA	70%	1,000-766,667	2
AFRICA	West Africa	Niger	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	10	NA	2013	Traveler	Symptomatic	NA	NA		NA	2
AFRICA	West Africa	Nigeria	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	6	NA	2013	Traveler	Symptomatic	34-42	NA		NA	2
AFRICA	West Africa	Nigeria	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France/Malaria Reference Laboratory, London, UK	91	NA	2014	Traveler	Symptomatic	NA	NA	63%	NA	2/3
AFRICA	West Africa	Nigeria	University of Ibadan, Ibadan, Nigeria	49	Ibadan	2009	Resident	Asymptomatic	2-97	44.9%		40-117,866	2
AFRICA	West Africa	Nigeria	University of Ibadan, Ibadan, Nigeria	153	Ibadan	2009	Resident	Symptomatic	4-90	48.6%		40-470,000	2
AFRICA	West Africa	Senegal	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	63	NA	2013	Traveler	Symptomatic	NA	NA		NA	2
AFRICA	West Africa	Senegal	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	4	NA	2014	Traveler	Symptomatic	NA	NA		NA	2
AFRICA	West Africa	Senegal	Institut Pasteur de Dakar, Dakar, Senegal	6	Dakar	2013	Resident	Symptomatic	10-28	83%	57%	120-7,746	2
AFRICA	West Africa	Senegal	Institut Pasteur de Dakar, Dakar, Senegal	102	Tambacounda	2012	Resident	Symptomatic	0,1-52	48.4%		68-199,200	2
AFRICA	West Africa	Senegal	Institut de Recherche Biomédicale des Armées, Marseille, France	138	Dakar	2012	Resident	Symptomatic	5-89	63%		40-120,000	3

AFRICA	West Africa	Sierra Leone	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	5	NA	2013	Traveler	Symptomatic	NA	NA		NA	2
AFRICA	West Africa	Sierra Leone	Malaria Reference Laboratory, London, UK	32	NA	2014	Traveler	Symptomatic	NA	NA	0%	NA	3
AFRICA	West Africa	Togo	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	26	NA	2013	Traveler	Symptomatic	NA	NA		NA	2
AFRICA	West Africa	Togo	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	4	NA	2014	Traveler	Symptomatic	NA	NA		NA	2
AFRICA	West Africa	Togo	Malaria Reference Laboratory, London, UK	2	NA	2014	Traveler	Symptomatic	NA	NA		NA	3
AFRICA	West Africa	Togo	WHO, Global Malaria Programme, Geneva, Switzerland	143	Lomé	2013	Resident	Symptomatic	6-59	42%	94%	2,187-208,385	3
AFRICA	West Africa	Togo	WHO, Global Malaria Programme, Geneva, Switzerland	163	Niamtougou	2012	Resident	Symptomatic	6-59	55.2%		2,172-235,000	3
AFRICA	West Africa	Togo	WHO, Global Malaria Programme, Geneva, Switzerland	170	Sokodé	2012	Resident	Symptomatic	6-59	51.2%		2,026-240,000	3
ASIA	Central Asia	Afghanistan	WHO, Global Malaria Programme, Geneva, Switzerland	24	Kunar	2012	Resident	Symptomatic	3-74	46%	98%	NA	1
ASIA	Central Asia	Afghanistan	WHO, Global Malaria Programme, Geneva, Switzerland	38	Kunar	2013	Resident	Symptomatic	1-70	59%		NA	1
ASIA	Central Asia	Iran	Institut Pasteur d'Iran, Tehran, Iran	21	Chabahar	2013	Resident	Symptomatic	NA	81%		NA	2
ASIA	Central Asia	Iran	Institut Pasteur d'Iran, Tehran, Iran	4	Iranshahr	2013	Resident	Symptomatic	NA	75%	100%	NA	2
ASIA	Central Asia	Iran	Institut Pasteur d'Iran, Tehran, Iran	25	Saravan	2013	Resident	Symptomatic	NA	92%		NA	2
ASIA	Central Asia	Iran	Institut Pasteur d'Iran, Tehran, Iran	28	Sarbaz	2013	Resident	Symptomatic	NA	82%		NA	2
ASIA	East Asia	China	Institut Pasteur of Shanghai Chinese Academy of sciences, Shanghai, China	94	Jiangsu	2013	Resident	Symptomatic	17-60	100%		208-533,333	2
ASIA	East Asia	China	Institut Pasteur of Shanghai Chinese Academy of sciences, Shanghai, China	6	Tengchong	2008	Resident	Symptomatic	33-45	100%		3,755-59,050	2
ASIA	East Asia	China	Institut Pasteur of Shanghai Chinese Academy of sciences, Shanghai, China	5	Tengchong	2009	Resident	Symptomatic	20-43	80%		480-83,400	2
ASIA	East Asia	China	Institut Pasteur of Shanghai Chinese Academy of sciences, Shanghai, China	4	Tengchong	2010	Resident	Symptomatic	12-50	100%		1,760-821,700	2
ASIA	East Asia	China	Institut Pasteur of Shanghai Chinese Academy of sciences, Shanghai, China	3	Tengchong	2011	Resident	Symptomatic	21-27	100%		162-5,076	2
ASIA	East Asia	China	Institut Pasteur of Shanghai Chinese Academy of sciences, Shanghai, China	14	Tengchong	2012	Resident	Symptomatic	20-43	64%	93%	810-22,165	2
ASIA	East Asia	China	Institut Pasteur of Shanghai Chinese Academy of sciences, Shanghai, China	1	Tengchong	2013	Resident	Symptomatic	53	100%		7,453	2
ASIA	East Asia	China	Institut Pasteur of Shanghai Chinese Academy of sciences, Shanghai, China	14	Yingjiang	2011	Resident	Symptomatic	21-46	100%		120-494,600	2
ASIA	East Asia	China	Institut Pasteur of Shanghai Chinese Academy of sciences, Shanghai, China	8	Yingjiang	2012	Resident	Symptomatic	41-60	100%		2,431-55,720	2
ASIA	East Asia	China	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	2	Yunnan	2004	Resident	Symptomatic	NA	NA		NA	3

ASIA	East Asia	China	WHO, Global Malaria Programme, Geneva, Switzerland	10	Yingjiang	2013	Resident	Symptomatic	NA	NA		NA	3
ASIA	East Asia	China	WHO, Global Malaria Programme, Geneva, Switzerland	26	Yingjiang	2010	Resident	Symptomatic	12-49	73%		560-821,700	3
ASIA	East Asia	China	WHO, Global Malaria Programme, Geneva, Switzerland	29	Yingjiang	2014	Resident	Symptomatic	10-54	77%		860-225,000	3
ASIA	East Asia	Myanmar	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	13	Kachin	2007	Resident	Symptomatic	12-47	54%		NA	3
ASIA	East Asia	Myanmar	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	44	Kachin	2008	Resident	Symptomatic	NA	NA		NA	3
ASIA	East Asia	Myanmar	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	79	Kachin	2009	Resident	Symptomatic	3-47	78.2%		NA	3
ASIA	East Asia	Myanmar	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	7	Kachin	2010	Resident	Symptomatic	NA	NA		NA	3
ASIA	East Asia	Myanmar	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	8	Kachin	2012	Resident	Symptomatic	NA	NA		NA	3
ASIA	East Asia	Myanmar	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	46	Kachin	2013	Resident	Symptomatic	NA	NA		NA	3
ASIA	East Asia	Myanmar	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	6	Wa State	2007	Resident	Symptomatic	NA	NA	66%	NA	3
ASIA	East Asia	Myanmar	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	16	Wa State	2008	Resident	Symptomatic	7-27	33%		NA	3
ASIA	East Asia	Myanmar	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	3	Wa State	2010	Resident	Symptomatic	NA	NA		NA	3
ASIA	East Asia	Myanmar	Department of Entomology, Pennsylvania State University, Pennsylvania, USA	1	Wa State	2011	Resident	Symptomatic	NA	NA		NA	3
ASIA	East Asia	Myanmar	WHO, Global Malaria Programme, Geneva, Switzerland	63	Pyin Oo Lwin	2014	Resident	Symptomatic	8-65	73%		1063-14,824	1
ASIA	East Asia	Myanmar	WHO, Global Malaria Programme, Geneva, Switzerland	61	Tamu	2014	Resident	Symptomatic	12-62	60%		2,888-14,664	1
ASIA	South Asia	Bangladesh	Medical University of Vienna, Vienna, Austria	18	Bandarban	2011	Resident	Symptomatic	10-58	83%		NA	2
ASIA	South Asia	Bangladesh	Medical University of Vienna, Vienna, Austria	277	Bandarban	2012	Resident	Symptomatic	10-74	NA	32%	NA	2
ASIA	South Asia	Bangladesh	WHO, Global Malaria Programme, Geneva, Switzerland	38	Lama	2014	Resident	Symptomatic	7-90	80,50 %		3360-47,556	1
ASIA	South Asia	Nepal	WHO, Global Malaria Programme, Geneva, Switzerland	7	Dhangadi	2014	Resident	Symptomatic	19-35	100%		1040-27,778	1
ASIA	South Asia	Nepal	WHO, Global Malaria Programme, Geneva, Switzerland	6	Kanchanpur	2014	Resident	Symptomatic	29-55	83%		2,964-99,999	1
ASIA	South Asia	Nepal	WHO, Global Malaria Programme, Geneva, Switzerland	6	Mahakali Zonal Hospital	2013	Resident	Symptomatic	29-55	83%	100%	2,964-99,999	1
ASIA	South Asia	Nepal	WHO, Global Malaria Programme, Geneva, Switzerland	5	Seti Zonal Hospital	2014	Resident	Symptomatic	19-35	100%		1040-27,778	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	45	Battambang	2012	Resident	Symptomatic	NA	NA		NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	36	Battambang	2013	Resident	Symptomatic	NA	NA	0%	NA	1

ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	19	Kampong Speu	2012	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	2	Kampong Speu	2013	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	57	Kampong Thom	2012	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	8	Kampot	2013	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	9	Kampot	2014	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	17	Kratie	2013	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	5	Kratie	2014	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	17	Mondolkiri	2013	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	1	Mondolkiri	2014	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	48	Oddar Meanchey	2012	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	59	Oddar Meanchey	2013	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	4	Oddar Meanchey	2014	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	155	Pailin	2012	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	58	Pailin	2013	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	12	Pailin	2014	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	13	Preah Vihear	2013	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	6	Preah Vihear	2013	Resident	Asymptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	4	Preah Vihear	2014	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	69	Pursat	2012	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	3	Pursat	2013	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	48	Rattanakiri	2012	Resident	Symptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	70	Rattanakiri	2012	Resident	Asymptomatic	NA	NA	NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	59	Rattanakiri	2013	Resident	Symptomatic	NA	NA	NA	1

ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	32	Rattanakiri	2013	Resident	Asymptomatic	NA	NA		NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	20	Stung Treng	2013	Resident	Asymptomatic	NA	NA		NA	1
ASIA	Southeast Asia	Cambodia	Institut Pasteur du Cambodge, Phnom Penh, Cambodia	6	Stung Treng	2013	Resident	Asymptomatic	NA	NA		NA	1
ASIA	Southeast Asia	Indonesia	Eijkman Institute for Molecular Biology, Jakarta, Indonesia	23	Sumba	2011	Resident	Symptomatic	3-54	45%	96%	360-200,000	2
ASIA	Southeast Asia	Indonesia	Eijkman Institute for Molecular Biology, Jakarta, Indonesia	87	Sumba	2012	Resident	Symptomatic	1-59	53%		120-480,000	2
ASIA	Southeast Asia	Lao PDR	Institut Pasteur du Laos, Vientiane, Lao PDR	5	Xepon, Savannakhet	2013	Resident	Symptomatic	7-27	60%	99%	NA	2
ASIA	Southeast Asia	Lao PDR	Institut Pasteur du Laos, Vientiane, Lao PDR	42	Xepon, Savannakhet	2013	Resident	Asymptomatic	4-63	52%		NA	2
ASIA	Southeast Asia	Lao PDR	WHO, Global Malaria Programme, Geneva, Switzerland	26	Champasak	2013	Resident	Symptomatic	12-50	96%		1,247-47,424	1
ASIA	Southeast Asia	Lao PDR	WHO, Global Malaria Programme, Geneva, Switzerland	49	Saravanh	2013	Resident	Symptomatic	3-42	59%		1,448-186,920	1
ASIA	Southeast Asia	Philippines	Research Institute for Tropical Medicine, Manila, Philippines	117	Palawan	2013	Resident	Symptomatic	1-65	53%	100%	64-83,619	2
ASIA	Southeast Asia	Philippines	Research Institute for Tropical Medicine, Manila, Philippines	3	Tawi-Tawi	2013	Resident	Symptomatic	11-45	66%		455-17,931	2
ASIA	Southeast Asia	Thailand	Thammasat University, Bangkok, Thailand	11	Mae Sot	2006	Resident	Symptomatic	19-55	73%		NA	2
ASIA	Southeast Asia	Thailand	Thammasat University, Bangkok, Thailand	2	Mae Sot	2008	Resident	Symptomatic	35-37	0%		NA	2
ASIA	Southeast Asia	Thailand	Thammasat University, Bangkok, Thailand	129	Mae Sot	2009	Resident	Symptomatic	18-60	49%		NA	2
ASIA	Southeast Asia	Thailand	Thammasat University, Bangkok, Thailand	2	Ranong	2009	Resident	Symptomatic	38-39	50%		NA	2
ASIA	Southeast Asia	Thailand	Thammasat University, Bangkok, Thailand	6	Ranong	2010	Resident	Symptomatic	18-45	50%		NA	2
ASIA	Southeast Asia	Thailand	Mahidol Vivax Research Unit, Bangkok, Thailand	43	Sai Yok District, Kanchanaburi Province	2013	Resident	NA	10-55	77%	91%	NA	2
ASIA	Southeast Asia	Thailand	Mahidol Vivax Research Unit, Bangkok, Thailand	10	Sai Yok District, Kanchanaburi Province	2014	Resident	NA	27-47	40%		NA	2
ASIA	Southeast Asia	Thailand	Mahidol Vivax Research Unit, Bangkok, Thailand	1	Suan Pheung District, Ratchaburi Province	2013	Resident	NA	45	0%		NA	2
ASIA	Southeast Asia	Thailand	Mahidol Vivax Research Unit, Bangkok, Thailand	3	Suan Pheung District,	2014	Resident	NA	7-36	33%		NA	2

												Ratchaburi Province	
ASIA	Southeast Asia	Vietnam	WHO, Global Malaria Programme, Geneva, Switzerland	177	NA	2014	Resident	NA	NA	NA	0%	NA	1
OCEANIA	Oceania	Papua New Guinea	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	1	NA	2013	Traveler	Symptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	1	Chimbu	2013	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	17	East New Britain	2014	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	7	East Sepik	2014	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	2	Eastern Highlands	2013	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	1	Enga	2013	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	2	Gulf	2014	Resident	Asymptomatic	NA	NA	74%	NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	3	Madang	2013	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	1	Manus	2013	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	2	Morobe	2013	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	10	New Ireland	2014	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	4	Oro	2014	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Papua New Guinea	Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea	5	West Sepik	2014	Resident	Asymptomatic	NA	NA		NA	2
OCEANIA	Oceania	Solomon Islands	Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia / National Vector Borne Disease Control Program, Solomon Islands	15	Auki	2012-2013	Resident	Symptomatic	NA	NA		1,200-160,000	2
OCEANIA	Oceania	Solomon Islands	Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia / National Vector Borne Disease Control Program, Solomon Islands	29	Tetere	2012-2013	Resident	Symptomatic	NA	NA	0%	2,526-241,600	2
S. AMERICA	South America	Brazil	Fundação de Medicina Tropical, Manaus, Brazil	30	Manaus	1997	Resident	Symptomatic	NA	NA		NA	1
S. AMERICA	South America	Brazil	Fundação de Medicina Tropical, Manaus, Brazil	29	Manaus	2000	Resident	Symptomatic	NA	NA		NA	1
S. AMERICA	South America	Brazil	Fundação de Medicina Tropical, Manaus, Brazil	3	Manaus	2001	Resident	Symptomatic	NA	NA	8%	NA	1
S. AMERICA	South America	Brazil	Fundação de Medicina Tropical, Manaus, Brazil	36	Manaus	2003	Resident	Symptomatic	NA	NA		NA	1
S. AMERICA	South America	Brazil	Fundação de Medicina Tropical, Manaus, Brazil	33	Manaus	2009	Resident	Symptomatic	NA	NA		NA	1

S. AMERICA	South America	Brazil	Fundação de Medicina Tropical, Manaus, Brazil	2	Manaus	2012	Resident	Symptomatic	NA	NA		NA	1
S. AMERICA	South America	Brazil	Fundação de Medicina Tropical, Manaus, Brazil	4	Manaus	2012	Resident	Asymptomatic	NA	NA		NA	1
S. AMERICA	South America	Brazil	Fundação de Medicina Tropical, Manaus, Brazil	86	Manaus	2013	Resident	Symptomatic	NA	NA		NA	1
S. AMERICA	South America	Brazil	Fundação de Medicina Tropical, Manaus, Brazil	14	Manaus	2013	Resident	Asymptomatic	NA	NA		NA	1
S. AMERICA	South America	Colombia	Caucaseco Scientific Reasearch Center, Cali, Colombia	99	Quibdo	2012	Resident	Symptomatic	5-79	52%		4-127,008	2
S. AMERICA	South America	Colombia	Caucaseco Scientific Reasearch Center, Cali, Colombia	40	Tierralta	2012	Resident	Symptomatic	4-65	72.5%	100%	2-18,685	2
S. AMERICA	South America	Colombia	Caucaseco Scientific Reasearch Center, Cali, Colombia	396	Tumaco	2012	Resident	Symptomatic	5-96	48.5%		2-100,000	2
S. AMERICA	South America	Ecuador	Malaria Reference Laboratory, London, UK	1	NA	2014	Traveler	Symptomatic	NA	NA	0%	NA	3
S. AMERICA	South America	French Guiana	Centre National de Référence du Paludisme, Hôpital Bichat Claude-Bernard, Paris, France	5	NA	2013	Traveler	Symptomatic	5-13	NA		NA	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	96	Cayenne	2012	Resident	Symptomatic	5-61	72%		50-840,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	39	Cayenne	2013	Resident	Symptomatic	5-57	69.2%		50-695,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	11	Kourou	2012	Resident	Symptomatic	17-55	91%		1,000-50,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	5	Kourou	2013	Resident	Symptomatic	24-44	100%		5,000-20,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	3	Maripa-Soula	2012	Resident	Symptomatic	29-36	66%		50-155,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	11	Maripa-Soula	2013	Resident	Symptomatic	1-50	64%	97%	500-90,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	1	Papaïchton	2012	Resident	Symptomatic	27	100%		24,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	5	Papaïchton	2013	Resident	Symptomatic	25-37	80%		2,000-47,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	3	Rémire-Montjoly	2012	Resident	Symptomatic	7-16	33%		1,600-85,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	7	Saint Laurent du Maroni	2012	Resident	Symptomatic	23-38	71.5%		400-19,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	12	Saint Laurent du Maroni	2013	Resident	Symptomatic	16-40	42%		1,200-81,600	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	4	Saint-Georges	2012	Resident	Symptomatic	16-37	100%		10,000-40,000	2
S. AMERICA	South America	French Guiana	Institut Pasteur de la Guyane, Cayenne, French Guiana	1	Saint-Georges	2013	Resident	Symptomatic	43	100%		24,000	2
S. AMERICA	South America	Peru	Naval Medical Research Unit 6, Iquitos, Peru	51	Loreto	2012	Resident	Symptomatic	6-72	54%	54%	71-49,800	3

S. AMERICA	South America	Peru	Naval Medical Research Unit 6, Iquitos, Peru	24	Loreto	2013	Resident	Symptomatic	14-78	50%		12-60,768	3
S. AMERICA	South America	Venezuela	Malaria Reference Laboratory, London, UK	1	NA	2014	Traveler	Symptomatic	NA	NA	0%	NA	3
14037										56%			

Table S5. Full data set listing the number of tested samples, the number of samples with interpretable sequences, the number of samples with 3D7 non-reference allele sequences, the number of samples with non-synonymous or synonymous mutations, the number of polyclonal infections and the genetic diversity parameters (number of haplotypes, H; nucleotide diversity, $\pi \times 10^{-3}$; haplotype diversity, Hd and Tajima's D test) detailed by continent, regions and country, KARMA study 2014

Continent	Region	Country	No. Blood samples	Samples with interpretable sequences			Samples with non-reference 3D7 allele sequence			Samples with non-synonymous mutations			Samples with synonymous mutations			No. polyclonal infections	No. sequences included in the genetic diversity analysis	H	π (SD) $\times 10^{-3}$	Hd (SD)	No. of allele with mutation detected as		Tajima's D test
				No.	%	CI95%	No.	%	CI95%	No.	%	CI95%	No.	%	CI95%						S	NS	
WORLD			14037	13157	93,7%	1250	9,5%	8.8-9.9%	1087	8,3%	7.6-8.6%	174	1,3%	1.1-1.6%	111	13268	186	0,26	0,1824 (0,0045)	58	88	1,032	
AFRICA			10207	9434	92,4%	287	3,0%	2.7-3.5%	128	1,4%	1.1-1.6%	169	1,8%	1.5-2.1%	108	9542	150	0,09	0,0661 (0,0036)	58	61	1,006	
AFRICA	Central Africa		3276	3072	93,8%	97	3,2%	2.7-4.0%	49	1,6%	1.2-2.2%	56	1,8%	1.4-2.5%	44	3116	70	0,10	0,072 (0,006)	30	39	1,041	
AFRICA	Central Africa	Cameroon	911	901	98,9%	26	2,9%	1.9-4.2%	11	1,2%	0.6-2.2%	17	1,9%	1.1-3.0%	10	911	19	0,09	0,061 (0,011)	11	7	0,877	
AFRICA	Central Africa	Central African Republic	469	423	90,2%	28	6,6%	4.6-9.8%	19	4,5%	2.7-7.0%	14	3,3%	1.8-5.5%	21	444	40	0,27	0,184 (0,025)	15	24	1,090	
AFRICA	Central Africa	Chad	33	33	100,0%	2	6,1%	0.7-21.9%	1	3,0%	0.1-16.9%	1	3,0%	0.1-16.9%	0	33	3	0,17	0,119 (0,076)	1	1	1,000	
AFRICA	Central Africa	Congo	72	71	98,6%	2	2,8%	0.3-10.2%	0	0,0%	0-5.2%	2	2,8%	0.3-10.2%	1	72	3	0,08	0,055 (0,037)	2	0	-	
AFRICA	Central Africa	Democratic Republic of Congo	1288	1230	95,5%	32	2,6%	2.5-2.7%	14	1,1%	1.1-1.2%	18	1,5%	1.4-1.5%	11	1241	21	0,07	0,052 (0,009)	10	10	1,003	
AFRICA	Central Africa	Equatorial Guinea	7	7	100,0%	1	14,3%	0.4-79.6%	0	0,0%	0-52.7%	1	14,3%	0.4-79.6%	1	8	2	0,35	0,250 (0,180)	1	0	-	
AFRICA	Central Africa	Gabon	496	407	82,1%	6	1,5%	0.5-3.2%	4	1,0%	0.3-2.5%	3	0,7%	0.2-2.1%	0	407	6	0,04	0,029 (0,012)	1	4	1,842	
AFRICA	Eastern Africa		1360	1314	96,6%	30	2,3%	1.5-3.2%	13	1,0%	0.5-1.7%	17	1,3%	0.7-2.1%	11	1325	20	0,07	0,049 (0,008)	12	7	0,849	
AFRICA	East Africa	Burundi	1	1	100,0%	0	0,0%	-	0	0,0%	-	0	0,0%	-	0	1	1	-	-	0	0	-	
AFRICA	East Africa	Ethiopia	146	126	86,3%	0	0,0%	0-2.9%	0	0,0%	0-2.9%	0	0,0%	0-2.9%	0	126	1	-	-	0	0	-	
AFRICA	East Africa	Kenya	198	184	92,9%	8	4,3%	1.9-8.6%	6	3,3%	1.2-7.1%	2	1,1%	0.1-3.9%	4	188	5	0,13	0,093 (0,029)	2	2	0,839	
AFRICA	East Africa	Rwanda	293	292	99,7%	11	3,8%	1.9-6.7%	4	1,4%	0.4-3.5%	7	2,4%	1.0-4.9%	5	297	12	0,12	0,086 (0,023)	6	5	0,957	
AFRICA	East Africa	Sudan	5	5	100,0%	0	0,0%	-	0	0,0%	-	0	0,0%	-	0	5	1	-	-	0	0	-	
AFRICA	East Africa	South Sudan	1	1	100,0%	0	0,0%	-	0	0,0%	-	0	0,0%	-	0	1	1	-	-	0	0	-	
AFRICA	East Africa	Somalia	186	186	100,0%	0	0,0%	0-2.0%	0	0,0%	0-2.0%	0	0,0%	0-2.0%	0	186	1	-	-	0	0	-	
AFRICA	East Africa	Tanzania	236	236	100,0%	0	0,0%	0-1.6%	0	0,0%	0-1.6%	0	0,0%	0-1.6%	0	236	1	-	-	0	0	-	
AFRICA	East Africa	Uganda	294	283	96,3%	11	3,9%	1.9-6.7%	3	1,1%	0.2-3.1%	8	2,8%	1.2-5.6%	2	285	9	0,11	0,076 (0,022)	7	1	0,431	

AFRICA	Indian Ocean		631	608	96,4%	20	3,3%	2.0-5.1%	14	2,3%	1.2-3.9%	6	1,0%	0.4-2.1%	5	613	13	0,11	0,08 (0,015)	3	9	1,480
AFRICA	Indian Ocean	Comoros	354	352	99,4%	14	4,0%	2.2-6.7%	13	3,7%	2.0-6.3%	1	0,3%	0-1.6%	4	356	11	0,00	0,098 (0,022)	2	8	1,579
AFRICA	Indian Ocean	Madagascar	277	256	92,4%	6	2,3%	0.8-5.1%	1	0,4%	0-2.2%	5	2,0%	0.6-4.6%	1	257	4	0,00	0,054 (0,019)	2	1	0,819
AFRICA	Southern Africa		365	344	94,2%	22	6,4%	4.0-9.7%	13	3,8%	2.0-6.5%	10	2,9%	1.4-5.3%	15	359	24	0,19	0,135 (0,025)	9	14	1,120
AFRICA	Southern Africa	Angola	34	34	100,0%	0	0,0%	0-10.8%	0	0,0%	0-10.8%	0	0,0%	0-10.8%	1	35	1	-	-	0	0	-
AFRICA	Southern Africa	Malawi	13	13	100,0%	1	7,7%	0.2-42.8%	0	0,0%	0-28.4%	1	7,7%	0.2-42.8%	0	13	2	0,21	0,154 (0,126)	1	0	-
AFRICA	Southern Africa	Mozambique	5	5	100,0%	0	0,0%	-	0	0,0%	-	0	0,0%	-	0	5	1	-	-	0	0	-
AFRICA	Southern Africa	South Africa	2	2	100,0%	0	0,0%	-	0	0,0%	-	0	0,0%	-	0	2	1	-	-	0	0	-
AFRICA	Southern Africa	Zambia	304	283	93,1%	20	7,1%	4.3-10.9%	13	4,6%	2.4-7.8%	8	2,8%	1.2-5.6%	14	297	24	0,22	0,149 (0,029)	9	14	1,109
AFRICA	Southern Africa	Zimbabwe	7	7	100,0%	1	14,3%	0.3-79.6%	0	0,0%	0-52.7%	1	14,3%	0.3-79.6%	0	7	2	0,40	0,286 (0,196)	1	0	-
AFRICA	Western Africa		4575	4096	89,5%	118	2,9%		39	1,0%		80	2,0%		33	4129	59	0,08	0,059 (0,005)	31	21	0,934
AFRICA	West Africa	Benin	265	234	88,3%	13	5,6%	2.9-9.5%	2	0,9%	0.1-3.1%	11	4,7%	2.3-8.4%	1	235	8	0,15	0,107 (0,028)	5	2	0,757
AFRICA	West Africa	Burkina Faso	612	589	96,2%	14	2,4%	1.3-4.0%	2	0,3%	0-1.3%	12	2,0%	1.0-3.6%	0	589	11	0,07	0,047 (0,012)	8	2	0,610
AFRICA	West Africa	Gambia	12	12	100,0%	1	8,3%	-	1	8,3%	-	0	0,0%	-	0	12	2	0,23	0,167 (0,134)	0	1	-
AFRICA	West Africa	Ghana	37	37	100,0%	0	0,0%	0-10.0%	0	0,0%	0-10.0%	0	0,0%	0-10.0%	0	37	1	-	-	0	0	-
AFRICA	West Africa	Guinea	87	86	98,9%	4	4,7%	1.2-11.8%	3	3,5%	0.7-10.1%	1	1,2%	0-6.4%	0	86	5	0,13	0,091 (0,043)	1	3	1,559
AFRICA	West Africa	Guinea Bissau	3	3	100,0%	0	0,0%	-	0	0,0%	-	0	0,0%	-	0	3	1	-	-	0	0	-
AFRICA	West Africa	Ivory Coast	1157	1083	93,6%	33	3,0%	2.1-4.3%	10	0,9%	0.4-1.7%	24	2,2%	1.4-3.3%	13	1096	28	0,09	0,065 (0,010)	15	12	0,954
AFRICA	West Africa	Liberia	1	1	100,0%	0	0,0%	-	0	0,0%	-	0	0,0%	-	0	1	1	-	-	0	0	-
AFRICA	West Africa	Mali	467	465	99,6%	7	1,5%	0.6-3.1%	2	0,4%	0-1.6%	5	1,1%	0.3-2.5%	5	470	8	0,04	0,030 (0,011)	6	1	0,487
AFRICA	West Africa	Mauritania	1	1	100,0%	0	0,0%	-	0	0,0%	-	0	0,0%	-	0	1	1	-	-	0	0	-
AFRICA	West Africa	Niger	776	521	67,1%	22	4,2%	2.6-6.4%	7	1,3%	0.5-2.8%	15	2,9%	1.6-4.7%	11	532	16	0,12	0,088 (0,017)	9	6	0,889
AFRICA	West Africa	Nigeria	299	273	91,3%	7	2,6%	1.0-5.3%	3	1,1%	0.2-3.2%	4	1,5%	0.4-3.8%	3	276	7	0,07	0,05 (0,018)	3	3	1,015
AFRICA	West Africa	Senegal	313	246	78,6%	2	0,8%	0.1-2.9%	0	0,0%	0-1.5%	2	0,8%	0.1-2.9%	0	246	3	0,02	0,016 (0,011)	2	0	-
AFRICA	West Africa	Sierra Leone	37	37	100,0%	0	0,0%	0-10.0%	0	0,0%	0-10.0%	0	0,0%	0-10.0%	0	37	1	-	-	0	0	-
AFRICA	West Africa	Togo	508	508	100,0%	15	3,0%	1.6-4.9%	9	1,8%	0.8-3.4%	6	1,2%	0.4-2.6%	0	508	10	0,08	0,058 (0,015)	5	4	0,897
ASIA			2678	2623	97,9%	960	36,6%	33.9-38.7%	957	36,5%	33.8-38.6%	4	0,2%	0-0.4%	3	2626	45	0,86	0,543 (0,009)	3	41	1,795
ASIA	Central Asia		140	138	98,6%	3	2,2%	0-6.4%	3	2,2%	0-6.4%	0	0,0%	-	0	138	4	0,06	0,043 (0,024)	0	3	-
ASIA	Central Asia	Afghanistan	62	62	100,0%	1	1,6%	0-9.0%	1	1,6%	0-9.0%	0	0,0%	-	0	62	2	0,04	0,032 (0,031)	0	1	-
ASIA	Central Asia	Iran	78	76	97,4%	2	2,6%	0-9.5%	2	2,6%	0-9.5%	0	0,0%	-	0	76	3	0,07	0,052 (0,035)	0	2	-
ASIA	East Asia		563	558	99,1%	217	38,9%	38.4-39.4%	216	38,7%	38.2-39.2%	1	0,2%	0-1.0%	0	558	19	0,87	0,551 (0,018)	1	17	2,073
ASIA	East Asia	China	216	215	99,5%	56	26,0%	19.7-33.8%	55	25,6%	19.3-33.3%	1	0,5%	0-2.6%	0	215	11	0,64	0,423 (0,037)	1	9	1,677
ASIA	East Asia	Myanmar	347	343	98,8%	161	46,9%	46.2-47.7%	161	46,9%	46.2-47.7%	0	0,0%	0-1.1%	0	343	14	0,99	0,605 (0,019)	0	13	-
ASIA	South Asia		357	340	95,2%	3	0,9%	0-2.6%	3	0,9%	0-2.6%	0	0,0%	0-1.1%	0	340	5	0,03	0,023 (0,012)	0	4	-

ASIA	South Asia	Bangladesh	333	318	95,5%	3	0,9%	0-2.7%	3	0,9%	0-2.7%	0	0,0%	0-1.2%	0	318	5	0,03	0,025 (0,012)	0	4	-
ASIA	South Asia	Nepal	24	22	91,7%	0	0,0%	0-16.8%	0	0,0%	0-16.8%	0	0,0%	0-16.8%	0	22	1	-	-	0	0	-
ASIA	Southeast Asia		1618	1587	98,1%	737	46,4%	43.1-50.0%	735	46,3%	43.0-49.8%	3	0,2%	0-0.6%	3	1590	27	0,89	0,571 (0,007)	3	23	1,462
ASIA	Southeast Asia	Cambodia	882	882	100,0%	586	66,4%	61.2-72.0%	586	66,4%	61.2-72.0%	0	0,0%	-	0	882	13	0,89	0,545 (0,012)	0	12	-
ASIA	Southeast Asia	Indonesia	110	106	96,4%	1	0,9%	0-5.2%	1	0,9%	0-5.2%	0	0,0%	0-3.5%	0	106	2	0,03	0,019 (0,018)	0	1	-
ASIA	Southeast Asia	Lao PDR	122	120	98,4%	25	20,8%	13.5-30.7%	24	20,0%	13.0-30.0%	1	0,8%	0-4.6%	1	121	5	0,52	0,351 (0,051)	1	3	0,628
ASIA	Southeast Asia	Philippines	120	99	82,5%	1	1,0%	0-5.6%	0	0,0%	-	1	1,0%	0-5.6%	0	99	2	0,03	0,02 (0,020)	1	0	-
ASIA	Southeast Asia	Thailand	207	205	99,0%	54	26,3%	19.8-34.4%	54	26,3%	19.8-34.4%	0	0,0%	-	0	205	7	0,65	0,43 (0,039)	0	6	-
ASIA	Southeast Asia	Vietnam	177	175	98,9%	70	40,0%	31.0-50.5%	69	39,4%	31.0-50.0%	1	0,6%	0-3.2%	2	177	11	1,00	0,606 (0,036)	1	9	1,613
OCEANIA			100	86	86,0%	2	2,3%	0-8.4%	1	1,2%	0-6.4%	1	1,2%	0-6.4%	0	86	3	0,06	0,046 (0,031)	1	1	1,000
OCEANIA	Oceania	Papua New Guinea	56	43	76,8%	1	2,3%	0-12.9%	0	0,0%	-	1	2,3%	-	0	43	2	0,06	0,047 (0,044)	1	0	-
OCEANIA	Oceania	Solomon Islands	44	43	97,7%	1	2,3%	0-12.9%	1	2,3%	-	0	0,0%	-	0	43	2	0,06	0,047 (0,044)	0	1	-
S. AMERICA			1052	1014	96,4%	1	0,1%	0-0.5%	1	0,1%	0-0.5%	0	0,0%	-	0	1014	2	0,003	0,002 (0,002)	0	1	-
S. AMERICA	South America	Brazil	237	237	100,0%	1	0,4%	0-2.3%	1	0,4%	0-2.3%	0	0,0%	-	0	237	2	0,01	0,008 (0,008)	0	1	-
S. AMERICA	South America	Colombia	535	523	97,8%	0	0,0%	0-0.7%	0	0,0%	0-0.7%	0	0,0%	-	0	523	1	-	-	0	0	-
S. AMERICA	South America	Ecuador	1	1	100,0%	0	0,0%	-	0	0,0%	-	0	0,0%	-	0	1	1	-	-	0	0	-
S. AMERICA	South America	French Guiana	203	183	90,1%	0	0,0%	0-2.0%	0	0,0%	0-2.0%	0	0,0%	-	0	183	1	-	-	0	0	-
S. AMERICA	South America	Peru	75	69	92,0%	0	0,0%	0-5.3%	0	0,0%	0-5.3%	0	0,0%	-	0	69	1	-	-	0	0	-
S. AMERICA	South America	Venezuela	1	1	100,0%	0	0,0%	-	0	0,0%	-	0	0,0%	-	0	1	1	-	-	0	0	-

Table S6. List of the most frequent NS-mutations (private mutants observed once are excluded) ranked by their relative frequency and their distribution by continent and country, KARMA study 2014.

NS-mutation	No. of samples		by continents				by countries (No. of samples)
	Total (%)	by continents					
		Africa	Asia	Oceania	South America		
C580Y*	602 (54.9%)	-	602	-	-	Cambodia (515), Vietnam (34), Thailand (33), Lao PDR (17), Myanmar (3)	
F446I*	154 (14.0%)	-	154	-	-	Myanmar (116), China (38)	
R539T*	43 (3.9%)	-	43	-	-	Cambodia (35), Lao PDR (6), Myanmar (2)	
A578S	42 (3.8%)	41	1	-	-	Thailand (1), Benin (1), Burkina Faso (1), Cameroon (4), CAR (1), Chad (1), Comoros (7), Congo DR (3), Guinea (2), Ivory Coast (3), Kenya (5), Mali (1), Niger (4), Togo (4), Uganda (3), Zambia (1)	
Y493H*	32 (2.9%)	-	32	-	-	Cambodia (24), Vietnam (8)	
P574L*	23 (2.1%)	-	23	-	-	Myanmar (10), Thailand (9), China (4)	
P553L*	21 (1.9%)	-	21	-	-	China (3), Myanmar (3), Cambodia (2), Thailand (1), Vietnam (12)	
N458Y*	16 (1.5%)	-	16	-	-	Myanmar (8), Thailand (8)	
R561H	14 (1.3%)	1	13	-	-	Myanmar (13), Congo DR (1)	
I543T*	8 (0.7%)	-	8	-	-	Cambodia (1), Vietnam (7)	
S522C	7 (0.6%)	7	-	-	-	CAR (1), Congo DR (1), Gabon (1), Kenya (1), Togo (3)	
V589I	6 (0.5%)	6	-	-	-	Benin (1), Burkina Faso (1), Cameroon (1), CAR (1), Kenya (1), Madagascar (1)	
A481V	4 (0.4%)	-	3	-	1	China (3), Brazil (1)	
V534A	3 (0.3%)	3	-	-	-	Congo DR (3)	
F583L	3 (0.3%)	3	-	-	-	CAR (1), Ivory Coast (1), Zambia (1)	
G665S	3 (0.3%)	3	-	-	-	Cameroon (1), Guinea (1), Nigeria (1)	
K503N	3 (0.3%)	-	3	-	-	Vietnam (3)	
D584V	3 (0.3%)	-	3	-	-	Cambodia (3)	
C469Y	3 (0.3%)	-	3	-	-	Myanmar (1), China (2)	
F495L	2 (0.2%)	1	1	-	-	Myanmar (1), Comoros (1)	
G592R	2 (0.2%)	1	-	1	-	Nigeria, Salomon Islands	
Y482S	2 (0.2%)	2	-	-	-	Cameroon (2)	
I552M	2 (0.2%)	2	-	-	-	CAR (2)	
Q613E	2 (0.2%)	2	-	-	-	Congo DR (2)	
D641G	2 (0.2%)	2	-	-	-	CAR (2)	
C532S	2 (0.2%)	2	-	-	-	Ivory Coast (1), Togo (1)	
A557S	2 (0.2%)	2	-	-	-	Congo DR (1), Togo (1)	
E596K	2 (0.2%)	2	-	-	-	Congo DR (1), Zambia (1)	
T474I	2 (0.2%)	-	2	-	-	Vietnam (2)	
F483S	2 (0.2%)	-	2	-	-	China (2)	
P527H	2 (0.2%)	-	2	-	-	Thailand (2)	
V568G*	2 (0.2%)	-	2	-	-	Vietnam (2)	
E605K	2 (0.2%)	-	2	-	-	Vietnam (1), China (1)	
L492S	2 (0.2%)	-	2	-	-	Myanmar (1), China (1)	
V510M	2 (0.2%)	1	1	-	-	Bangladesh (1), Ivory Coast (1)	
N537D	2 (0.2%)	1	1	-	-	China (1), CAR (1)	

Continent-shared mutants are highlighted in orange, inter-Asian country-shared mutants in green, intra-Asian country-shared mutants in pale green, inter-African country-shared mutants in blue and intra-African country-shared mutants in pale blue.

* C580Y, Y493H, R539T, I543T are validated/confirmed artemisinin resistance mutations; F446I, P441L, N458Y, P553L, V568G, P574L are associated with clinical artemisinin resistance^{9,20,26,31,42} (see reference 28).

3-digit country codes are provided in the next sheet

Country Name	Country Code	Country Name	Country Code	Country Name	Country Code
Afghanistan	AFG	Gabon	GAB	Nigeria	NGA
Angola	AGO	Gambia	GMB	Papua New Guinea	PNG
Bangladesh	BGD	Ghana	GHA	Peru	PER
Benin	BEN	Guinea	GIN	Philippines	PHL
Brazil	BRA	Guinea Bissau	GNB	Rwanda	RWA
Burkina Faso	BFA	Indonesia	IDN	Senegal	SEN
Burundi	BDI	Iran	IRN	Sierra Leone	SLE
Cambodia	KHM	Ivory Coast	CIV	Solomon Islands	SLB
Cameroon	CMR	Kenya	KEN	Somalia	SOM
Central African Republic	CAF	Lao PDR	LAO	South Africa	ZAF
Chad	TCD			South Sudan	SSD
China	CHN	Liberia	LBR	Sudan	SDN
Colombia	COL	Madagascar	MDG	Tanzania	TZA
Comoros	COM	Malawi	MWI	Thailand	THA
Congo	COG	Mali	MLI	Togo	TGO
Democratic Republic of Congo	COD	Mauritania	MRT	Uganda	UGA
Ecuador	ECU	Mozambique	MOZ	Venezuela	VEN
Equatorial Guinea	GNQ	Myanmar	MMR	Vietnam	VNM
Ethiopia	ETH	Nepal	NPL	Zambia	ZMB
French Guiana	GUF	Niger	NER	Zimbabwe	ZWE


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159_H32 TTCTCTTTCTCCAATCTTTTAT~
159_H33 TTCTCTTTCTCCAATcTTTTATTACATCTTCTTTCTCTTTCTCCAATCTTTTATcACATCTTC~ ca
159_H34 TTCTCTTTCTCCAATCTTTTATTACATCTTCTTTCTCTTTCTCCAATCTTTTAT~
159_H35 TTCTCTTTCTCCAATCTTTTATTACATCTTCTTTCTCTTTCTCCAATCTTTTATTACATCTTCTTTCTCTTTC~
159_H36 TTCTCTTTTTCGAACCCTTTTATTACATCTTCTTTCTCTTTCTCCAATCTTTTATTACATCTTCTTTCTCTTTCCCAATCTTTTATTACATCTTCTT
159_H37 TTCTCTTTCTCCAATCTTTTATTACATCTTCTTTCTCTTTCTCCAATCTTTTAT~
159_H38 TTCTCTTTCTCCAATCTTTTATTACATCTTCTTTCTCTTTCTCCAATCTTTTAT~
159_H39 TTCTCTTTCTCCAATCTTTTATTACATCTTCTTTCTCTTTCTCCAATCTTTTAT~
159_H40 TTCTCTTTTTCGAACCCTTTTATTACATCTTCTTTCTCTTTCTCCAATCTTTTATTACATCTTCTTTCTCTTTC~
159_H41 TTCTCTTTCTCCAATCTTTTAT~
159_H42 TTCTCTTTCTCCAATCTTTTATTACATCTTCTTTCTCTTTCTCCAATCTTTTAT~

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          710      720      730      740
...|...|...|...|...|...|...|...|.
159_3D7 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H01 ~CACATCTCCAGATGTTCC
159_H02 ~CACATCTCCAGATGTTCC
159_H03 ~CACATCTCCAGATGTTCC
159_H04 ~CACATCTCCAGATGTTCC
159_H05 ~CACATCTCCAGATGTTCC
159_H06 ~CACATCTCCAGATGTTCC
159_H07 ~TCCAATCTTTTATCaCaTCCTCCAGATGTTCC
159_H08 ~CACATCTCCAGATGTTCC
159_H09 ~CaCaTCCTCCAGATGTTCC
159_H10 ~CACATCTCCAGATGTTCC
159_H11 ~CaCaTCCTCCAGATGTTCC
159_H12 ~CACATCTCCAGATGTTCC
159_H13 ~TCCAATCTTTTATCaCaTCCTCCAGATGTTCC
159_H14 ~TCCAATCTTTTATCACATCTCCAGATGTTcC
159_H15 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H16 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H17 ~CACATCTCCAGATGTTCC
159_H18 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H19 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H20 ~CACATCTCCAGATGTTCC
159_H21 ~CACATCTCCAGATGTTCC
159_H22 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H23 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H24 ~CACATCTCCAGATgTTCC
159_H25 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H26 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H27 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H28 ~CACATCTCCAGATGTTCC
159_H29 ~CaCaTCCTCCAGATGTTCC
159_H30 ~CACATCTCCAGATGTTCC
159_H31 ~CACATCTCCAGATGTTCC
159_H32 ~CACATCTCCAGATGTTCC
159_H33 gaTgTTcTCCAATCTTTTATCACATCTCCAGATGTTCC
159_H34 ~CACATCTCCAGATGTTCC
159_H35 ~TCCAATCTTTTATCACATCTCCAGATGTTCC
159_H36 TCTCTTTCCCAATCTTTTATCACATCTCCAGATGTTCC
159_H37 ~CACATCTCCAGATGTTCC
159_H38 ~CACATCTCCAGATGTTCC
159_H39 ~CACATCTCCAGATGTTCC
159_H40 ~TCCAATCTTTTATCACATCTCCAGATGTTCC

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159 H41 ~~~~~CACATCTCCAGATGTTCC
159 H42 ~~~~~CACATCTCCAGATGTTCC

Table S9. Full data listing the PF3D7_1337500 (K13_151) and PF3D7_1339700 (K13_159) alleles, located 200 kb upstream from K13 on chromosome 13 and their flanking haplotype number by K13 mutants (C580Y, Y493H, R539T, I543T, P553L, P574L, E605K, F446I, N458Y, R561H, A578S, S522C, V589I) in 359 continent- or country-shared samples collected in the KARMA study 2014 and previously in Cambodia in 2002 and 2004-2005 (C580Y). Colored backgrounds indicate individual countries.

C580Y

Continent	Region	Country	Resident/ Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
ASIA	Southeast Asia	Cambodia	Resident	Battambang	2013	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Battambang	2013	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Kampong Thom	2012	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Kampong Thom	2012	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Kampong Thom	2012	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Kampong Thom	2012	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2013	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2014	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2014	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2013	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Mondulkiri	2014	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Mondulkiri	2013	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Mondulkiri	2013	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Oddar Meanchey	2012	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2002	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2002	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2002	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2002	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2002	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2002	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2002	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2002	C580Y	tgt to tat	151_H02	159_H25	151_H02/159_H25	29

ASIA	Southeast Asia	Cambodia	Resident	Kampong Thom	2012	C580Y	tgt to tat	151_H05	159_H06	151_H05/159_H06	36
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2013	C580Y	tgt to tat	151_H06	159_H06	151_H06/159_H06	37
ASIA	Southeast Asia	Thailand	Resident	Sai Yok District, Kanchanaburi Province	2013	C580Y	tgt to tat	151_H07	159_H05	151_H07/159_H05	42
ASIA	Southeast Asia	Thailand	Resident	Sai Yok District, Kanchanaburi Province	2013	C580Y	tgt to tat	151_H07	159_H05	151_H07/159_H05	42
ASIA	Southeast Asia	Thailand	Resident	Sai Yok District, Kanchanaburi Province	2013	C580Y	tgt to tat	151_H07	159_H05	151_H07/159_H05	42
ASIA	Southeast Asia	Thailand	Resident	Sai Yok District, Kanchanaburi Province	2013	C580Y	tgt to tat	151_H07	159_H05	151_H07/159_H05	42
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2013	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2014	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2013	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2013	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2014	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2013	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Vietnam	Resident	Gia Lai province	2013	C580Y	tgt to tat	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2012	C580Y	tgt to tat	151_H07	159_H09	151_H07/159_H09	45

ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	C580Y	tgt to tat	151_H07	159_H13	151_H07/159_H13	46
ASIA	Southeast Asia	Cambodia	Resident	Kampt	2013	C580Y	tgt to tat	151_H07	159_H25	151_H07/159_H25	49
ASIA	Southeast Asia	Cambodia	Resident	Stung Treng	2013	C580Y	tgt to tat	151_H07	159_H25	151_H07/159_H25	49
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2012	C580Y	tgt to tat	151_H07	159_H32	151_H07/159_H32	50
ASIA	Southeast Asia	Cambodia	Resident	Kampong Speu	2012	C580Y	tgt to tat	151_H07	159_H34	151_H07/159_H34	51
ASIA	Southeast Asia	Cambodia	Resident	Kampong Speu	2012	C580Y	tgt to tat	151_H07	159_H34	151_H07/159_H34	51
ASIA	Southeast Asia	Cambodia	Resident	Kampong Speu	2012	C580Y	tgt to tat	151_H08	159_H06	151_H08/159_H06	56
ASIA	Southeast Asia	Cambodia	Resident	Kampong Speu	2012	C580Y	tgt to tat	151_H08	159_H06	151_H08/159_H06	56
ASIA	Southeast Asia	Cambodia	Resident	Mondulkiri	2013	C580Y	tgt to tat	151_H08	159_H06	151_H08/159_H06	56
ASIA	Southeast Asia	Cambodia	Resident	Battambang	2012	C580Y	tgt to tat	151_H08	159_H09	151_H08/159_H09	57
ASIA	Southeast Asia	Cambodia	Resident	Oddar Meanchey	2012	C580Y	tgt to tat	151_H08	159_H09	151_H08/159_H09	57
ASIA	Southeast Asia	Cambodia	Resident	Oddar Meanchey	2012	C580Y	tgt to tat	151_H08	159_H09	151_H08/159_H09	57
ASIA	Southeast Asia	Cambodia	Resident	Oddar Meanchey	2012	C580Y	tgt to tat	151_H08	159_H09	151_H08/159_H09	57
ASIA	Southeast Asia	Cambodia	Resident	Oddar Meanchey	2012	C580Y	tgt to tat	151_H08	159_H09	151_H08/159_H09	57
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2013	C580Y	tgt to tat	151_H08	159_H09	151_H08/159_H09	57
ASIA	Southeast Asia	Cambodia	Resident	Rattanakiri	2013	C580Y	tgt to tat	151_H08	159_H25	151_H08/159_H25	59
ASIA	Southeast Asia	Cambodia	Resident	Rattanakiri	2013	C580Y	tgt to tat	151_H08	159_H25	151_H08/159_H25	59
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	C580Y	tgt to tat	151_H08	159_H34	151_H08/159_H34	61
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	C580Y	tgt to tat	151_H08	159_H34	151_H08/159_H34	61
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	C580Y	tgt to tat	151_H08	159_H34	151_H08/159_H34	61
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	C580Y	tgt to tat	151_H08	159_H34	151_H08/159_H34	61
ASIA	Southeast Asia	Cambodia	Resident	Mondulkiri	2013	C580Y	tgt to tat	151_H09	159_H06	151_H09/159_H06	62

Y493H

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype ID
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H04	159_H35	151_H04/159_H35	35

ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H04	159_H35	151_H04/159_H35	35
ASIA	Southeast Asia	Cambodia	Resident	Kampong Thom	2012	Y493H	tac to cac	151_H07	159_H03	151_H07/159_H03	41
ASIA	Southeast Asia	Cambodia	Resident	Kampong Thom	2012	Y493H	tac to cac	151_H07	159_H03	151_H07/159_H03	41
ASIA	Southeast Asia	Cambodia	Resident	Kampong Thom	2012	Y493H	tac to cac	151_H07	159_H03	151_H07/159_H03	41
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2012	Y493H	tac to cac	151_H07	159_H03	151_H07/159_H03	41
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	Y493H	tac to cac	151_H07	159_H03	151_H07/159_H03	41
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H07	159_H08	151_H07/159_H08	44
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2012	Y493H	tac to cac	151_H07	159_H34	151_H07/159_H34	51
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	Y493H	tac to cac	151_H07	159_H34	151_H07/159_H34	51
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	Y493H	tac to cac	151_H07	159_H34	151_H07/159_H34	51
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	Y493H	tac to cac	151_H07	159_H34	151_H07/159_H34	51
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	Y493H	tac to cac	151_H07	159_H34	151_H07/159_H34	51
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	Y493H	tac to cac	151_H07	159_H34	151_H07/159_H34	51
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H07	159_H35	151_H07/159_H35	52
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H07	159_H35	151_H07/159_H35	52
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H07	159_H35	151_H07/159_H35	52
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H07	159_H35	151_H07/159_H35	52
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H07	159_H35	151_H07/159_H35	52
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H07	159_H35	151_H07/159_H35	52
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	Y493H	tac to cac	151_H07	159_H35	151_H07/159_H35	52

ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	R539T	aga to aca	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	R539T	aga to aca	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pursat	2012	R539T	aga to aca	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Rattanakiri	2013	R539T	aga to aca	151_H07	159_H06	151_H07/159_H06	43
ASIA	Southeast Asia	Cambodia	Resident	Pailin	2012	R539T	aga to aca	151_H09	159_H06	151_H09/159_H06	62
ASIA	Southeast Asia	Cambodia	Resident	Oddar Meanchey	2012	R539T	tgt to tat	151_H09	159_H06	151_H09/159_H06	62

I543T

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
ASIA	Southeast Asia	Cambodia	Resident	Rattanakiri	2012	I543T	att to act	151_H07	159_H09	151_H07/159_H09	45
ASIA	Southeast Asia	Vietnam	Resident	Gia Lai province	2013	I543T	att to act	151_H07	159_H09	151_H07/159_H09	45
ASIA	Southeast Asia	Vietnam	Resident	Gia Lai province	2013	I543T	att to act	151_H07	159_H09	151_H07/159_H09	45
ASIA	Southeast Asia	Vietnam	Resident	Gia Lai province	2013	I543T	att to act	151_H07	159_H09	151_H07/159_H09	45
ASIA	Southeast Asia	Vietnam	Resident	Gia Lai province	2013	I543T	att to act	151_H07	159_H09	151_H07/159_H09	45
ASIA	Southeast Asia	Vietnam	Resident	Gia Lai province	2013	I543T	att to act	151_H09	159_H09	151_H09/159_H09	63

P553L

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
ASIA	Southeast Asia	Cambodia	Resident	Kratie	2013	P553L/WT	cgg to ctg	151_3D7	159_H06	151_3D7/159_H06	1
ASIA	Southeast Asia	Thailand	Resident	Mae Sot	2009	P553L	cgg to ctg	151_3D7	159_H09	151_3D7/159_H09	3
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	cgg to ctg	151_H04	159_H06	151_H04/159_H06	32
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	cgg to ctg	151_H04	159_H06	151_H04/159_H06	32
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	cgg to ctg	151_H06	159_H15	151_H06/159_H15	38
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	cgg to ctg	151_H06	159_H15	151_H06/159_H15	38
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	cgg to ctg	151_H06	159_H15	151_H06/159_H15	38
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	cgg to ctg	151_H06	159_H15	151_H06/159_H15	38

ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	ccg to ctg	151_H06	159_H15	151_H06/159_H15	38
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	ccg to ctg	151_H06	159_H15	151_H06/159_H15	38
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	ccg to ctg	151_H06	159_H15	151_H06/159_H15	38
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	ccg to ctg	151_H06	159_H15	151_H06/159_H15	38
ASIA	Southeast Asia	Vietnam	Resident	Dak Nong province	2013	P553L	ccg to ctg	151_H06	159_H15	151_H06/159_H15	38
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	P553L	ccg to ctg	151_H09	159_H03	151_H09/159_H03	66

P574L

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
ASIA	Southeast Asia	Thailand	Resident	Mae Sot	2006	P574L	cct to ttc	151_H03	159_H32	151_H03/159_H32	30
ASIA	Southeast Asia	Thailand	Resident	Suan Pheung District, Ratchaburi Province	2014	P574L	cct to ctt	151_H04	159_H04	151_H04/159_H04	31
ASIA	Southeast Asia	Thailand	Resident	Suan Pheung District, Ratchaburi Province	2014	P574L	cct to ctt	151_H04	159_H04	151_H04/159_H04	31
ASIA	East Asia	China	Resident	Tengchong	2008	P574L	cct to ctt	151_H07	159_H01	151_H07/159_H01	40
ASIA	Southeast Asia	Thailand	Resident	Sai Yok District, Kanchanaburi Province	2013	P574L	cct to ctt	151_H07	159_H32	151_H07/159_H32	50
ASIA	Southeast Asia	Thailand	Resident	Sai Yok District, Kanchanaburi Province	2013	P574L	cct to ctt	151_H07	159_H32	151_H07/159_H32	50
ASIA	East Asia	China	Resident	Tengchong	2012	P574L	cct to ctt	151_H08	159_H05	151_H08/159_H05	55
ASIA	Southeast Asia	Thailand	Resident	Ranong	2009	P574L	cct to ttc	151_H08	159_H32	151_H08/159_H32	60
ASIA	Southeast Asia	Thailand	Resident	Ranong	2010	P574L	cct to ttc	151_H08	159_H32	151_H08/159_H32	60
ASIA	East Asia	China	Resident	Yingjiang	2011	P574L	cct to ctt	151_H09	159_H34	151_H09/159_H34	64

E605K

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	E605K	gaa to aaa	151_H08	159_H01	151_H08/159_H01	53
ASIA	Southeast Asia	Vietnam	Resident	Binh Phuoc province	2013	E605K	gaa to aaa	151_H08	159_H01	151_H08/159_H01	53
ASIA	East Asia	China	Resident	Tengchong	2009	E605K	gaa to aaa	151_H08	159_H03	151_H08/159_H03	54

F446I

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_3D7	159_H28	151_3D7/159_H28	19
ASIA	East Asia	China	Resident	Tengchong	2008	F446I	ttt to att	151_H01	159_H28	151_H01/159_H28	27
ASIA	East Asia	China	Resident	Tengchong	2012	F446I	ttt to att	151_H04	159_H06	151_H04/159_H06	32
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_3D7	159_H39	151_3D7/159_H39	69
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_3D7	159_H39	151_3D7/159_H39	69
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_3D7	159_H42	151_3D7/159_H42	71
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_3D7	159_H42	151_3D7/159_H42	71
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_3D7	159_H42	151_3D7/159_H42	71
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_H04	159_H03	151_H04/159_H03	72
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73

ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H04	159_H05	151_H04/159_H05	73
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H05	159_H28	151_H05/159_H28	75
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_H08	159_H28	151_H08/159_H28	77
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H08	159_H28	151_H08/159_H28	77
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H08	159_H28	151_H08/159_H28	77
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H08	159_H28	151_H08/159_H28	77
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H08	159_H28	151_H08/159_H28	77
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H08	159_H42	151_H08/159_H42	79
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	F446I	ttt to att	151_H09	159_H35	151_H09/159_H35	80
ASIA	East Asia	Myanmar	Resident	Tamu	2014	F446I	ttt to att	151_H09	159_H35	151_H09/159_H35	80

N458Y

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	N458Y	aat to tat	151_H05	159_H21	151_H05/159_H21	76
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	N458Y	aat to tat	151_H05	159_H40	151_H05/159_H40	78
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	N458Y	aat to tat	151_H05	159_H40	151_H05/159_H40	78
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	N458Y	aat to tat	151_H05	159_H40	151_H05/159_H40	78

R561H

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	R561H	cgt to cat	151_3D7	159_H40	151_3D7/159_H40	72
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	R561H	cgt to cat	151_3D7	159_H40	151_3D7/159_H40	72
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	R561H	cgt to cat	151_3D7	159_H40	151_3D7/159_H40	72
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	R561H	cgt to cat	151_3D7	159_H40	151_3D7/159_H40	72
ASIA	East Asia	Myanmar	Resident	Tamu	2014	R561H	cgt to cat	151_3D7	159_H40	151_3D7/159_H40	72
ASIA	East Asia	Myanmar	Resident	Tamu	2014	R561H	cgt to cat	151_3D7	159_H40	151_3D7/159_H40	72
ASIA	East Asia	Myanmar	Resident	Tamu	2014	R561H	cgt to cat	151_3D7	159_H40	151_3D7/159_H40	72
ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	R561H	cgt to cat	151_H08	159_H41	151_H08/159_H41	80

ASIA	East Asia	Myanmar	Resident	Pyin Oo Lwin	2014	R561H	cgt to cat	151_H08	159_H41	151_H08/159_H41	80
ASIA	East Asia	Myanmar	Resident	Tamu	2014	R561H	cgt to cat	151_H08	159_H41	151_H08/159_H41	80
ASIA	East Asia	Myanmar	Resident	Tamu	2014	R561H	cgt to cat	151_H08	159_H41	151_H08/159_H41	80

A578S

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
AFRICA	West Africa	Ivory Cost	Resident	NA	2013	A578S	gct to tct	151_3D7	159_H07	151_3D7/159_H07	2
AFRICA	Central Africa	Chad	Traveler	NA	2013	A578S	gct to tct	151_3D7	159_H10	151_3D7/159_H10	4
AFRICA	Indian Ocean	Comoros	Resident	Grande Comore_Foumbouni	2011	A578S	gct to tct	151_3D7	159_H11	151_3D7/159_H11	5
AFRICA	Indian Ocean	Comoros	Resident	Grande Comore_Moroni	2011	A578S	gct to tct	151_3D7	159_H11	151_3D7/159_H11	5
AFRICA	East Africa	Kenya	Resident	Ahero	2011	A578S	gct to tct	151_3D7	159_H12	151_3D7/159_H12	6
AFRICA	Central Africa	Cameroon	Resident	NA	2013	A578S	gct to tct	151_3D7	159_H13	151_3D7/159_H13	7
AFRICA	West Africa	Guinea	Traveler	NA	2014	A578S	gtc to atc	151_3D7	159_H14	151_3D7/159_H14	8
AFRICA	Central Africa	DRC	Resident	Kinshasa	2013	A578S	gct to tct	151_3D7	159_H16	151_3D7/159_H16	9
AFRICA	Indian Ocean	Comoros	Resident	Grande Comore_Moroni	2013	A578S	gct to tct	151_3D7	159_H17	151_3D7/159_H17	10
AFRICA	West Africa	Ivory Cost	Resident	NA	2014	A578S	gtc to atc	151_3D7	159_H19	151_3D7/159_H19	11
AFRICA	West Africa	Niger	Resident	Maradi, Madarounfa	2013	A578S	gct to tct	151_3D7	159_H20	151_3D7/159_H20	12
AFRICA	West Africa	Benin	Traveler	NA	2014	A578S	gct to tct	151_3D7	159_H21	151_3D7/159_H21	13
AFRICA	West Africa	Niger	Resident	Niamey	2013	A578S	gct to tct	151_3D7	159_H22	151_3D7/159_H22	14
AFRICA	East Africa	Kenya	Resident	Ahero	2013	A578S/WT	gct to tct	151_3D7	159_H23	151_3D7/159_H23	15
AFRICA	West Africa	Niger	Resident	Niamey	2013	A578S	gct to tct	151_3D7	159_H23	151_3D7/159_H23	15
AFRICA	Central Africa	DRC	Resident	Kinshasa	2013	A578S	gct to tct	151_3D7	159_H25	151_3D7/159_H25	16
AFRICA	Central Africa	Cameroon	Resident	Yaounde	2013	A578S	gct to tct	151_3D7	159_H26	151_3D7/159_H26	17
AFRICA	Southern Africa	Zambia	Resident	NA	2012	A578S	gct to tct	151_3D7	159_H27	151_3D7/159_H27	18
AFRICA	West Africa	Guinea	Traveler	NA	2013	A578S	gct to tct	151_3D7	159_H28	151_3D7/159_H28	19
AFRICA	West Africa	Niger	Resident	Maradi, Madarounfa	2013	A578S	gct to tct	151_3D7	159_H28	151_3D7/159_H28	19

AFRICA	West Africa	Burkina Faso	Resident	Colsama	2012	A578S/WT	gct to tct	151_3D7	159_H29	151_3D7/159_H29	20
AFRICA	West Africa	Mali	Resident	NA	2013	A578S/WT	gct to tct	151_3D7	159_H30	151_3D7/159_H30	21
AFRICA	Central Africa	Cameroon	Resident	Yaounde	2013	A578S	gct to tct	151_3D7	159_H31	151_3D7/159_H31	22
AFRICA	Central Africa	CAR	Resident	Bangui	2009	A578S	gct to tct	151_3D7	159_H31	151_3D7/159_H31	22
AFRICA	East Africa	Uganda	Resident	Mbarara	2010	A578S	gct to tct	151_3D7	159_H32	151_3D7/159_H32	23
AFRICA	East Africa	Uganda	Resident	Mbarara	2010	A578S	gct to tct	151_3D7	159_H33	151_3D7/159_H33	24
AFRICA	East Africa	Uganda	Resident	Mbarara	2010	A578S	gct to tct	151_3D7	159_H37	151_3D7/159_H37	26
AFRICA	Central Africa	Cameroon	Resident	NA	2013	A578S	gct to tct	151_H02	159_H23	151_H02/159_H23	28
AFRICA	East Africa	Kenya	Resident	Ahero	2012	A578S	gct to tct	151_H06	159_H24	151_H06/159_H24	39
AFRICA	East Africa	Kenya	Resident	Ahero	2012	A578S	gct to tct	151_H07	159_H18	151_H07/159_H18	47
AFRICA	Central Africa	DRC	Resident	Kinshasa	2013	A578S	gct to tct	151_H07	159_H23	151_H07/159_H23	48
AFRICA	Indian Ocean	Comoros	Resident	Grande Comore_Foumbouni	2013	A578S	gct to tct	151_H07	159_H35	151_H07/159_H35	52
ASIA	Southeast Asia	Thailand	Resident	Mae Sot	2009	A578S	gct to tct	151_H08	159_H10	151_H08/159_H10	58
ASIA	Southeast Asia	Bangladesh	Resident	Khagrachari	2009-2013	A578S	gct to tct	151_H04	159_H38	151_H04/159_H38	69
ASIA	Southeast Asia	Bangladesh	Resident	Khagrachari	2009-2013	A578S	gct to tct	151_3D7	159_H38	151_3D7/159_H38	70

S522C

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
AFRICA	East Africa	Kenya	Resident	Ahero	2012	S522C	agt to tgt	151_3D7	159_H20	151_3D7/159_H20	12
AFRICA	Central Africa	Gabon	Traveler	NA	2013	S522C	gct to tct	151_3D7	159_H23	151_3D7/159_H23	15
AFRICA	Central Africa	CAR	Traveler	NA	2013	S522C/WT	agt to tgt	151_3D7	159_H36	151_3D7/159_H36	25

V589I

Continent	Region	Country	Resident /Travelers	Sample Location	Year of collection	K13 allele	Nucleotide change	K13_151 allele	K13_159 allele	Haplotypes	Flanking Haplotype_ID
AFRICA	West Africa	Burkina Faso	Resident	Colsama	2012	V589I	gtc to atc	151_3D7	159_H23	151_3D7/159_H23	15
AFRICA	Central Africa	CAR	Resident	Bangui	2009	V589I	gtc to atc	151_3D7	159_H23	151_3D7/159_H23	15

AFRICA	Indian Ocean	Madagascar	Resident	Toamasina	2012	V589I	gtc to atc	151_3D7	159_H23	151_3D7/159_H23	15
AFRICA	Central Africa	Cameroon	Resident		2013	V589I/WT	gtc to atc	151_3D7	159_H23	151_3D7/159_H23	15

NA: Not available

Table S10. List of the flanking haplotypes shared by different K13 NS-mutations by continent and country, KARMA study 2014-2015.

Flanking Haplotype ID	K13 allele (No. of isolates)		Continental distribution	Country location	
12	A578S (1)	S522C (1)	African background	Niger/Kenya	
15	A578S (2)	S522C (1)	V589I (4)	African background	Niger/Kenya/Gabon/Burkina Faso/CAR/Madagascar/Cameroon
19	F446I (1)	A578S (2)	Asian/African background	Niger/Guinea/Myanmar	
32	F446I (1)	P553L (2)	Asian background	China/Vietnam	
43	C580Y (17)	R539T (26)	Y493H (1)	Asian background	Cambodia/Vietnam
45	C580Y (1)	I543T (6)	Asian background	Cambodia/Vietnam	
50	C580Y (1)	P574L (2)	Asian background	Cambodia/Thailand	
51	C580Y (2)	Y493H (7)	Asian background	Cambodia/Vietnam	
52	A578S (1)	Y493H (8)	Asian/African background	Cambodia/Comoros	
62	C580Y (1)	R539T (2)	Asian background	Cambodia	
69	A578S (1)	F446I (2)	Asian background	Bangladesh/Myanmar	
72	F446I (2)	R561H	Asian background	Myanmar	