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Supplementary information

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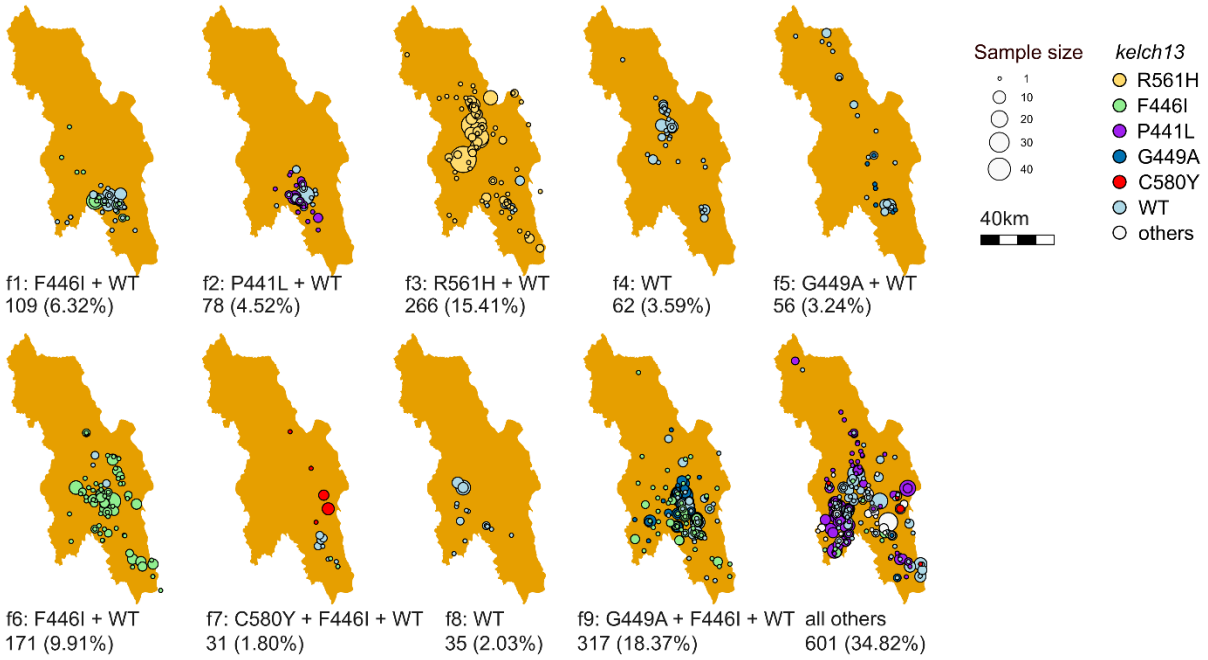
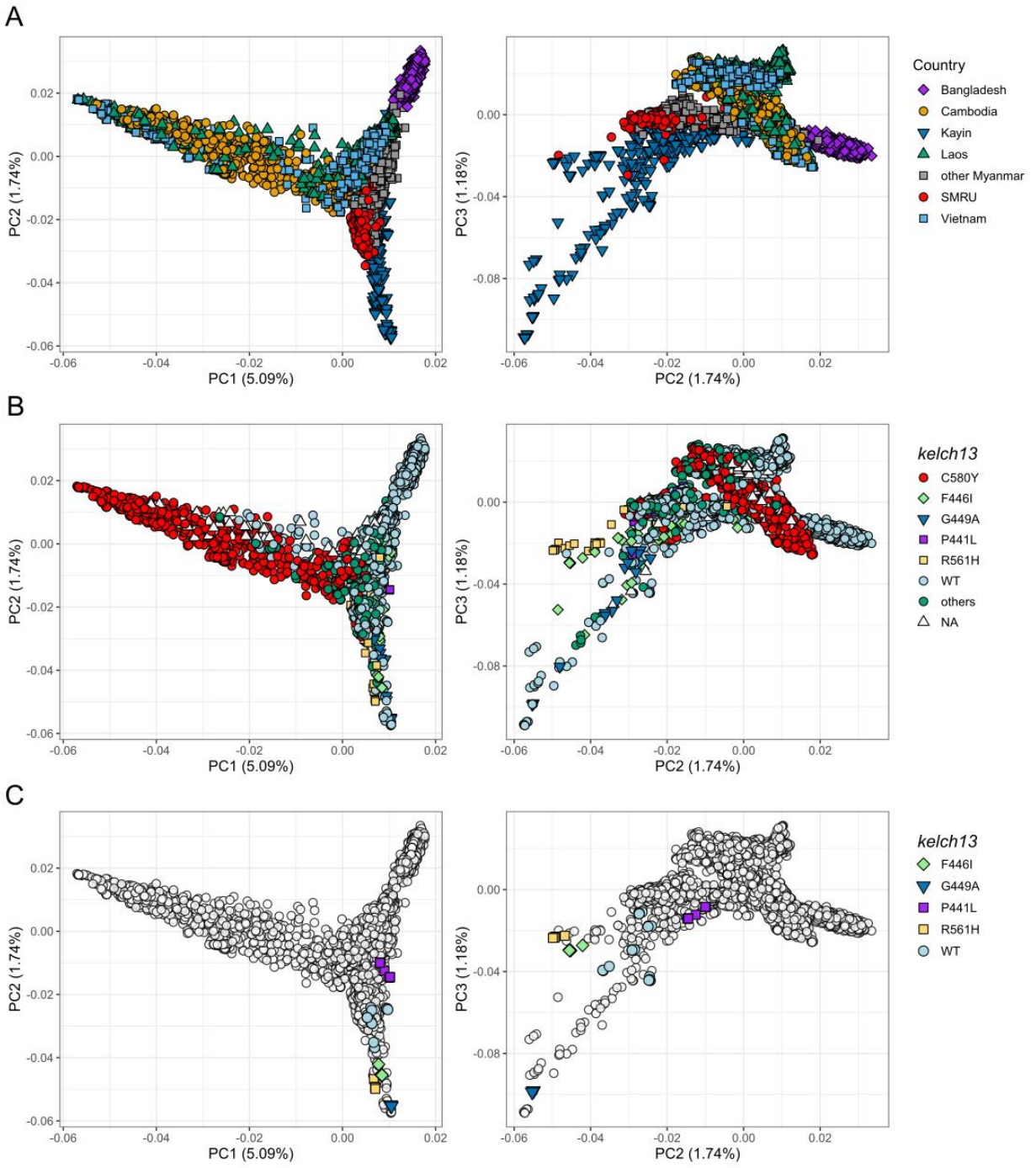
Impact of intensive control on malaria population genomics under elimination settings in Southeast Asia

In the format provided by the authors and unedited

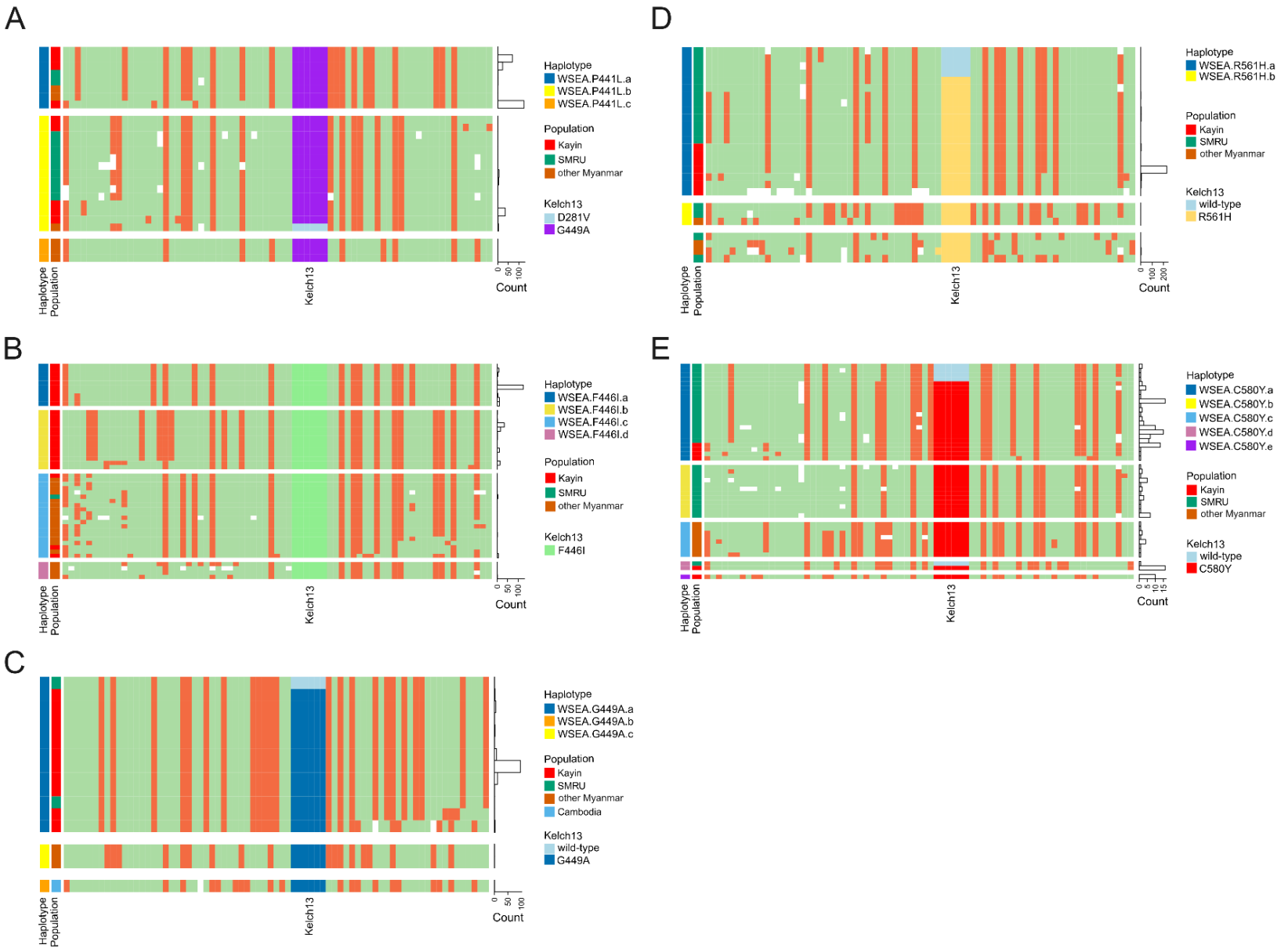


Supplementary Figure 1. Geographic distribution of closely related parasite families. Families are defined as a group of parasites that share over 45% of their genome ($r \geq 0.45$).



Supplementary Figure 2. Principal component analysis (PCA) comparing Southeast Asian populations.

(A, B) PCA plots of the first three components. Each point represents a sample, which was colored according to the geographical origin (A) or *kelch13* alleles (B). (C) Placement of the top ten unique genomes from Kayin state in PCA plots.


A
Haplotype
WSEA.P441L.a
WSEA.P441L.b
WSEA.P441L.c
Population
Kayin
SMRU
other Myanmar
Kelch13
D281V
G449A
Haplotype
Population
Kelch13
Count
B
Haplotype
WSEA.F446I.a
WSEA.F446I.b
WSEA.F446I.c
WSEA.F446I.d
Population
Kayin
SMRU
other Myanmar
Kelch13
F446I
C
Haplotype
WSEA.G449A.a
WSEA.G449A.b
WSEA.G449A.c
Population
Kayin
SMRU
other Myanmar
Cambodia
Kelch13
wild-type
G449A
D
Haplotype
WSEA.R561H.a
WSEA.R561H.b
Population
Kayin
SMRU
other Myanmar
Kelch13
wild-type
R561H
E
Haplotype
WSEA.C580Y.a
WSEA.C580Y.b
WSEA.C580Y.c
WSEA.C580Y.d
WSEA.C580Y.e
Population
Kayin
SMRU
other Myanmar
Kelch13
wild-type
C580Y

Supplementary Figure 3. Compare *kelch13* haplotypes from Southeast Asia.

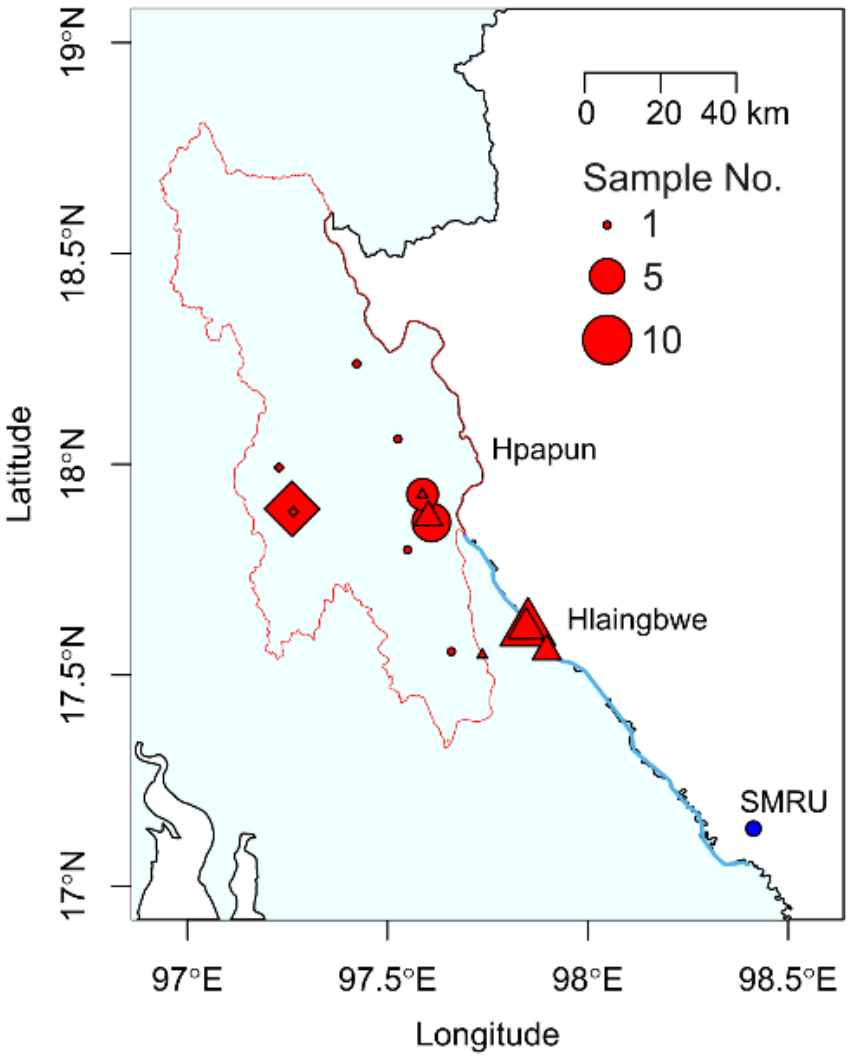
(A) P441L. Two *kelch13* haplotypes carrying P441L mutation were detected in Kayin. Both of them have also been found either in SMRU or other Myanmar regions, despite their low allele frequency in those regions.

(B) F446I. Three F446I haplotypes were observed in Kayin. The most common two haplotypes were only found in Kayin and were at high allele frequencies (9.72% and 5.22%), suggesting that they originated locally and have not been transmitted to other locations. The third F446I haplotype was more common in north Myanmar with only few cases found in Kayin.

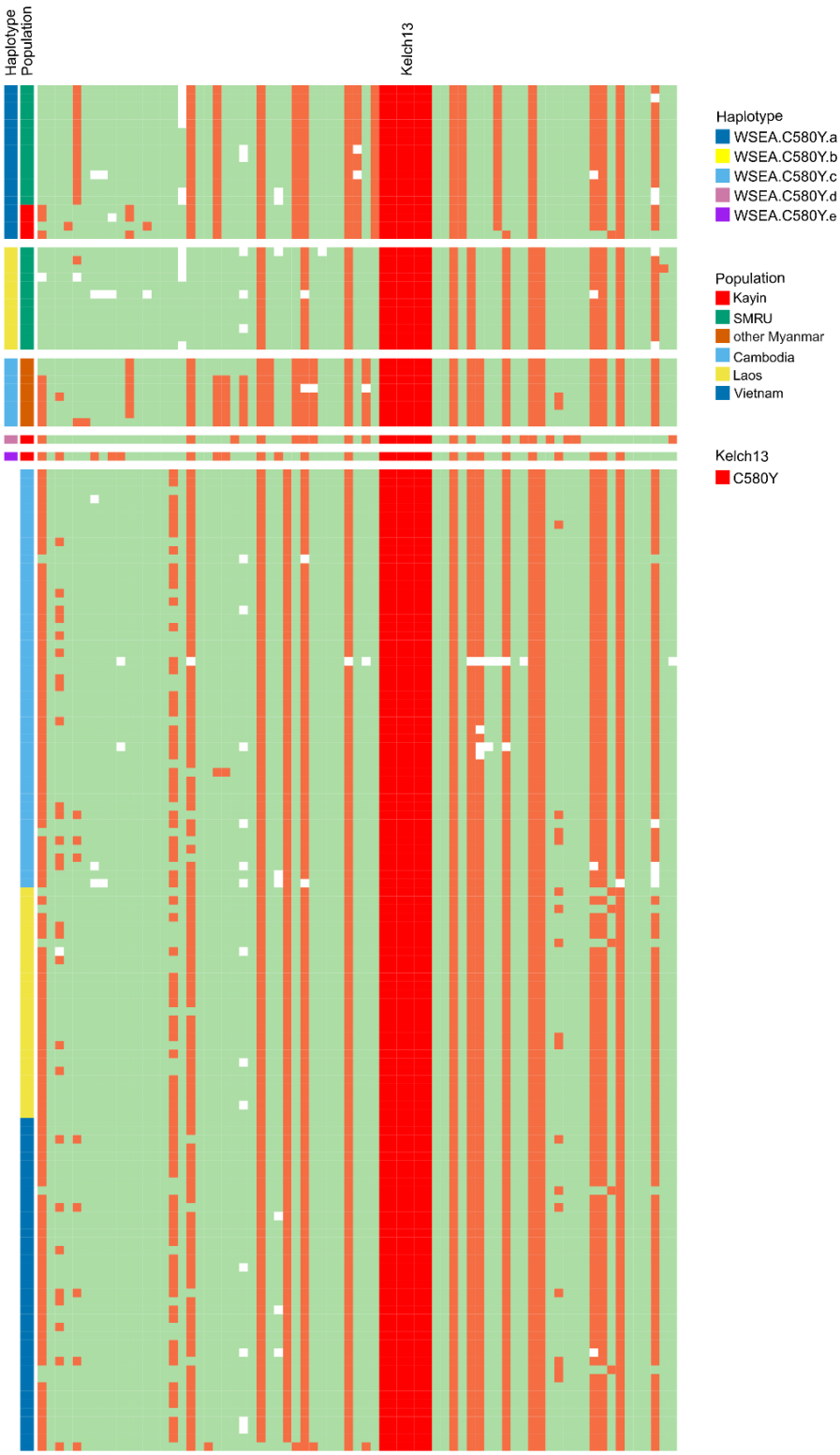
(C) G449A. One unique haplotype carrying G449A was detected in Kayin and also observed in in SMRU. The same haplotype carrying wild-type *kelch13* was found from SMRU in 2001, suggesting it might have originated from the SMRU region. However, we cannot locate where the G449A mutation took place.

(D) R561H. Multiple haplotypes have been found to be associated with the R561H mutation in western SE Asia, but only one of them was found in Kayin (named WSEA.R561H.a). The *kelch13* wild-type version of WSEA.R561H.a haplotype was detected from SMRU in 2002 and 2004, while the *kelch13*-R561H on this haplotype was not detected until 2012. Comparing the wild-type and mutant WSEA.R561H.a from SMRU, the Kayin R561H haplotype has been broken down by recombination, suggesting the spread of this haplotype was not a recent event.

(E) C580Y. Four haplotypes were detected, with three of them found in Kayin. Two of the haplotypes were detected in both Kayin and SMRU, and one of them was dominant *kelch13* mutant alleles in SMRU.



Supplementary Figure 4. Distribution of samples carrying *kelch13-C580Y* haplotypes in Kayin state.
Three *kelch13*-C580 haplotypes (represented by different shapes) were identified in Kayin state. Two haplotypes (circles and triangles) were also observed among patients attending Shoklo Malaria Research Unit (SMRU) clinics. The *kelch13*-C580Y allele was at highly frequency (≥ 90%) at malaria posts in Hlaingbwe Township (located between SMRU and Hpapun Township), but less common (<10%) in Hpapun Township (outlined in red).



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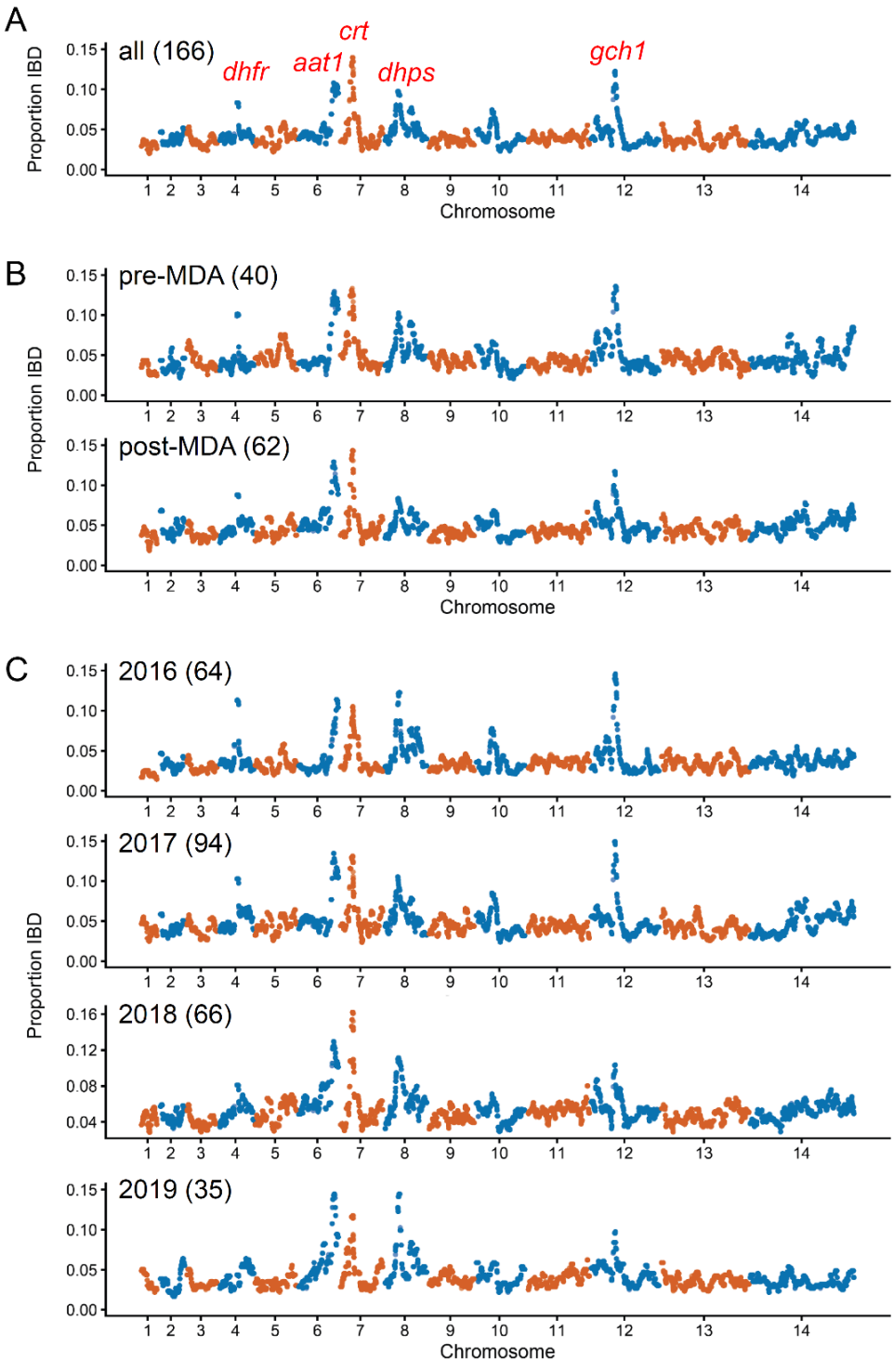
Supplementary Figure 5. Compare *kelch13*-C580Y haplotypes from Southeast Asia. No *kelch13*-C580Y haplotype was shared between west and east southeast Asia.



Supplementary Figure 6. Genome-wide scan of selection using shared IBD.
(A) Proportion of pairwise identity-by-descent (IBD) at each genomic position among 166 unique genomes. Strong IBD peaks are observed at known antimalarial resistance loci (*dhfr*, *aat1*, *crt*, *dhps*, *gch1*). (B) Comparison of IBD profiles between pre-MDA (n = 40) and post-MDA (n = 62) samples. (C) Annual IBD profiles for samples collected from 2016 to 2019. Only 13 unique genomes were available for 2020, so this year was excluded from analysis.