

TABLE S1. Lineage, parasitological, treatment, genotyping and antimalarial resistance profile of *Plasmodium falciparum* C2A in *Aotus* monkeys

| Passage Level | ID | Inoculation Date | Donor | Inoculum Preservative description | Inoculation route | Inoculum Size | Day of Patency | Peak Asexual Parasitemia x uL x 10 ³ | Day of Peak | Day of primary Treatment | Primary treatment administration route | Day of Clearance | Days to clear from end of primary treatment | Primary treatment disposition | Day of Recrudescence | Day of Retreatment | Final Disposition | Treatment regimen (mg per kg/day:Day Pt) | Production of Gametocytes Yes or No | Gametocyte day of patency | Gametocyte Peak x 10 ³ | Gametocyte Pt Day of Peak | Gametocyte day of clearance | Gametocyte day of recrudescence | |
|---------------|-------------|------------------|-------|-----------------------------------|-------------------|-----------------------|----------------|---|-------------|--------------------------|--|------------------|---|-------------------------------|----------------------|--------------------|-------------------|---|-------------------------------------|---------------------------|-----------------------------------|---------------------------|-----------------------------|---------------------------------|--|
| I | TM92CA-WR9R | | | | | | | | | | | | | | | | | | | | | | | | |
| I | 89005 | 12/14/98 | | Culture | IP | nd | 73 | 10.50 | 84 | | | 90 | | | | | self-cured | None | Yes | 77 | 0.01 | 77 | 106 | | |
| II | 92015 | 2/26/99 | 89005 | Citrate | IV | >10 | 2 | 20.12 | 22 | 73 | Oral | 93 | 20 | cured | | | cured | MQ (40/3:73) | Yes | 6 | 260 | 82 | 7, 22, 33, 93 | 16, 24, 74 | |
| III | 92034 | 5/7/99 | 92015 | Citrate | IV | 18120 | 1 | 85.12 | 11 | 11 | Oral | 55 | 43 | failed | 95 | | self-cured | MQ (20/1:11) | Yes | 5 | >0.01 | 14 | 7, 43 | 12 | |
| III | 24058 | 11/24/09 | 92015 | Glycerol-EDTA | IP | 42280 | 19 | 56.43 | 27 | 27 | Oral/IV | 31 | 2 | cured | | | cured | MQ (40/1:27), AS_IV (30/3:27) | Yes | 27 | >0.01 | 29 | 30 | | |
| III | 24058 | 11/24/09 | 92015 | Glycerol-EDTA | IP | 42280 | | | | | | | | | | | | | | | | | | | |
| IV | 93014 | 8/12/99 | 92034 | Citrate | IV | >10 | 3 | 121.50 | 8 | 8 | | 41 | 30 | failed | | 22, 42 | died | ART (8/3:8)/(16/3:22), QN (20/2:43) | Yes | 15 | 0.01 | 15 | 19, 21, 34, 37 | 20, 27, 36 | |
| IV | 26008 | 12/21/09 | 24058 | RPMI | IV | 5.0 x 10 ⁶ | 1 | 50.27 | 8 | 9 | Oral/IV | 13 | 2 | cured | | | self-cured | MQ (40/1:9), AS_IV (33/3:9) | Yes | 9 | >0.01 | 9 | 11 | | |
| IV | 26048A | 12/21/09 | 24058 | RPMI | IV | 5.0 x 10 ⁶ | 1 | 0.35 | 4 | | | 8 | | | | | self-cured | None | No | | | | | | |
| V | 12801 | 5/2/02 | 93014 | Glycerol-EDTA | IP | 121500 | 7 | 113.52 | 25 | 26 | Oral | | | | | 33, 46, 48 | died | MQ (20/1:26), QN (20/3:33), QN (20/2:40), P226 (40/3:48) | No | | | | | | |
| VI | 12907 | 5/24/02 | 12801 | Citrate | IV | 4860 | 2 | 121.50 | 11 | 14 | Oral | 39 | 20 | failed | | 26, 38 | cured | QN (20/5:14), P526 (20/3:26), MQ (40/1:38) | No | | | | | | |
| VII | 12804 | 6/7/02 | 12907 | Citrate | IV | 23500 | 1 | 72.42 | 6 | 11 | Oral | | | | | 12 | | QN (20/1:11), P526 (10/3:12) | No | | | | | | |
| VIII | 13112 | 6/18/02 | 12804 | Citrate | IV | 27750 | 1 | 87.75 | 6 | 7 | Oral | | | failed | | 13 | died | WR283178/40/3:7), MQ (40/1:13) | No | | | | | | |
| VIII | 12753 | 7/13/07 | 12907 | Glycerolate | IV | 121510 | 15 | 6.59 | 21 | 21 | Oral | 28 | 7 | failed | 70 | 26, 81 | cured | MQ (40/1:21), AS_IV (20/3:26), MQ (40/1:81)/AS (8/3:81) | No | | | | | | |
| VIII | 90025 | 8/3/07 | 12753 | Citrate | IV | 6590 | 2 | 1.13 | 7 | 60 | Oral | 17 | | | | | cured | MQ (40/1:60), AS/8/3:60) | No | | | | | | |
| VIII | 24049 | 4/17/08 | 12753 | Glycerolate | IV | 6590 | 4 | 266.76 | 12 | 12 | IV | 24 | 10 | failed | 45 | 21, 69 | cured | AS_IV (20/3:12), MAL (25/3:21), AS_IV (20/3:69), MQ (40/1:69) | No | | | | | | |
| IX | 26006 | 4/7/09 | 24049 | Glycerolate | IV | 266,760 | | 115.25 | 7 | 8 | Oral/IV | 19 | 9 | failed | 14 | 17 | cured | MQ (40/1:8), AS_IV (20/3:8), MQ (40/1:17), AS_IV (20/3:17) | No | | | | | | |
| X | 26058 | 4/15/09 | 26006 | RPMI | IV | 5.0 x 10 ⁶ | 2 | 104.31 | 11 | 11 | Oral | 28 | 17 | failed | 20 | 27 | cured | MQ(40/1:11), AS_IV(20/3:27), MQ(40/2:29) | No | | | | | | |
| X | 26033 | 4/15/09 | 26006 | RPMI | IV | 5.0 x 10 ⁶ | 2 | 272.74 | 9 | 9 | Oral | 23 | 14 | failed | | 16 | cured | MQ(40/1:9), AS(33/3:16) | No | | | | | | |
| X | 26028 | 4/15/09 | 26006 | RPMI | IV | 5.0 x 10 ⁶ | 1 | 449.73 | 9 | 9 | Oral | 23 | 12 | failed | | 21 | cured | AS(33/3:9), AS_IV(20/3:21), MQ(40/1:23) | No | | | | | | |
| X | 26045 | 4/15/09 | 26006 | RPMI | IV | 5.0 x 10 ⁶ | 2 | 110.58 | 11 | 11 | Oral | 23 | 12 | failed | | 21 | cured | AS(33/3:11), AS_IV(20/3:21), MQ (40/1:23) | No | | | | | | |
| X | 26063 | 4/15/09 | 26006 | RPMI | IV | 5.0 x 10 ⁶ | 2 | 177.84 | 9 | 9 | Oral | 28 | 17 | failed | | 27 | cured | MQ (40/1:9), AS (33/3:9), AS_IV (20/3:27), MQ (40/1:29) | No | | | | | | |
| X | 26025 | 4/15/09 | 26006 | RPMI | IV | 5.0 x 10 ⁶ | 2 | 106.02 | 10 | 10 | Oral | 24 | 12 | failed | 20 | | cured | MQ(40/1:10), AS(33/3:12), MQ (40/1:29) | No | | | | | | |
| X | 23042A | 4/15/09 | 26006 | RPMI | IV | 5.0 x 10 ⁶ | 2 | 0.34 | 17 | 16 | Oral | 18 | -1 | cured | | | cured | AS(33/3:16), MQ(40/1:18) | No | | | | | | |
| MIN | | | | | | | 1 | 0.34 | 4 | 7 | | 8 | -1 | | | | | | | 5 | | | | 9 | |
| Q1 | | | | | | | 1 | 17.715 | 7.75 | 9 | | 19 | 7.5 | | | | | | | 5.75 | | | | 12.75 | |
| Median | | | | | | | 2 | 96.03 | 10.5 | 11 | | 24 | 12 | | | | | | | 12 | | | | 22 | |
| Q3 | | | | | | | 3.5 | 121.5 | 18 | 19.75 | | 39 | 19.25 | | | | | | | 39.5 | | | | 78.25 | |
| MAX | | | | | | | 73 | 449.73 | 84 | 73 | | 93 | 43 | | | | | | | 77 | | | | 82 | |

λ = Spleen intact
 * = Repeat
 ** = PfPR

Primer sequences

MDR1-T1F 5'-TATGCATTTGTGGGAGAATCAG-3'

MDR1-T1R 5'-CTCCTTCGGTTGGATCATAAAG-3'

LDH-T1F 5'-AGGACAATATGGACACTCCGAT-3' and

LDH-T1R 5'-TTTCAGCTATGGCTTCATCAA-3'

1F: 5'-ATGGAAGGAGAAAAAGTAAAAACAAAAGCAAATAG-3'

2F: 5'-GGTAGGTGATTTAAGAATTACATTTATTAATTGGT-3'; 3F: 5'-

CATTCCCATTAGTATTTTGTATAGGTG-3'

1R: 5'-TTATATATTTGCTATTAACCGGAGTGACCAAATCTG-3'

1R': 5'-TTA TAT ATT TGC TAT TAA AAC GGA GTG-3'

2R: 5'-AGCCTTATAATCATAGTTATTACCACCAAAAACG-3'

3R: 5'-TGTTGGTATTCATAATTGATGGAGAATTC-3'

PFB0075c-F 5'-GGGCGGCCGCATGAAAATATGAGAAGTTTAAAG-3'

PFB0075c-R 5'-CCGCTAGCACTAGTGAATATAATAAAAATTACGATGGAGAA-3'

PF11710w-F 5'-CCTGAACACTTGAAAATGGAAA-3'

PF11710w-R 5'-AAACGAAAAGATTGAAATGGA-3'

PF11755c-F 5'-ACCTGATCCTAGTGTACCCTCTCT-3'

PF11755c-R 5'-GAAGAACTTGTACTTGGTTTAGCCG-3'

PF11780w-F 5'-AAAACACTAGTATGTTTTTATGTAGGTTATGAG-3'

PF11780w-R 5'-AAACTTAAGCTCTCAGATTCATGTACATAAC-3'

Table S3. Average parasite day of clearance of *Plasmodium falciparum* infections in splenectomized or spleen intact Aotus monkeys after treatment with mefloquine and artesunate alone or in combination

| Aotus infection groups | | | | | |
|--|-------------------------|-----------|-----------|-----------------|-----------------|
| <i>P. falciparum</i> strain | C2A | C2A | C2A | C2A | C2A |
| Passage level | III-IV | X | X | X | X |
| Splenectomized | <i>y</i> | <i>y</i> | <i>y</i> | <i>y</i> | <i>n</i> |
| Treatment regimens | | | | | |
| Drug | AS / MQ | MQ | AS | AS / MQ | AS / MQ |
| mg/Kg x (days) | 33 (3) / 40 (1) | 40 (1) | 33 (3) | 33 (3) / 40 (1) | 33 (3) / 40 (1) |
| Route | <i>i.v.</i> / <i>po</i> | <i>po</i> | <i>po</i> | <i>po</i> | <i>po</i> |
| Treatment outcome (individual Aotus day of clearance*) | | | | | |
| | 5 | 15** | 15** | 15 | 3 |
| | 5 | 17** | 13** | 20** | - |
| | - | - | - | - | - |
| Average | 5 | 16 | 14 | 17.5 | 3 |

* = day after initiation of treatment

** = did not clear with primary treatment

AS = artesunate

i.v. = intravenously

nd = not determine

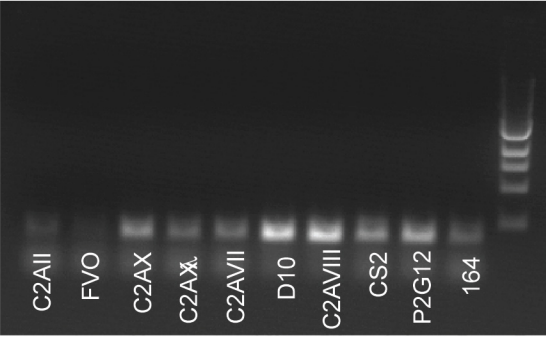
MQ = mefloquine

po = *per os* (orally)

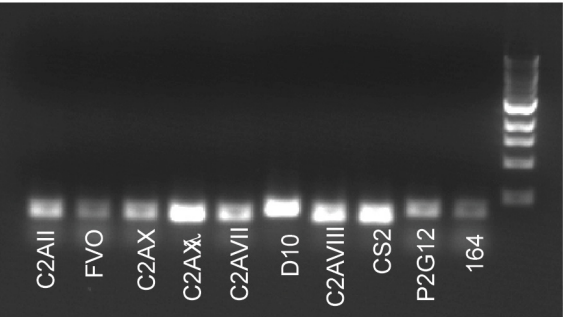
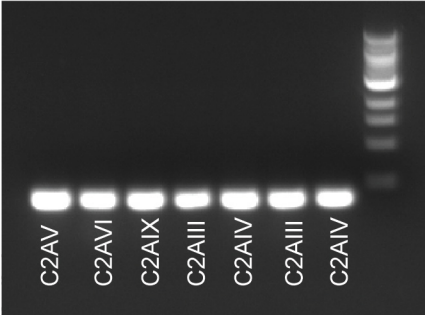
y = yes; *n* = no

Genomic analysis of chromosomes 2 and 9

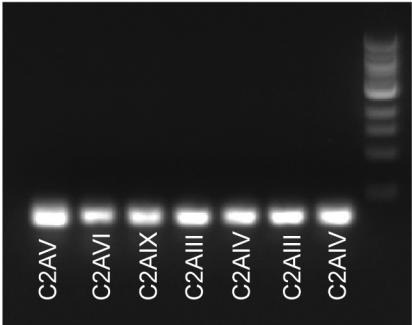
Chromosome 2



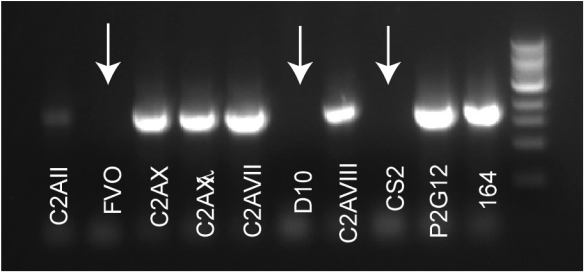
PFB0075c (Hyp9)



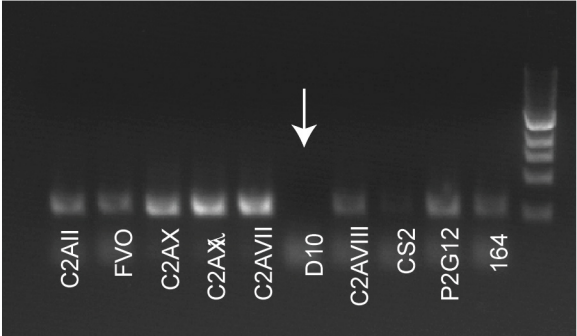
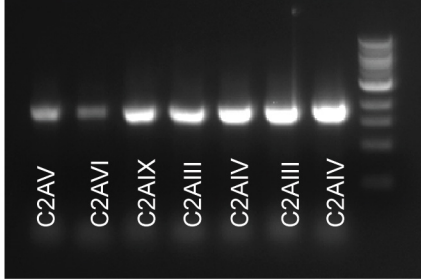
PFB0100c (KAHRP)



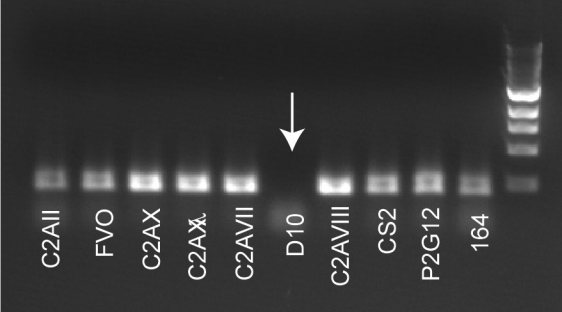
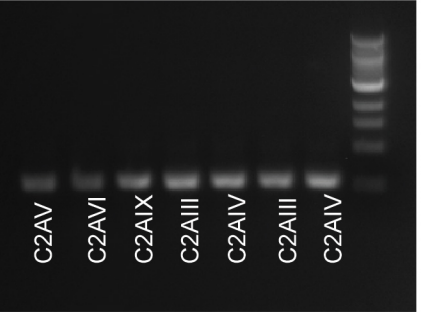
Chromosome 9



PFI1710w (GDV1)



PFI1755c (Rex3)



PFI1780w (PHISTc)

