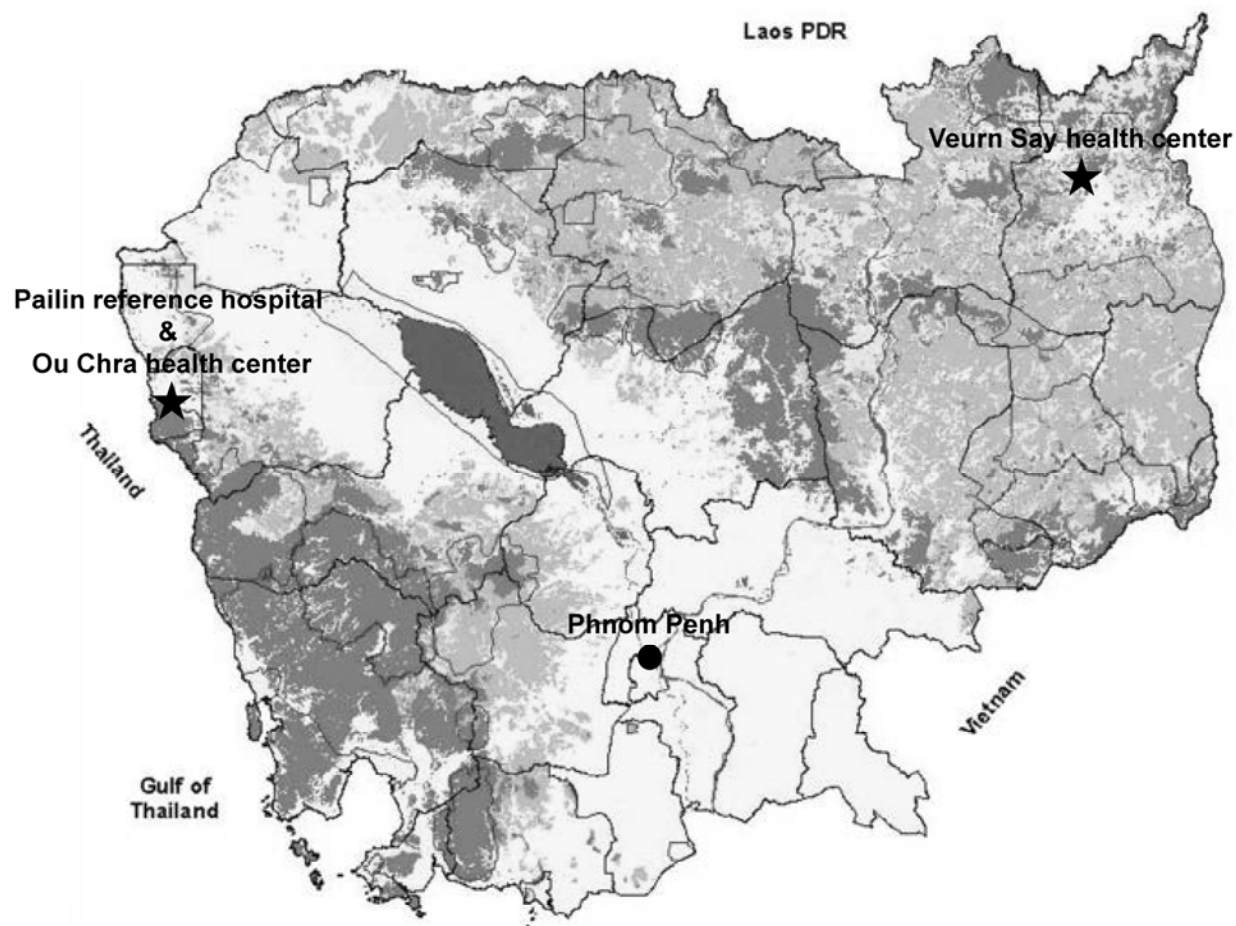


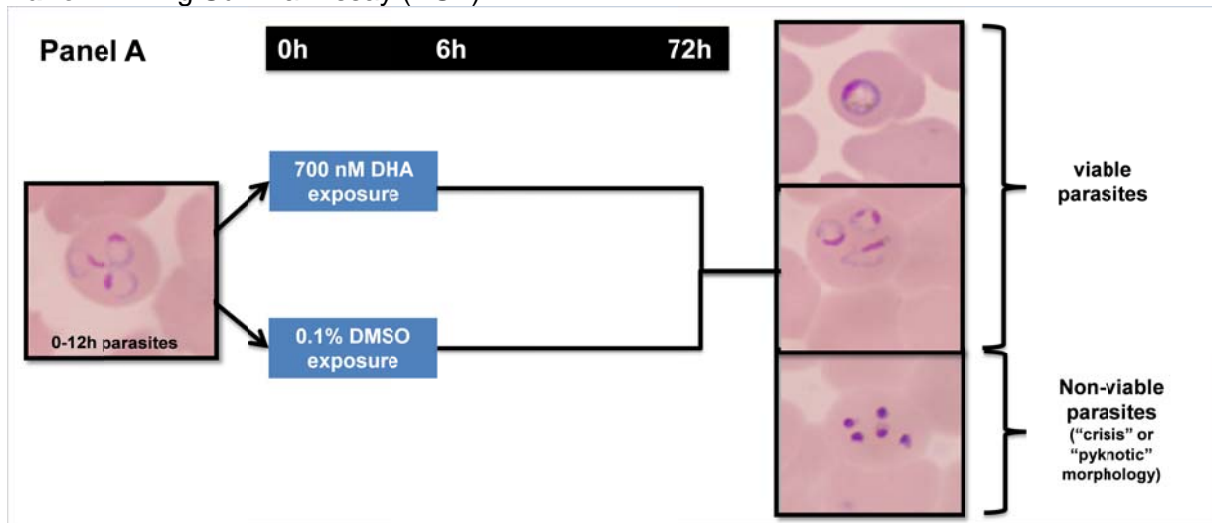
**Figure S1.** *P. falciparum* isolates collection sites, Cambodia, 2010-2011.



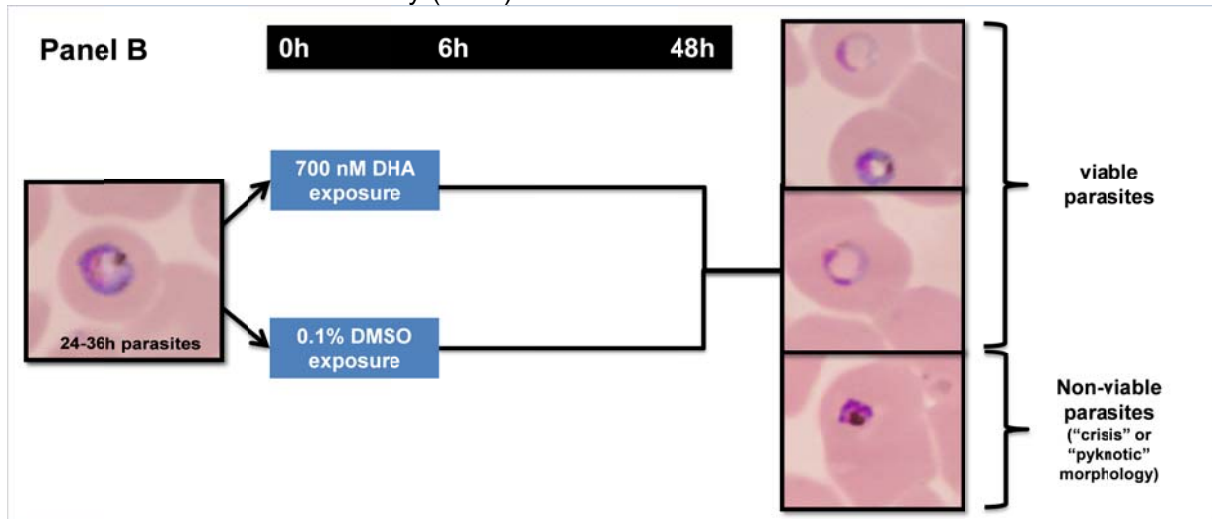
*P. falciparum* isolates were collected from malaria infected patients in Pailin (artemisinin-resistant area in the western Cambodia) and Ratanakiri (artemisinin-susceptible area in the Eastern Cambodia). Blood samples collected in ACD tubes from patients enrolled in the antimalarial drug resistance surveillance network (conducted by CNM and Institut Pasteur in Cambodia), in TRAC project (conducted by Mahidol-Oxford Tropical Medicine Research Unit) and therapeutic efficacy studies (conducted by CNM and WHO) were transported to Phnom Penh at 4°C within 24-48 hours.

**Figure S2.** Detailed protocols used to explore parasite stages susceptibility to DHA.

**Panel A:** Ring Survival Assay (RSA)



**Panel B:** Mature Survival Assay (MSA).



Synchronized parasites by 5%-sorbitol treatments were exposed 6 hours to 700 nM DHA (~2% parasitemia, 2% hematocrit, 2 ml final volume). Exposed parasites were then washed and resuspended in culture medium. Non-exposed parasites used as controls were exposed 6 hours to 0.1% DMSO and processed in the same conditions. Susceptibility to DHA was assessed microscopically (thin films) by estimating the percentage of viable parasites that had developed into second generation of rings or trophozoites, 66-hours or 42-hours following exposure of ring-stages or mature-stages, respectively. Each smear was read by two independent microscopists (50 consecutive x100 field, ~250 red blood cells per field) and results were expressed as the ratio of the parasite density found in exposed and non-exposed cultures.

**Table S1.** Ring survival assay (RSA) data of parasites from Pailin, Ratanakiri and reference clones (W2, 3D7, HB3, G15 and 7G8).

ID IPC	No. experiment	Site	66 hours post-exposure (6 hours - 700 nM DHA) reading of								RSA				Growth control
			exposed ring-stages				non-exposed ring-stages				Data	Average	SD	RSD	
			M1*	M2**	Mean	SD	M1*	M2**	Mean	SD					
5145	1	Pailin	2.02	2.03	2.02	0.007	11.23	14.9	13.06	2.59	15.4				3.4
	2	Pailin	0.7	0.68	0.69	0.01	5.3	5.56	5.43	0.18	12.7	14.2	1.4	9.9	2.1
	3	Pailin	1.96	1.22	1.59	0.52	11.0	11.0	11.0	0.0	14.4				1.5
4970	1	Pailin	0.5	0.35	0.42	0.10	2.76	2.21	2.48	0.38	17.1				1.2
	2	Pailin	0.37	0.42	0.39	0.03	2.55	2.6	2.57	0.03	15.4	15.5	1.5	9.8	2.2
	3	Pailin	0.25	0.4	0.32	0.10	2.5	2.12	2.31	0.26	14.0				1.9
4992	1	Pailin	1.02	1.21	1.11	0.13	6.66	8.5	7.58	1.30	14.7				4.3
	2	Pailin	0.36	0.41	0.38	0.03	2.56	2.71	2.63	0.11	14.6	13.8	1.4	10.5	2.7
	3	Pailin	0.78	0.82	0.80	0.03	7.0	6.2	6.6	0.56	12.1				3.0
4248	1	Pailin	0.48	0.67	0.57	0.13	7.9	7.1	7.5	0.56	7.6				3.2
	2	Pailin	0.81	0.65	0.73	0.11	10.4	8.6	9.5	1.27	7.6	7.0	1.0	14.3	3.8
	3	Pailin	0.35	0.33	0.34	0.01	6.4	5.1	5.75	0.91	5.9				3.4
5035	1	Pailin	0.11	0.18	0.14	0.04	2.13	2.17	2.15	0.02	6.7				2.5
	2	Pailin	0.29	0.27	0.28	0.01	3.52	3.15	3.33	0.26	8.4	7.0	1.2	18.0	2.2
	3	Pailin	0.17	0.22	0.19	0.03	3.5	3.1	3.3	0.28	5.9				1.9
5100	1	Pailin	0.05	0.03	0.04	0.01	1.14	1.02	1.08	0.08	3.6				1.7
	2	Pailin	0.12	0.17	0.14	0.03	2.79	2.8	2.79	0.007	5.2	4.2	0.9	21.6	1.9
	3	Pailin	0.12	0.08	0.1	0.03	2.8	2.55	2.67	0.17	3.7				1.7
5160	1	Pailin	0.42	0.3	0.36	0.08	3.16	2.96	3.06	0.14	11.7				1.4
	2	Pailin	0.75	0.7	0.72	0.03	3.23	3.05	3.14	0.12	23.0	19.6	6.8	34.8	1.6
	3	Pailin	0.87	0.77	0.82	0.07	3.6	3.2	3.4	0.28	24.1				2.4
5168	1	Pailin	0.58	0.58	0.58	0.0	4.0	3.57	3.78	0.30	15.3				3.5
	2	Pailin	0.48	0.57	0.52	0.06	2.81	3.08	2.94	0.19	17.9	14.1	4.4	31.0	1.8
	3	Pailin	0.23	0.23	0.23	0.0	2.53	2.4	2.46	0.09	9.3				1.9
5208	1	Pailin	0.12	0.14	0.13	0.008	3.5	3.35	3.425	0.10	3.9	3.9	-	-	1.5
4971	1	Pailin	0.73	0.69	0.71	0.03	4.0	3.85	3.92	0.10	18.1				1.9
	2	Pailin	0.5	0.7	0.6	0.14	4.34	4.15	4.24	0.13	14.1	17.4	2.9	17.1	1.9
	3	Pailin	1.0	1.3	1.15	0.21	5.42	6.1	5.76	0.48	19.9				2.5
5188	1	Ratanakiri	0.005	0.24	0.12	0.16	4.1	3.55	3.82	0.38	3.20				2.6
	2	Ratanakiri	0.04	0.21	0.12	0.12	4.1	5.87	4.98	1.25	2.49	3.3	0.9	27.7	1.5
	3	Ratanakiri	0.06	0.24	0.15	0.12	3.45	3.55	3.50	0.06	4.33				1.8
3592	1	Ratanakiri	0.07	0.12	0.10	0.03	4.42	5.25	4.83	0.58	2.1				1.4
	2	Ratanakiri	0.04	0.06	0.04	0.01	3.5	3.85	3.67	0.24	1.3	1.6	0.4	23.1	3.5
	3	Ratanakiri	0.08	0.06	0.07	0.01	5.36	4.8	5.08	0.39	1.4				2.8
	4	Ratanakiri	0.1	0.17	0.13	0.05	9.0	8.5	8.75	0.35	1.6				2.4
5150	1	Ratanakiri	0.03	0.05	0.04	0.01	4.05	3.2	3.62	0.6	1.1				1.8
	2	Ratanakiri	0.008	0.03	0.02	0.01	4.26	3.9	4.08	0.25	0.5	0.7	0.3	42.4	2.1
	3	Ratanakiri	0.01	0.02	0.015	0.007	2.45	2.2	2.325	0.17	0.6				1.3
5055	1	Ratanakiri	0.005	0.008	0.006	0.002	3.72	4.18	3.95	0.32	0.2	0.2	-	-	1.4
4974	1	Ratanakiri	0.02	0.03	0.02	0.009	2.54	2.64	2.59	0.07	0.9				2.0
	2	Ratanakiri	0.04	0.05	0.04	0.007	4.18	4.03	4.10	0.10	1.1	1.3	0.3	27.2	1.9
	3	Ratanakiri	0.01	0.1	0.05	0.06	3.9	3.2	3.55	0.49	1.6				2.0
	4	Ratanakiri	0.02	0.1	0.06	0.05	4.0	3.9	3.95	0.07	1.6				1.8
5152	1	Ratanakiri	0.02	0.03	0.02	0.008	4.0	3.56	3.78	0.31	0.6	0.6	-	-	2.8
5159	1	Ratanakiri	0.02	0.01	0.01	0.007	2.9	2.4	2.65	0.35	0.6	0.6	-	-	1.5
4880	1	Ratanakiri	0.02	0.05	0.03	0.02	2.28	2.89	2.58	0.43	1.3	1.3	-	-	2.2
5207	1	Ratanakiri	0.02	0.03	0.02	0.009	1.95	2.4	2.17	0.31	1.1	1.1	-	-	2.0
4914	1	Ratanakiri	0.02	0.1	0.06	0.05	2.38	2.25	2.31	0.09	2.5	2.5	-	-	1.8
3D7	1	Reference clone	0.009	0.03	0.01	0.01	2.38	2.25	2.31	0.09	0.8	0.8	-	-	1.9
G15	1	Reference clone	0.1	0.15	0.12	0.03	3.6	3.5	3.55	0.07	3.5	3.5	-	-	1.7
W2	1	Reference clone	0.82	1.05	0.93	0.16	16.4	18.3	17.35	1.34	5.3	5.3	-	-	4.9
7G8	1	Reference clone	0.08	0.06	0.07	0.01	3.92	4.12	4.02	0.14	1.7	1.7	-	-	3.4
HB3	1	Reference clone	0.03	0.01	0.02	0.01	3.2	3.0	3.1	0.14	0.6	0.6	-	-	2.8

\*M1: Microscopist 1; \*\*M2: Microscopist 2; SD: Standard deviation; RSD: Relative Standard deviation; Growth control (=parasite density in non-exposed culture/initial parasite density).

Parasite densities at H0 ranged from 0.8% to 4.7% (mean: 1.9%, 95%CI: 1.7%-2.2%) and were not significantly different between both sites (Pailin, mean: 1.7%, range: 0.8%-2.9%, 95%CI: 1.4%-2.0% and Ratanakiri, mean: 1.9%, range: 1.1%-3.7%, 95%CI: 1.5%-2.4%).