

1 **Supplementary Materials**

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3 **Cellular aging dynamics after acute malaria infection: A 12-months**
4 **longitudinal study**

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Supplementary Figures

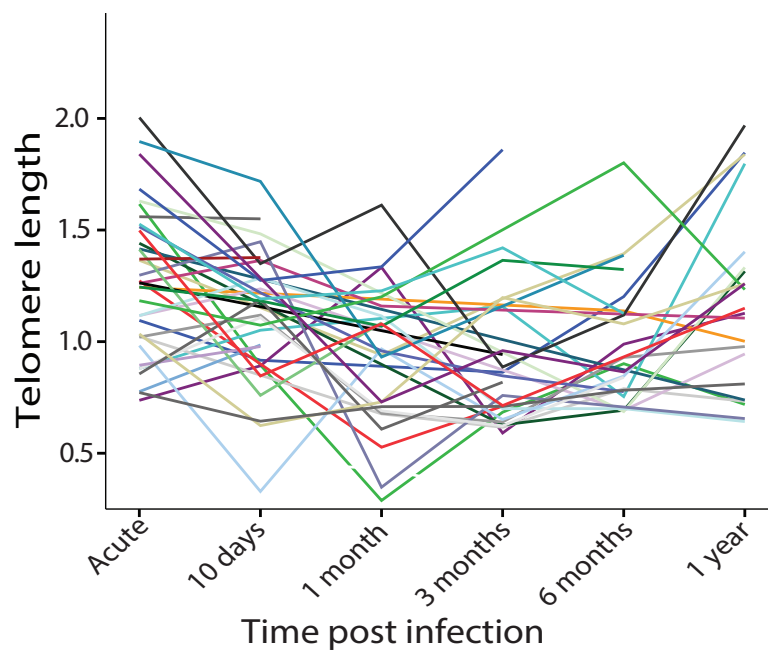
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38 **Fig. S1**

39 Telomere length (T/S ratio) dynamics in blood of travelers followed one year after a
40 successfully treated *P. falciparum* malaria infection. Each line represents an individual patient's
41 telomere dynamics.

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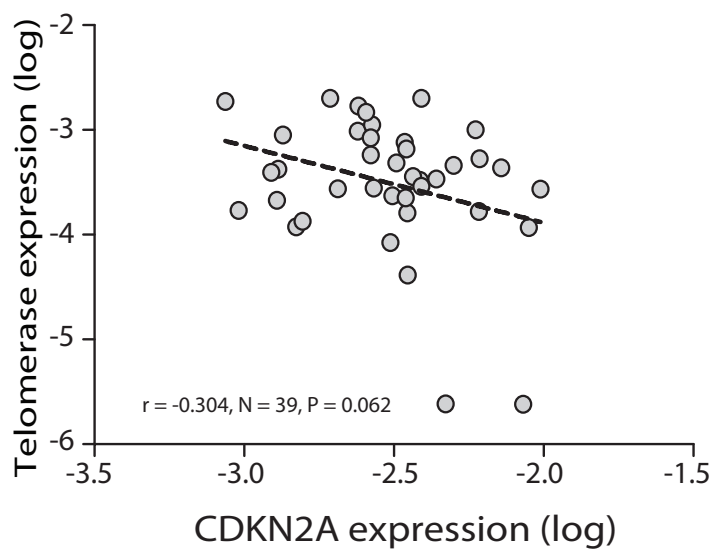
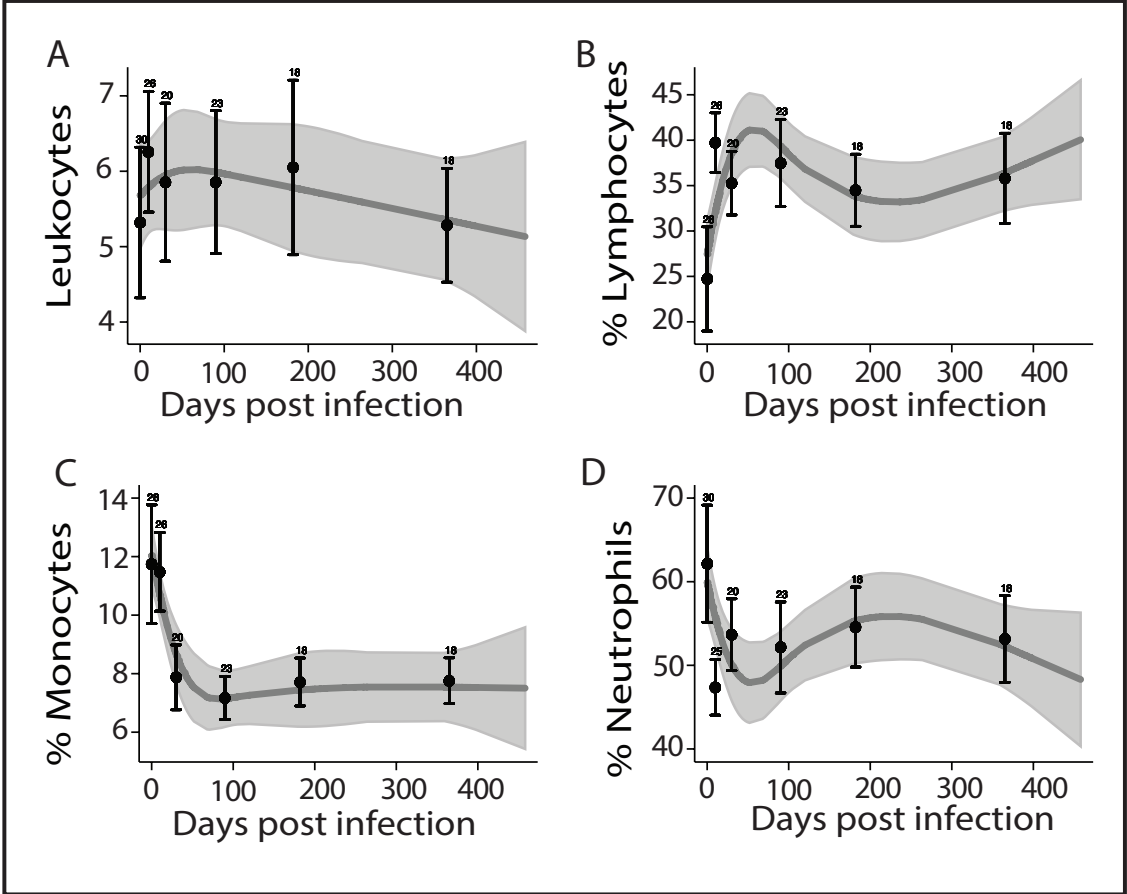


Fig. S2

Relationship between CDKN2A and telomerase expression (Pearson correlation, adjusted for cluster robust Standard Errors) in blood of subset of travelers (n=8) with RNA samples followed over one year after a successfully treated *P. falciparum* malaria infection.

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85 **Fig. S3**

86 Total leukocyte count (assuming 5×10^6 erythrocytes per microliter whole blood) and proportion
87 of different cell types in blood (%) over a one year follow up study in human travelers with
88 successfully treated single malaria infection: (A) Leukocytes, (B) Lymphocytes, (C) Monocytes
89 and (D) Neutrophils. Solid black lines denote the mixed model predicted mean proportion of
90 cells (at the actual measurement time points) and the shaded gray areas denote the 95% CI of
91 the model prediction. Black points denote the observed mean proportion of cells at each time
92 point (pooled data at expected measurement day) and error bars denote the 95% CI of the mean.
93 Numbers on each error bar represents the sample size. Lymphocytes, monocytes and
94 neutrophils are presented as the % proportion of total leukocytes.

Supplementary Tables

Table S1: Paired t-tests predicting telomere length dynamics in blood in travelers over a year follow up. Mean difference of telomere length levels are presented as (Mean diff) and 95% confidence interval of mean difference as (95% CI).

	<i>Day 10</i>	<i>1 month</i>	<i>3 months</i>	<i>6 months</i>	<i>12 months</i>
Acute (0)	Mean diff = -0.14 95% CI = -0.02 - -0.25 N = 30, p = 0.022	Mean diff = -0.36 95% CI = -0.19 - -0.25 N = 25, p < 0.001	Mean diff = -0.34 95% CI = -0.19 - -0.48 N = 26, p < 0.001	Mean diff = -0.26 95% CI = -0.09 - -0.43 N = 24, p = 0.004	Mean diff = -0.07 95% CI = 0.12 - -0.26 N = 23, p = 0.460
Day 10		Mean diff = -0.11 95% CI = 0.07 - -0.31 N = 21, p = 0.233	Mean diff = -0.10 95% CI = 0.07 - -0.27 N = 20, p = 0.243	Mean diff = -0.07 95% CI = 0.11 - -0.26 N = 19, p = 0.411	Mean diff = 0.14 95% CI = 0.41 - -0.12 N = 17, p = 0.277
1 months			Mean diff = 0.10 95% CI = 0.17 - -0.15 N = 21, p = 0.902	Mean diff = 0.09 95% CI = 0.26 - -0.07 N = 18, p = 0.236	Mean diff = 0.21 95% CI = 0.38 - 0.03 N = 16, p = 0.022
3months				Mean diff = 0.07 95% CI = 0.17 - -0.25 N = 19, p = 0.134	Mean diff = 0.39 95% CI = 0.58 - 0.21 N = 17, p < 0.001
6 months					Mean diff = 0.26 95% CI = 0.45 - 0.06 N = 18, p = 0.011

Two tailed p-value significance level 0.05

Table S2: Paired t-tests predicting telomerase expression dynamics in blood in travelers over a year follow up. Mean difference of telomerase expression levels are presented as (Mean diff) and 95% confidence interval of mean difference as (95% CI).

	<i>Day 10</i>	<i>1 month</i>	<i>3 months</i>	<i>6 months</i>	<i>12 months</i>
Acute (0)	Mean diff = -2.64 95% CI = 0.03 - -5.31 N = 7, p = 0.052 ^a p = 0.042^b	Mean diff = -1.06 95% CI = -0.31 - -1.81 N = 7, p = 0.013^a p = 0.028^b	Mean diff = -0.59 95% CI = 0.03 - -1.21 N = 7, p = 0.059 ^a p = 0.028^b	Mean diff = -0.09 95% CI = 1.81 - -1.98 N = 7, p = 0.902 ^a p = 0.892 ^b	Mean diff = -1.26 95% CI = 0.67 - -3.21 N = 5, p = 0.145 ^a p = 0.138 ^b
Day 10		Mean diff = 1.62 95% CI = 4.25 - -1.00 N = 6, p = 0.173 ^a p = 0.173 ^b	Mean diff = 2.72 95% CI = 5.01 - 0.44 N = 6, p = 0.028^a p = 0.027^b	Mean diff = 1.91 95% CI = 5.32 - -1.49 N = 4, p = 0.171 ^a p = 0.067 ^b	Mean diff = 1.185 95% CI = 7.02 - -3.31 N = 4, p = 0.336 ^a p = 0.273 ^b
1 months			Mean diff = 0.53 95% CI = 1.51 - -0.44 N = 6, p = 0.219 ^a p = 0.345 ^b	Mean diff = 0.175 95% CI = 1.85 - -0.35 N = 5, p = 0.131 ^a p = 0.079 ^b	Mean diff = -0.36 95% CI = 1.47 - -2.21 N = 5, p = 0.609 ^a p = 0.685 ^b
3months				Mean diff = -0.37 95% CI = 1.99 - -2.07 N = 4, p = 0.957 ^a p = 0.715 ^b	Mean diff = -0.94 95% CI = 1.36 - -3.25 N = 4, p = 0.283 ^a p = 0.273 ^b
6 months					Mean diff = -1.55 95% CI = 0.43 - -3.15 N = 4, p = 0.054 ^a p = 0.068 ^b

Paired t-test^a, Wilcoxon signed-rank test^b
Two tailed p-value significance level 0.05

Table S3: Paired t-tests predicting CDKN2A expression dynamics in blood in travelers over a year follow up. Mean difference of CDKN2A levels are presented as (Mean diff) and 95% confidence interval of mean difference as (95% CI).

	<i>Day 10</i>	<i>1 month</i>	<i>3 months</i>	<i>6 months</i>	<i>12 months</i>
Acute (0)	Mean diff = 0.33 95% CI = 0.65 - 0.01 N = 7, p = 0.045^a p = 0.063 ^b	Mean diff = -0.13 95% CI = 0.36 - -0.62 N = 7, p = 0.539 ^a p = 0.499 ^b	Mean diff = -0.89 95% CI = -0.16 - -1.61 N = 7, p = 0.023^a p = 0.028^b	Mean diff = -0.77 95% CI = -0.32 - -1.22 N = 5, p = 0.009^a p = 0.043^b	Mean diff = -0.55 95% CI = -0.06 - -1.04 N = 5, p = 0.035^a p = 0.079 ^b
Day 10		Mean diff = -0.32 95% CI = 0.41 - -1.04 N = 6, p = 0.312 ^a p = 0.248 ^b	Mean diff = -1.12 95% CI = -0.14 - -2.35 N = 6, p = 0.034^a p = 0.046^b	Mean diff = -1.12 95% CI = -0.11 - -2.13 N = 4, p = 0.038^a p = 0.068 ^b	Mean diff = -1.10 95% CI = -0.18 - -2.02 N = 4, p = 0.031^a p = 0.067 ^b
1 months			Mean diff = -0.67 95% CI = 0.25 - -1.60 N = 6, p = 0.11 ^a p = 0.074 ^b	Mean diff = -0.50 95% CI = 0.45 - -1.44 N = 5, p = 0.224 ^a p = 0.224 ^b	Mean diff = -0.17 95% CI = 0.67 - -1.02 N = 5, p = 0.601 ^a p = 0.500 ^b
3months				Mean diff = -0.35 95% CI = 1.16 - -1.87 N = 4, p = 0.508 ^a p = 0.465 ^b	Mean diff = 0.45 95% CI = 2.04 - -1.13 N = 4, p = 0.430 ^a p = 0.465 ^b
6 months					Mean diff = 0.24 95% CI = 0.31 - 0.16 N = 4, p = 0.002^a p = 0.067 ^b

Paired t-test^a, Wilcoxon signed-rank test^b
Two tailed p-value significance level 0.05

Table S4: Relationship between telomerase expression and CDKN2A in multivariate mixed effects models, with time modeled as a restricted cubic spline (N = 39, patients = 8).

<i>Factors</i>	<i>Coef.</i>	<i>SE.</i>	<i>p-value</i>
Telomerase	-0.10	0.06	0.123
Age	0.02	0.09	0.378
Sex	-0.07	0.65	0.912
Foreign born	-0.21	1.09	0.846

*All analyses adjust for time (days since start of treatment), using cubic splines with 4 knots.
Two tailed p-value significance level 0.05*

Table S5: Relationship between differential proportion of leukocytes with telomere length in multivariate mixed effects models, with time modeled as a restricted cubic spline (N = 135, patients = 34).

<i>Factors</i>	<i>Coef.</i>	<i>SE.</i>	<i>p-value</i>
Leukocytes	-0.02	0.01	0.160
Lymphocytes	0.001	0.001	0.747
Monocytes	0.01	0.01	0.166
Neutrophils	-0.001	0.001	0.303

*All analyses adjust for time (days since start of treatment), using cubic splines with 4 knots.
Two tailed p-value significance level 0.05*