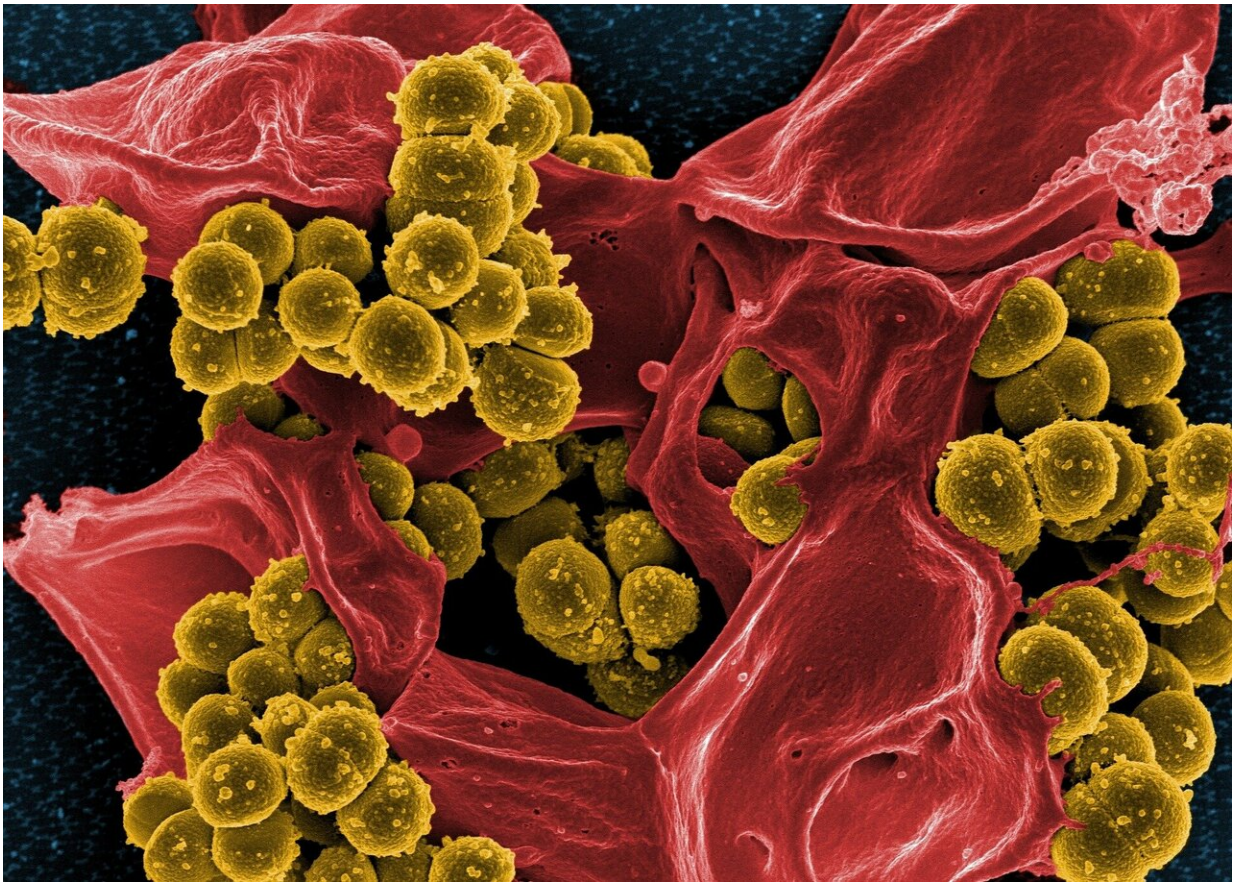


Malaria may shorten leukocyte telomeres among sub-Saharan Africans, study finds

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The length of telomeres in white blood cells, known as leukocytes, varies significantly among sub-Saharan African populations, [researchers report](#)

in *The American Journal of Human Genetics*. Moreover, leukocyte telomere length (LTL) is negatively associated with malaria endemicity and only partly explained by genetic factors.

"We highlight the contributions of genetic and environmental factors influencing LTL, and we have uncovered a potential role of malaria in shortening LTL across sub-Saharan Africa," says Sarah Tishkoff of the University of Pennsylvania, a co-senior author on the study.

"This association between malaria and LTL appears larger than any other known exposure or behavior that has been investigated in large-scale studies."

Telomeres are regions of repetitive DNA sequences that protect the ends of chromosomes from becoming frayed or tangled. LTL shows vast person-to-person variation, with individuals of African ancestry generally having longer LTL than non-Africans. It shortens with age and is a predictor of a range of aging-related diseases and mortality. LTL is a highly heritable human trait, and LTL variation at birth largely determines LTL variation throughout the life course.

"However, the majority of large-scale studies examining LTL variation among humans have focused primarily on populations of European ancestry," Tishkoff says.

"This under-representation of diverse populations hampers our ability to understand the genetic and environmental drivers of LTL variation and their effects on [telomere](#)-related disease risk."

In particular, little is known about the genetic, environmental, and evolutionary forces that have shaped the vast LTL variation across sub-Saharan African populations. This variation in LTL is largely explained by [genetic factors](#), but environmental factors could also play a role.

Exposure to *Plasmodium falciparum* malaria is one environmental factor of particular interest in impacting LTL, due to recent studies demonstrating a link between [malaria infection](#) and LTL.

While these studies suggest a link between malaria infection and telomere shortening, they rely on single, acute infection events where participants received rapid medical treatment. It remains unknown whether repeated malaria exposures throughout life in populations living in endemic regions has a lasting effect on LTL.

It is also unclear whether having longer leukocyte telomeres at birth in malaria endemic regions or regions with a high pathogen burden could be selectively advantageous.

To fill these knowledge gaps, Tishkoff and co-senior study author Abraham Aviv of Rutgers University examined LTL from diverse environmental contexts across Africa, including those where malaria is highly endemic. The authors extracted DNA from blood cells and genotyped individuals and measured LTL in 1,818 ethnically diverse adults from Tanzania, Botswana, Ethiopia, and Cameroon.

The results revealed significant variation in LTL among populations. The San hunter-gatherers from Botswana have the longest leukocyte telomeres, and the Fulani pastoralists from Cameroon have the shortest telomeres. Genetic factors explain roughly half of LTL variation among individuals.

Moreover, LTL is shorter in adults indigenous to regions of high malaria endemicity than in those indigenous to regions of low malaria endemicity. The potential impact of malaria endemicity on LTL reported in this study appears larger than previously identified [environmental factors](#) that impact LTL.

One potential mechanism by which malaria may shorten LTL may involve malaria-induced bouts of massive destruction of erythrocytes (i.e., [red blood cells](#)) and the process of making new cells to restore this loss.

"Circulating erythrocytes outnumber circulating leukocytes by approximately a thousand to one and comprise 84% of all somatic cells in the body," Tishkoff explains. "The telomere length reserves of the hematopoietic system are, thus, principally spent on building and maintaining the massive pool of about 25 trillion erythrocytes in the average human adult."

The authors say a longitudinal study in children and adults indigenous to regions of high and low malaria endemicity would provide more insightful information. "We propose that the effect of malaria on hematopoietic cell telomere shortening with age primarily unfolds during childhood, yet our LTL data are derived from adults," Tishkoff says.

"Clearly, the next step in testing the relationship between malaria and LTL is to characterize LTL dynamics in children born and raised in regions of high malaria endemicity versus those born and raised in regions of low or no malaria endemicity."

More information: Association Between Telomere Length and Falciparum Malaria Endemicity in Sub-Saharan Africans, *The American Journal of Human Genetics* (2024). [DOI: 10.1016/j.ajhg.2024.04.003](https://doi.org/10.1016/j.ajhg.2024.04.003). [www.cell.com/ajhg/fulltext/S0002-9297\(24\)00118-6](http://www.cell.com/ajhg/fulltext/S0002-9297(24)00118-6)

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