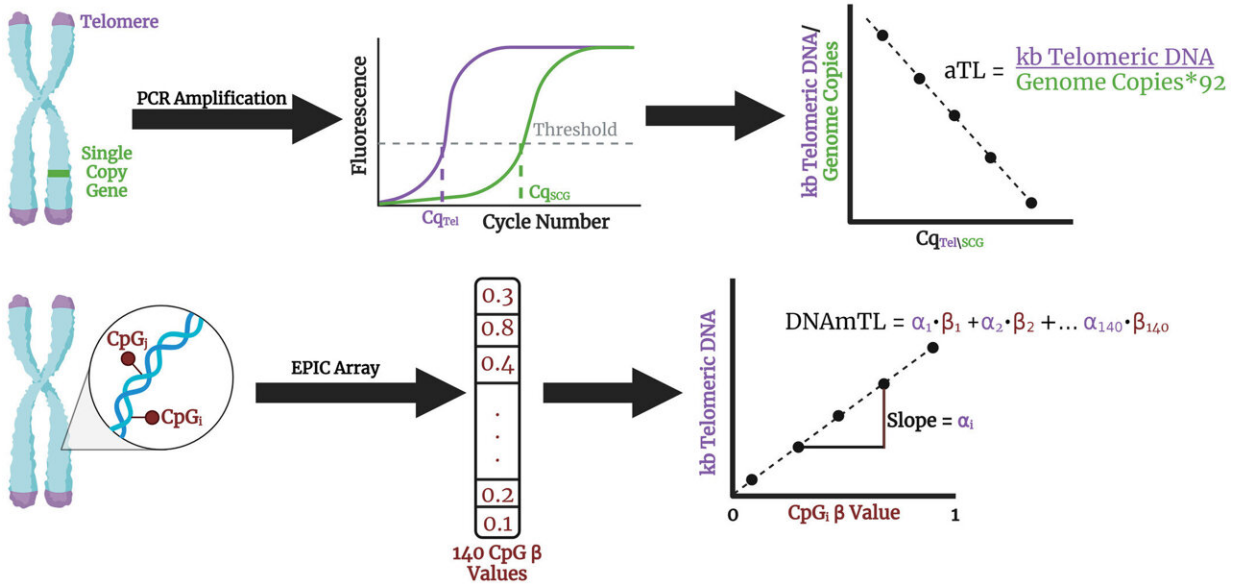
Calorie restriction study reveals complexities in how diet impacts aging

April 17 2024, by Aaron Wagner



Telomere Length Assessment in CALERIE. Assessment of aTL with qPCR involves quantifying levels of telomeric DNA content relative to the number of genomes using the single copy gene IFNB1. Credit: *Aging Cell* (2024). DOI: 10.1111/acel.14149

Penn State researchers may have uncovered another layer of complexity in the mystery of how diet impacts aging. A new study led by researchers in the Penn State College of Health and Human Development examined how a person's telomeres—sections of genetic bases that function like protective caps at the ends of chromosomes—were affected by caloric

restriction.

The team published their results in Aging Cell. Analyzing data from a two-year study of caloric restriction in humans, the researchers found that people who restricted their calories lost telomeres at different rates than the control group—even though both groups ended the study with telomeres of roughly the same length. Restricting calories by 20% to 60% has been shown to promote longer life in many animals, according to previous research.

Over the course of human life, every time a person's cells replicate, some telomeres are lost when chromosomes are copied to the new cell. When this happens, the overall length of the cell's telomeres becomes shorter. After cells replicate enough times, the protective cap of telomeres completely dissipates.

Then, the genetic information in the chromosome can become damaged, preventing future reproduction or proper function of the cell. A cell with longer telomeres is functionally younger than a cell with short telomeres, meaning that two people with the same chronological age could have different biological ages depending on the length of their telomeres.

Typical aging, stress, illness, genetics, diet and more can all influence how often cells replicate and how much length the telomeres retain, according to Idan Shalev, associate professor of biobehavioral health at Penn State. Shalev led the researchers who analyzed genetic samples from the national CALERIE study—the first randomized clinical trial of calorie restriction in humans.

Shalev and his team sought to understand the effect of caloric restriction on telomere length in people. Because telomere length reflects how quickly or slowly a person's cells are aging, examining telomere length could allow scientists to identify one way in which caloric restriction

may slow aging in humans.

"There are many reasons why caloric restriction may extend human lifespans, and the topic is still being studied," said Waylon Hastings, who earned his doctorate in biobehavioral health at Penn State in 2020 and was lead author of this study. "One primary mechanism through which life is extended relates to metabolism in a cell. When energy is consumed within a cell, waste products from that process cause oxidative stress that can damage DNA and otherwise break down the cell. When a person's cells consume less energy due to caloric restriction, however, there are fewer waste products, and the cell does not break down as quickly."

The researchers tested the telomere length of 175 research participants using data from the start of the CALERIE study, one year into the study and the end of the study after 24 months of caloric restriction. Approximately two-thirds of study participants participated in caloric restriction, while one-third served as a control group.

During the study, results showed that telomere loss changed trajectories. Over the first year, participants who were restricting caloric intake lost weight, and they lost telomeres more rapidly than the control group. After a year, the weight of participants on caloric restriction was stabilized, and caloric restriction continued for another year. During the second year of the study, participants on caloric restriction lost telomeres more slowly than the control group. At the end of two years, the two groups had converged, and the telomere lengths of the two groups was not statistically different.

"This research shows the complexity of how caloric restriction affects telomere loss," Shalev said. "We hypothesized that telomere loss would be slower among people on caloric restriction. Instead, we found that people on caloric restriction lost telomeres more rapidly at first and then

more slowly after their weight stabilized."

Shalev said the results raised a lot of important questions. For example, what would have happened to telomere length if data had been collected for another year? Study participants are scheduled for data collection at a 10-year follow-up, and Shalev said that he was eager to analyze those data when they become available.

Despite the ambiguity of the results, Shalev said there is promise for the potential health benefits of caloric restriction in humans. Previous research on the CALERIE data has demonstrated that caloric restriction may help reduce harmful cholesterol and lower blood pressure. For telomeres, the two-year timeline was not sufficient to show benefits, but those may still be revealed, according to Shalev and Hastings.

Three of Shalev's trainees, Hastings, current graduate student Qiaofeng Ye and former postdoctoral scholar Sarah Wolf, led the research under Shalev's guidance.

Hastings said the opportunity to lead this study was critical to his career.

"I was recently hired as an assistant professor in the Department of Nutrition at Texas A&M University, and I will begin that work in the fall semester," Hastings said. "Prior to this project, I had limited experience in nutrition. This project literally set the course of my career, and I am grateful to Dr. Shalev for trusting me with that responsibility."

More information: Waylon J. Hastings et al, Effect of long-term caloric restriction on telomere length in healthy adults: CALERIE™ 2 trial analysis, *Aging Cell* (2024). DOI: 10.1111/acel.14149

Provided by Pennsylvania State University