Telomere length predicts cancer risk

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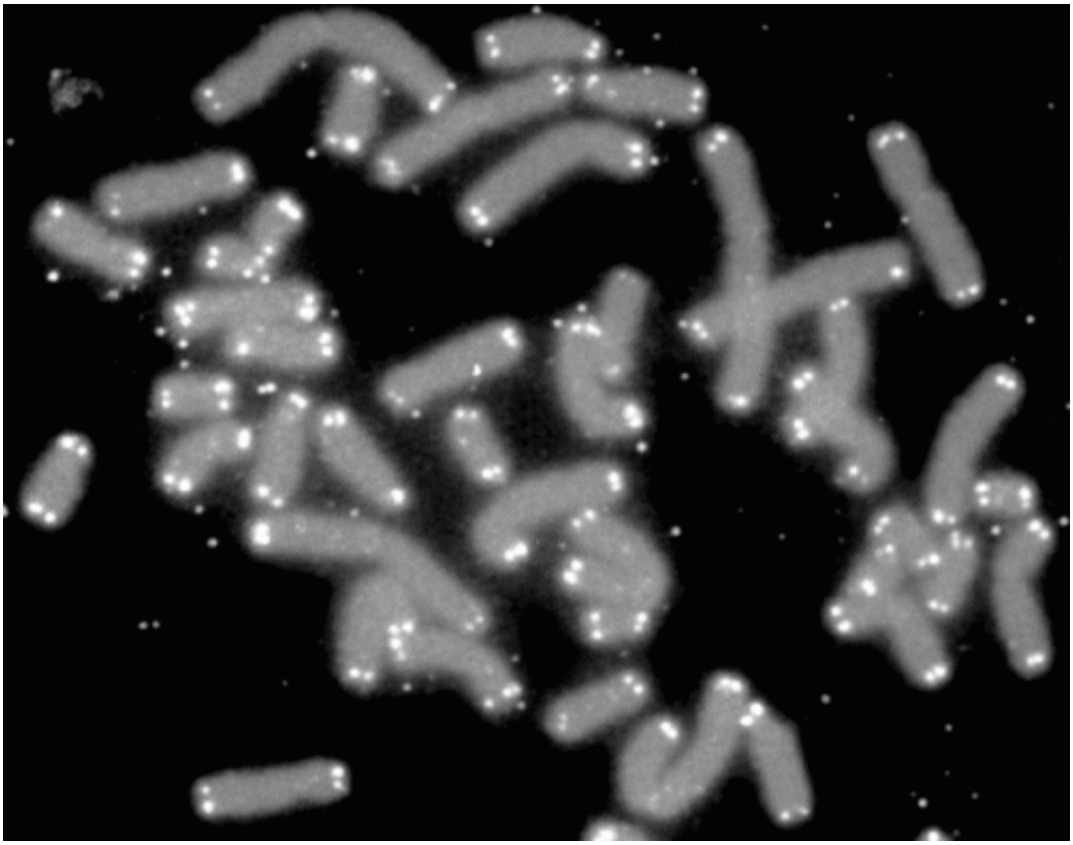

Human chromosomes (grey) capped by telomeres (white). Credit: PD-NASA; PD-USGOV-NASA

The length of the telomere "caps" of DNA that protect the tips of chromosomes may predict cancer risk and be a potential target for future therapeutics, University of Pittsburgh Cancer Institute (UPCI) scientists will report today at the AACR Annual Meeting in Washington, D.C.

Longer-than-expected telomeres—which are composed of repeated sequences of DNA and are shortened every time a cell divides—are associated with an increased cancer risk, according to research led by scientists from Pitt and Singapore.

"Telomeres and cancer clearly have a complex relationship," said Jian-Min Yuan, M.D., Ph.D., who holds the Arnold Palmer Endowed Chair in Cancer Prevention at UPCI and is lead or senior author on two studies being presented at AACR. "Our hope is that by understanding this relationship, we may be able to predict which people are most likely to develop certain cancers so they can take preventive measures and perhaps be screened more often, as well as develop therapies to help our DNA keep or return its telomeres to a healthy length."

Yuan and his colleagues analyzed blood samples and health data on more than 28,000 Chinese people enrolled in the Singapore Chinese Health Study, which has followed the health outcomes of participants since 1993. As of the end of 2015, 4,060 participants had developed cancer.

Participants were divided into five groups, based on how much longer their telomeres were than expected. The group with the longest telomeres had 33 percent higher odds of developing any cancer than the group with the shortest telomeres, after taking into account the effect of age, sex, education and smoking habits. That group also had 66 percent higher odds of developing lung cancer, 39 percent higher odds of developing breast cancer, 55 percent higher odds of developing prostate cancer and 37 percent higher odds of developing colorectal cancer. Of all the cancers, pancreatic had the largest increase in incidence related to longer telomeres, with participants in the highest one-fifth for telomere length at nearly 2.6 times the odds of developing pancreatic cancer, compared to those in the lowest one-fifth for telomere length. Only the risk of liver cancer went down with longer telomeres.

For three cancers, the risk was greatest for both the groups with extreme short and extreme long telomeres—creating a "U-shaped" risk curve. Participants in the group with the shortest telomere length had 63 percent higher odds of stomach cancer, 72 percent higher odds of bladder cancer and 115 percent higher odds of leukemia than the group in the middle of the curve. The group with the longest telomeres had 55 percent higher odds of stomach cancer, 117 percent higher odds of bladder cancer and 68 percent higher odds of leukemia.

"We had the idea for this study more than seven years ago, but it took the laboratory three months to finish quantifying telomere length for just 100 samples, which was not enough to draw any meaningful conclusions," said Yuan, also a professor of epidemiology at Pitt's Graduate School of Public Health. "Not even a decade later, we've been able to run nearly 30,000 samples in a year and draw these really robust insights, showing how far technology has come. Even more complicated will be linking telomere length to genome-wide analyses, which is on the horizon. We're on the cusp of gaining a truly remarkable understanding of the complicated biological phenomena that lead to cancer."

Provided by University of Pittsburgh Schools of the Health Sciences