

Are Telomere Tests Ready For Prime Time?

Companies are offering tests to gauge the length of telomeres, which they say may foretell our health. But some researchers question how useful they will be

Can the length of our telomeres, the protective caps at the ends of chromosomes that wear down as we get old, predict how well our bodies will age and our vulnerability to chronic diseases? Two new companies, both with heavyweight academic backing, are betting on it and have started or are planning to start performing telomere tests for the general public this year. But other leading telomere scientists say such tests are premature, if not virtually useless. On opposite sides of the issue are former collaborators Elizabeth Blackburn and Carol Greider, who, along with Jack Szostak of Harvard Medical School in Boston, shared the 2009 Nobel Prize in physiology or medicine for their telomere discoveries.

“Telomeres are an integrative indicator of health,” says Blackburn, a molecular biologist at the University of California, San Francisco (UCSF), who co-founded one of the companies, Telome Health in Menlo Park, California. Its Web site boasts that by knowing how long your telomeres are, you—and your doctor—might be able gauge your vulnerability to aging-related illnesses like heart disease and cancer and possibly tailor your lifestyle to improve the odds of staying healthy.

Greider and other critics disagree. “Do I think it’s useful to have a bunch of companies offering to measure telomere length so people can find out how old they are? No,” says Greider, who was a graduate student in Blackburn’s lab in the mid-1980s and is now a molecular biologist at Johns Hopkins University (JHU) School of Medicine in Baltimore, Maryland.

Telomeres perform a vital cellular job:

preventing chromosomes from sticking to each other. But their notoriety stems from their putative role in aging. Each time a cell divides, its telomeres typically shrink a little. Over many years and divisions, they can dwindle to nubs, spurring the cell to kill itself or stop dividing and enter a semi-retired state called replicative senescence. As more and more cells die or senesce, the skin, the lining of the intestines, and other tissues can gradually lose the capacity to replenish themselves. By curtailing tissue self-renewal, worn-down telomeres might promote the senescence of our bodies—although how much has been controversial. The length of our telomeres could serve as a life-span clock that reveals our biological age, providing a better indicator of our



Going public. Maria Blasco is a co-founder of one of two new companies offering tests of telomere length to patients.

Telltale tips. The glowing caps on these chromosomes are telomeres, which wear down as we get old.

physical deterioration than does our chronological age. Telomeres are “the best biomarker of aging we have,” says Jerry Shay, a cell biologist at the University of Texas Southwestern Medical Center in Dallas.

For some diseases, telomere measurements are already helping doctors tailor treatments and save lives, says cancer biologist and physician Mary Armanios of JHU School of Medicine. The beneficiaries are people who suffer from telomeropathies, inherited diseases that result in stumpy telomeres. Along with the rare dyskeratosis congenita, the telomeropathies include some cases of the blood disorder aplastic anemia and of idiopathic pulmonary fibrosis, progressive lung scarring that kills up to 40,000 people a year in the United States.

More uncertain is what value these tests will have for the general population—and whether doctors will be able to interpret the results. Right now, Telome Health is offering the service only to academic researchers, according to Calvin Harley, the company’s president and chief scientific officer. He was formerly chief scientific officer at Geron Corp., a biotech company that has been trying to develop telomere-lengthening drugs since the early 1990s. Harley says that later this year, individuals will be able to find out how long their telomeres are, probably by having their doctors submit a blood sample to Telome Health for analysis. The second company, Life Length of Madrid, also measures telomeres for researchers and has already launched patient testing, says co-founder Maria Blasco, a molecular biologist at the Spanish National Cancer Research Centre in Madrid.

What the measurements furnish, according to the companies, is a readout of a patient’s overall risk of developing age-related chronic diseases. Studies have linked undersized telomeres to cardiovascular disease, diabetes, Alzheimer’s disease, and cancer, among other chronic diseases. Although telomeres don’t necessarily foretell when we’ll die, Blackburn and colleagues reported in 2009 that their length correlates with the number of years elderly people remain healthy.

Very short telomeres might signal a health problem, Blasco says. They can also suggest who would profit from treatment. As an example, Harley points to the West of Scotland Primary Prevention Study, which for 20 years has been investigating

how to forestall heart disease in a group of middle-aged men with above-normal cholesterol levels. Men with the longest telomeres were half as likely to fall victim to heart disease as were men with punier telomeres. But the difference in susceptibility shrank after treatment with a cholesterol-lowering statin, researchers revealed in *The Lancet* in 2007, suggesting that the patients with the shortest telomeres gained the most. “Short telomeres are as or more predictive than conventional cardiovascular disease risk markers” such as cholesterol levels, Harley says.

Telomere tests also deliver a verdict on a patient’s lifestyle, Blasco says. A stack of studies suggests that not only age but also our habits and actions can affect telomere length. And unlike a gene variant that hikes disease risk, “telomeres are malleable,” Blackburn says.

Among the enemies of our telomeres, these studies indicate, are smoking, heavy drinking, and obesity. Long-term psychological stress might also take a toll. In 2004, Blackburn, UCSF health psychologist Elissa Epel, and colleagues reported that telomeres were shorter in women who said they were under the most pressure. More recent studies have connected childhood trauma and prolonged depression to truncated telomeres.

By contrast, telomeres tend to shrink more slowly with age in people who adopt healthy habits such as regular exercise. Longer telomeres are also associated with positive physiological measures like higher blood levels of omega-3 fatty acids, which are found in fish and might protect against heart disease. Epel, Blackburn, and colleagues reported last year that meditation revs up telomerase, a cellular enzyme that stretches telomeres. If tests point to dwindling telomeres, “people need to assess the probable causes of telomere shortening” and consider changing their lifestyle, says Epel, who is another of Telome Health’s co-founders.

Researchers involved with the two companies acknowledge some gaps in the evidence on the health impact of telomere length. The link between short telomeres and chronic illnesses rests on association studies that tease out correlations between

telomere length and disease incidence, not cause and effect. And the findings of these studies can be inconsistent, critics say. “At the moment, there are mixed results in some of these studies,” says cancer biologist Alan Meeker of JHU School of Medicine.

“Today, it isn’t clear how best to determine telomere length and exactly what it will tell you for 99% of people,” Greider says.

Molecular cell biologist Peter Lansdorp of the British Columbia Cancer Agency in Canada seconds her skepticism. In 2005, he started his own company, Repeat Diagnostics, which has been measuring telomeres for research projects and for patients suspected of having conditions such as dyskeratosis congenita. The company is not marketing tests to the general public, he



Predictive power. Elizabeth Blackburn (*right*) says telomere tests might reveal how well our bodies are aging. Longtime collaborator Carol Greider (*left*) is not so sure.



says: “I think we know too little to suggest that a person [with short telomeres] is at greater risk.”

The notion that changing how we live can alter telomere length also relies mainly on association studies, Epel concedes. So far, there are no telomere-stretching drugs, and the placebo-controlled, blinded studies that could nail down whether lifestyle interventions work are just getting under way. For example, Blackburn and colleagues are collaborating with researchers in the UCSF urology department to determine whether they can protect the telomeres of a group of men who have early prostate cancer and are therefore under stress. The patients will follow a regimen, designed by diet guru and UCSF professor Dean Ornish, that includes regular exercise, a low-fat diet, and activities such as yoga.

Measuring telomeres is tricky as well, experts say. Telome Health will use the quantitative polymerase chain reaction, or qPCR, which is fast and inexpensive, Harley says. Because most studies on telomere length in diseases opt for this technique, it should be easier to interpret patient results, he adds.

But Shay describes qPCR as “marginally useful” because it provides only the average telomere length for a group of cells. He says that two of the telomere-measuring companies asked him to consult for them, but he is offering his expertise to Life Length because he feels that it uses superior techniques. One method, called Q-FISH, involves tagging telomeres with fluorescent labels and analyzing images of the chromosomes. Unlike qPCR, he says, Q-FISH can identify extremely short telomeres within a cell. These run-down telomeres are the ones that can nudge the cell into senescence or suicide. Other researchers laud a different version of FISH developed by Lansdorp and colleagues. Called Flow-FISH, it relies on a flow cytometer to measure fluorescence and gauges average telomere length within an individual cell.

With all these claims and counterclaims, pediatrician and telomere biologist Abraham Aviv of the New Jersey Medical School in Newark has proposed that an independent organization, perhaps the U.S. National Institutes of Health, do an impartial analysis of the different techniques.

Whether patients will want the new tests depends in part on how much they cost and who will pay. Life Length charges €500 (about \$700), Blasco says. Telome Health has yet to set a price for the service, Harley says. Both scientists agree that the early market will likely be private clinics and “concierge physicians,” whose patients can afford to foot their own medical bills. But if the tests do turn out to have predictive power, Blasco says she hopes the Spanish national health system will cover the costs. U.S. insurance companies might do the same, Harley says.

But do we really want to know how long our telomeres are? Shay thinks many people do—but he’s not one of them. “I have no interest in knowing how long my telomeres are,” he says. “I’m afraid to ask.”

—MITCH LESLIE