

TeloYears™ Scientific Overview

About Telomeres

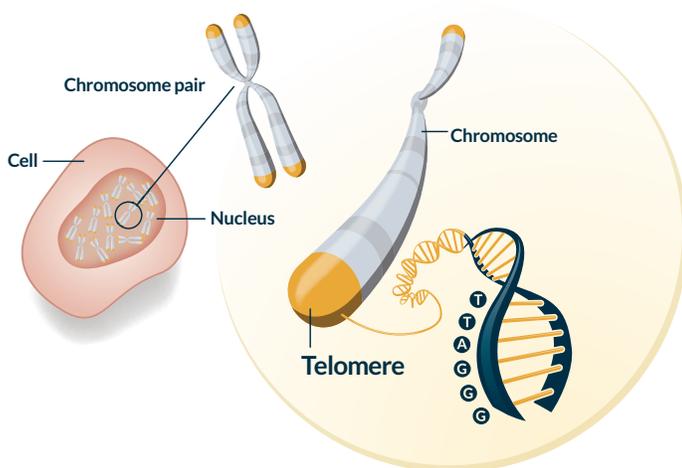


Figure 1. Telomeres, chromosomal end caps, protect genetic material

DNA, considered the building block of life, is found in the nucleus of nearly every cell in our bodies in small packages called chromosomes. Telomeres are the protective caps on the ends of these chromosomes that shorten with every cell division. Technically speaking, telomeres are repetitive stretches of the nucleotide base-pair sequence $TTAGGG^1$. If you imagine DNA as a long spiral ladder with millions of rungs, those repeated base-pair sequences are the last few thousand rungs on the ends of the ladder that keep it from “unzipping” as cells divide, thus protecting the

genes contained in the long stretches of sequences in the middle of the ladder. Telomeres help maintain the integrity of the chromosomes, preventing rearrangement that leads to failed replication or cell death.

Telomeres are a key part of the process that ensures DNA is accurately copied as your cells divide and reproduce. When we are born, our telomeres are at their longest. However, throughout our lives, with every cell division, telomeres lose a bit of their DNA until, over time, the cell cannot replicate and becomes “senescent,” the cellular equivalent of old age. This shortening process can be interpreted as an aging clock for the lifetime of the cell.



Figure 2. Gradual telomere loss naturally occurring in aging cells

Internal and External Factors That Accelerate Telomere Length Shortening

In addition to shortening due to normal cell replication, telomeres are subject to other factors that shorten them, such as oxidative stressⁱⁱ. Oxidative stress is an imbalance between the body's production of free radicals (reactive oxygen) and its ability to detoxify their harmful effects through antioxidants. Other factors that influence telomere length include inflammation, toxins, radiation, lifestyle and the environment. Some researchers and physicians think of telomere length as reflecting the cell's replicative capacity, where longer is betterⁱⁱⁱ, and may reflect the whole body's general health. Refer to the TeloYears Bibliography for more references.



Figure 3. Rapid telomere erosion due to oxidative stress induced by inflammation, toxins or radiation

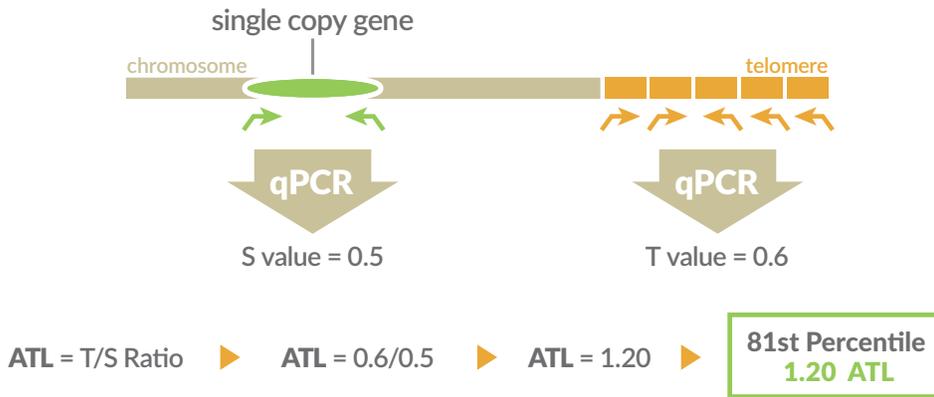
Measuring Telomeres

In the published scientific literature on telomere length, leukocytes (white blood cells) are the most frequently used cells. A single drop of blood contains thousands of leukocytes. They are not only easy to sample and analyze, but, as immune cells, are particularly sensitive to pathological stress. Thus, their overall health may better reflect the health of the whole organism. The TeloYears assay uses one drop of blood that the customer collects at home with a simple finger stick, similar to blood sample collection methods routinely used by diabetic patients to monitor their glucose levels.

The Telomere Diagnostics lab in Silicon Valley, California, has been qualified to perform high-complexity clinical testing and is certified by and regulated under the Clinical Laboratory Improvement Amendments (CLIA) Act^{iv}. There we measure telomere length using proprietary methods to analyze the DNA extracted from the leukocytes (white blood cells) in the finger stick blood sample (Figure 4).

We measure the average telomere length found in the DNA using qPCR (quantitative polymerase chain reaction), which is the most accurate method of measuring telomere length and by far the most referenced in the scientific literature. For our products, we use the “Cawthon qPCR assay” for average telomere length (ATL)^v. Using telomere specific primers in our assay protocol, we quantify the ratio of the telomeric signal (T) versus the single copy gene signal (S). This T/S ratio reflects the average length of the telomeres per cell in the sample. This ratio is routinely in the range of 0.80–1.20 and is indexed to a large reference range of healthy individuals.

We have developed proprietary methods to tackle the sensitive nature of the qPCR telomere length assay with regards to sample collection, storage, preparation, and assay conditions. Telomere Diagnostics uses multiple standards and normalization procedures to ensure the precision and accuracy of the assay.



Calculating Age in TeloYears

Generally speaking, your age in TeloYears is the age of a typical man or woman whose telomere length is similar to yours. More specifically, we measured average telomere length at the population level and used the results to build a

mathematical model by analyzing the mean, variance, and distribution of relevant sub populations. We use this model to calculate your age in TeloYears based on your own telomere length and model-derived factors applied to your actual age and gender. Likewise the model is used to calculate your telomere length as a percentile compared to a typical man or woman of your actual age^{vi}.

Telomeres in Space: The NASA Twins Study

You may have heard about NASA astronaut Captain Scott Kelly, who recently returned from a one-year trip to space. His twin brother Captain Mark, also a retired astronaut, remained on earth as the other half of an unprecedented experiment. The ongoing NASA Twins Study is the first to compare the cellular profiles of identical twin astronauts. Among other tests, they measured their telomeres to help evaluate how living the weightless lifestyle and space exposure to cosmic rays may have affected Scott differently than earth-bound Mark.

In particular, the experiment “Differential Effects on Telomeres and Telomerase in Twin Astronauts Associated with Spaceflight,” will assess changes in telomere length and the rate at which telomeres shorten “to provide a deeper understanding” of “an informative biomarker of aging and age-related pathologies (e.g., cardiovascular disease and cancer) that captures the interplay between genetics and lifestyle.”

Lead investigators Susan Bailey, PhD, Colorado State University, and Kerry George of Wyle Labs, hypothesize that accelerated telomere shortening will be associated with Scott, who spent nearly a year on the International Space Station (ISS), as compared to his twin Mark, who stayed on Earth to serve as ground control, in a duration and severity dependent manner^{vii}.

From the Nobel Prize to You

The new TeloYears genetic test is available through Telomere Diagnostics, a company founded by a scientist who shared the Nobel Prize for Physiology or Medicine in 2009 “for the discovery of how chromosomes are protected by telomeres and the enzyme telomerase.”^{viii} The pioneering team was also recognized for discovering the fundamental mechanisms of telomeres. They established the protective function of telomeres during cell replication, and discovered that the enzyme telomerase synthesizes telomere sequences and can lengthen telomeres in living cells. *See also Telomere Biology: A Short History.*

References

- i. Reddel RR: Telomere maintenance mechanisms in cancer: clinical implications. *Curr Pharm Des* 2014, 20(41):6361–6374.
- ii. Petersen S, Saretzki G, von Zglinicki T: Preferential accumulation of single-stranded regions in telomeres of human fibroblasts. *Exp Cell Res* 1998, 239(1):152–160.
- iii. Rode, L, et al. Peripheral Blood Leukocyte Telomere Length and Mortality Among 64 637 Individuals From the General Population, *JNCI J Natl Cancer Inst* (2015) 107(6): djv074.
- iv. CLIA license number 05D2041002.
- v. Cawthon, RM. Telomere measurement by quantitative PCR. *Nucleic Acids Research*, 2002. Vol. 30, No. 10 e47.
- vi. Data on File at Telomere Diagnostics, Inc.
- vii. [<http://qz.com/370729/astronaut-scott-kelly-will-return-from-a-year-in-space-both-older-and-younger-than-his-twin-brother/>]
- viii. The Nobel Prize in Physiology or Medicine 2009 Elizabeth H. Blackburn, Carol W. Greider, Jack W. Szostak: "how chromosomes are protected by telomeres and the enzyme telomerase" [http://www.nobelprize.org/nobel_prizes/medicine/laureates/2009/press.html]

For more information and to purchase TeloYears, visit www.teloyears.com

The TeloYears test is not intended for screening, diagnosing, treating or preventing diseases or medical conditions. The test is available for individuals between the ages of 20 to 80 within the United States, except for the state of New York.

The information provided by the TeloYears test should not be used to replace medically appropriate screening tests recommended based upon actual age or other risk factors, nor should the information be used to make decisions about diagnosis or treatment of diseases or medical conditions. The Telomere Diagnostics lab is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical testing. The performance characteristics of this test were determined by Telomere Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration.

Test reports are kept absolutely private according to our Privacy Policy and are available only in a fashion that maintains compliance with the HIPAA security rule, which regulates privacy and security of health information.