

# Telomere Analysis Technology<sup>®</sup>

## Results Report

SAMPLE CODE: USAK001006  
Report issue date: 05-13-2014

For research only

# Legal Notice

The present report and all data included herein are intended solely for the Recipient - who is identified in this report exclusively by reference to a numerical code - and for his/her personal use. This report may not be used for pharmaceutical or clinical purposes. Neither the report nor its contents may be interpreted as a recommendation for medical treatment or medication, nor do these constitute a medical treatment as such, nor may any such statement be derived from the report.

This report is not to be used for treatment purposes, and is only intended for the Recipient to review and discuss with his/her own physician. The information contained in the report does not constitute medical advice or a medical consultation. It is not intended for the diagnosis of health problems and is not a substitute for professional medical care. By no means is the present report intended to suggest the start of any kind of medical treatment, nor should it be considered a substitute for the independent opinion of a physician with regard to any health-related issue.

If the Recipient suffers from a persistent health problem or has any questions in that respect, we suggest he/she discuss the matter with his/her physician. Under no circumstances should the Recipient disregard the advice of his/her professional physician or delay recommended treatment due to the issuance of the present report.

The measurement of telomere length provided in this report was carried out in accordance with strict quality controls and the best technology available in the market at the time the report was issued. The mean variability of replicated samples has a coefficient of variation of approximately 5%.

The estimation of biological age is carried out based on telomeric measurements which Life Length performs on a sample of the general population using its advanced technology and which it stores in its database. At this time this information allows Life Length to estimate biological ages between 20 and 90, but Life Length does not yet possess enough information to estimate biological ages outside these ranges with sufficient statistical rigor. As Life Length expands its database with samples from individuals of ages greater and less than the aforementioned limits, its biological age estimation range will broaden.

Life Length assumes no responsibility for deviations in the results of analyses stemming from the non-viability or poor quality of blood sample provided by the Recipient and, in any case, should be considered as research. In addition, evaluation results, which shall depend upon the quality of the blood sample analyzed, may reflect temporary changes in the Recipient's state of health, due to a temporary sickness, or if he/she is undergoing medical treatment, among other factors. As a result, we recommend repeating the measurement at least on a yearly basis.

Life Length accepts no responsibility whatsoever for the use or utilization the applicant might make of the report and its results.

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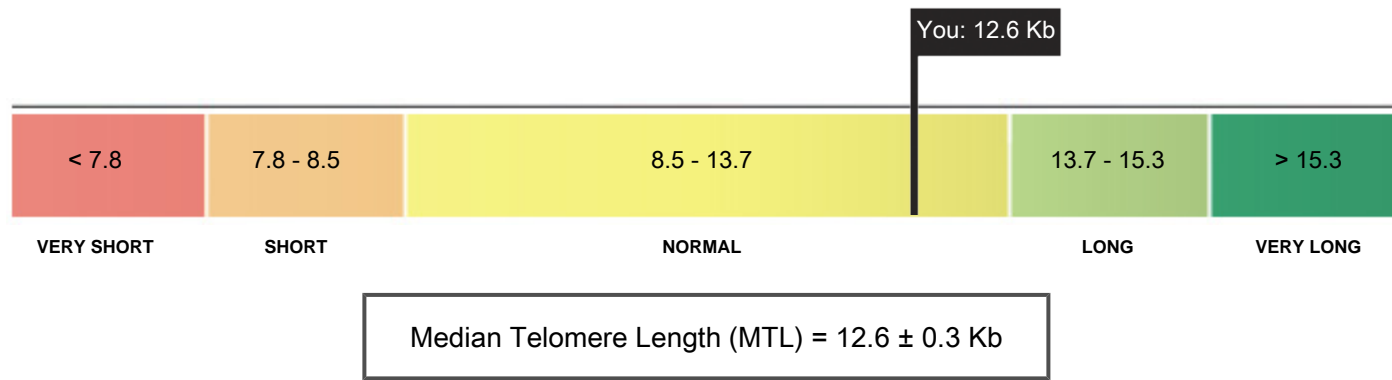
**Questions?**  
Contact Dr. London for further interpretation

Please record the code of the report for future measurements. Code: USAK001006

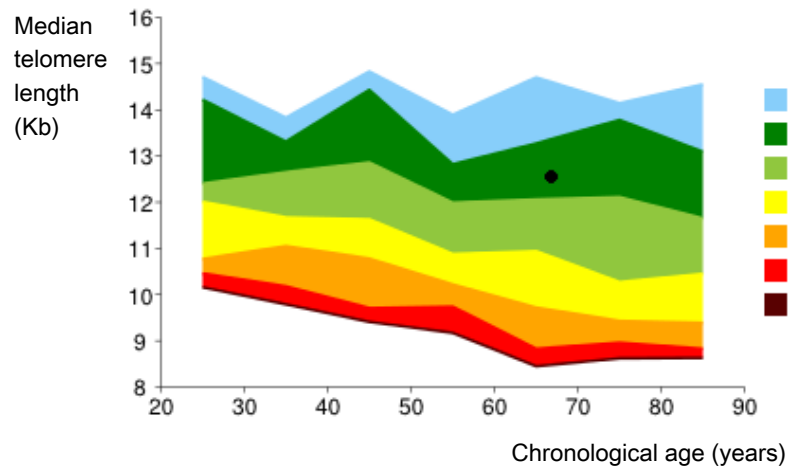
# 1. Your telomere length

Median Telomere Length: 12.6 Kb

Your median telomere length is estimated to be **normal** compared to Life Length's database population.



# 2. Median telomere length – Comparison by age band and percentiles



The adjacent graph shows a comparative analysis of the median telomere length in your sample compared with the control database.

Each line represents a specific percentile of our database.

For example, falling in the 75<sup>th</sup> percentile means that 25% of people of your age have a longer median telomere length than you.

It is therefore best if your results falls into one of the higher bands.

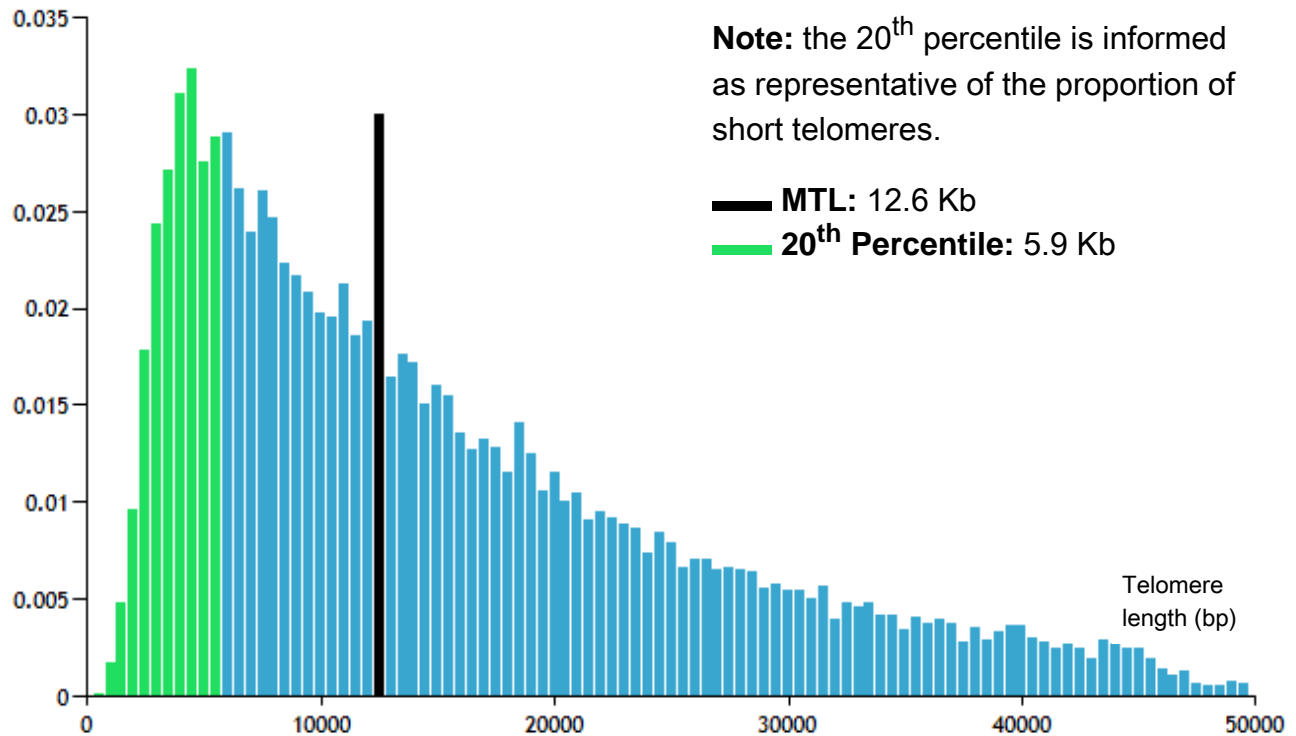
# 3. Your estimated biological age

Estimated Biological Age: 63.1 years old

Chronological Age: 67 years old

## Telomere length distribution of your sample

Relative  
frequency

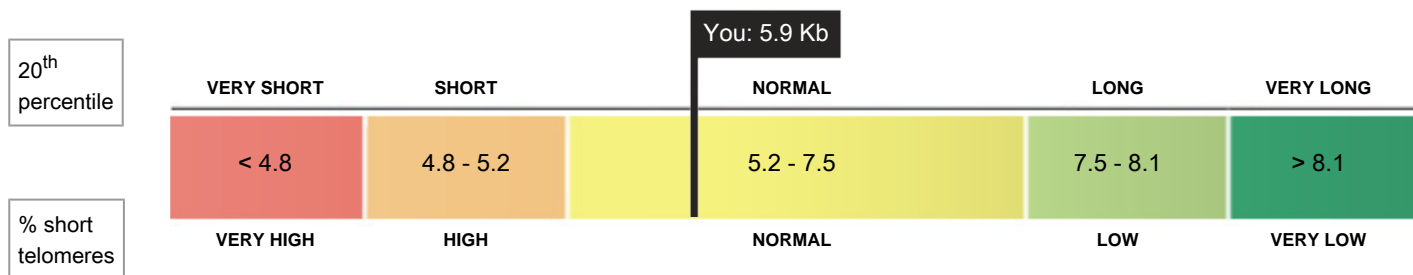


The histogram shows the distribution of telomere lengths in your cells. Bars represent the proportion of telomeres for every particular length (X axis). The 20<sup>th</sup> percentile indicates the particular length below which 20% of the telomeres have been observed. Therefore, if there are many bars in green, this indicates a relatively low abundance of short telomeres (we have to go up to a large length to cover 20% of the observations) while, if only a few bars are in green, this indicates a relatively high percentage of short telomeres. The median is also indicated in the histogram and it represents the 50<sup>th</sup> percentile of the distribution. This histogram also allows for the analysis of telomere length variability. A narrow histogram indicates relative homogeneity in telomere length, while a wider histogram indicates greater telomere length variability which, in turn, could suggest poor telomerase activity and telomere elongation by alternative lengthening mechanisms (i.e. recombination).

# Your 20<sup>th</sup> percentile / short telomeres

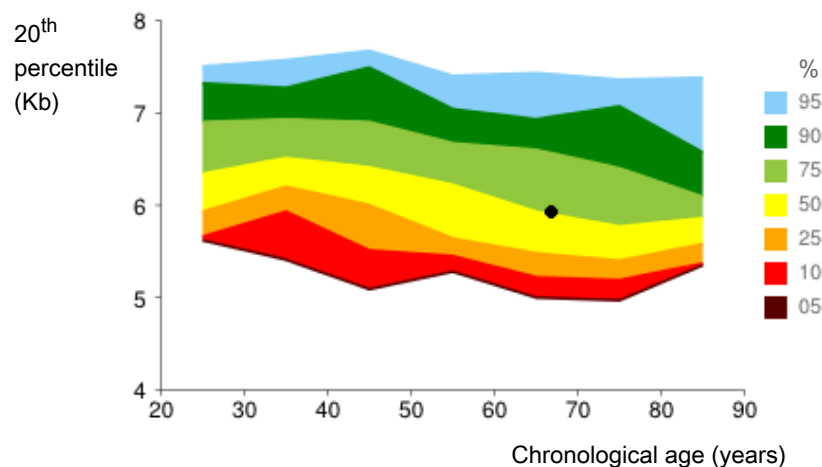
20<sup>th</sup> percentile: 5.9 Kb

Your 20<sup>th</sup> percentile is estimated to be **normal** compared to Life Length's database population. This implies that your percentage of short telomeres is **normal** compared to the same database.



**Note:** Please note that there may be higher variability associated with the measurement of the 20<sup>th</sup> percentile as compared to the corresponding median value between samples from the same individual due to the fact that measuring the shortest telomeres inherently has a lower statistical reliability.

## 20<sup>th</sup> percentile / short telomeres – Comparison by age band and percentiles



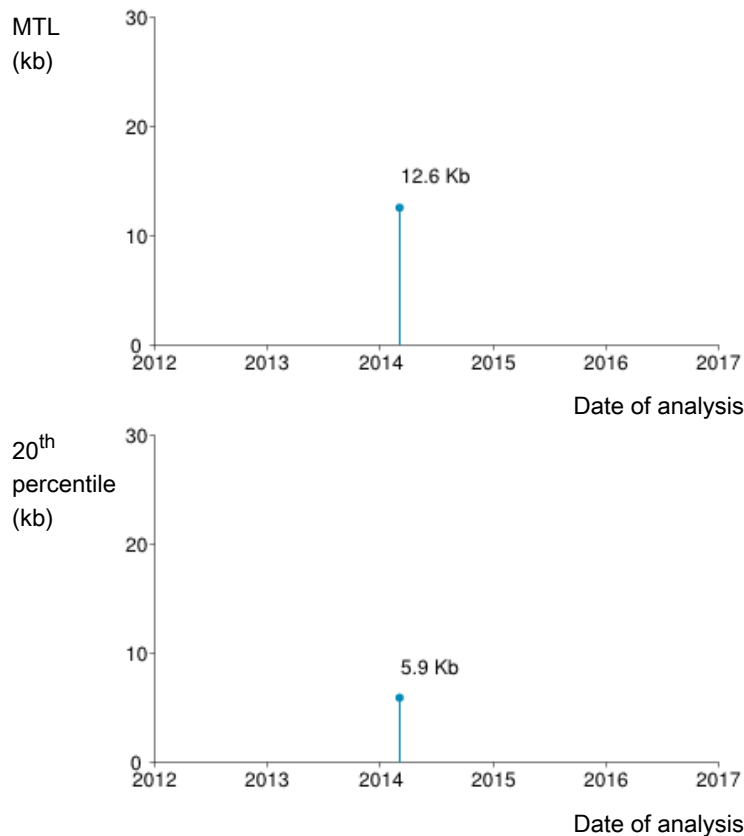
The adjacent graph shows a comparative analysis of your 20<sup>th</sup> percentile value (which represents your shortest telomeres) in your sample compared with the control database.

Each band represents a percentile of the control database.

Falling in the 75<sup>th</sup> percentile, for instance, means that 75% of the people of your age present shorter telomeres than you and, consequently, a higher degree of cellular aging than you.

It is therefore best if your results falls into one of the upper bands.

## Longitudinal analysis – MTL and 20<sup>th</sup> percentile

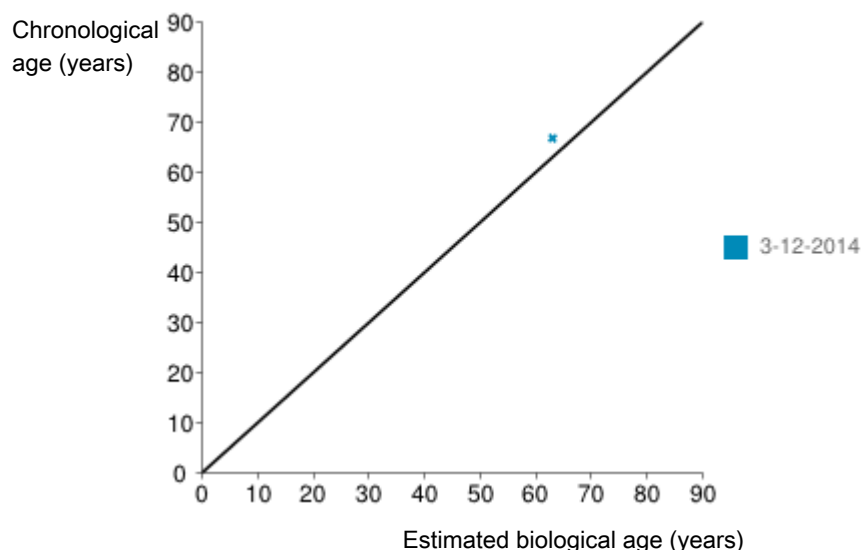


The adjacent graphs show the historic evolution of your results. Each spot represents an analysis that you have had.

The steeper the slopes of the lines, the faster the speed of telomere shortening and cellular aging.

We encourage you to take two or more tests in order for this information to become meaningful.

## Longitudinal analysis - Chronological age vs. biological age



The adjacent graph shows the longitudinal evolution of your biological age vs. your chronological age. Each spot represents an analysis you have had.

Spots above the line correspond to an estimated biological age lower than your chronological age.

Spots below the line correspond to an estimated biological age higher than your chronological age.

We suggest you take two or more tests in order for this information to become meaningful.

The list of factors below has been shown to play a role in telomere length and attrition in peer-reviewed scientific publications. This list does not pretend to be exhaustive or exclusive but lists some of the many conditions for which robust scientific validity appears to have been established.

If you authorized that your anonymous questionnaire responses be shared with your physician, then the report highlights in light blue those factors, whether good or bad, that affect you and the title of the publications which show the role of this factor in telomere biology. Please note that it is your physician who will aid you in the interpretation of these factors which may or may not play a role in your personal case.

Please also note that if you did not authorize Life Length to share your anonymous questionnaire responses with your physician, then the list appears without any highlighting.

FACTORS	CLICKABLE LINKS TO STUDIES
ALCOHOL	<ul style="list-style-type: none"> <li>Association between alcohol consumption in healthy midlife and telomere length in older men: the Helsinki Businessmen Study</li> <li>Shortened telomeres in individuals with abuse in alcohol consumption</li> </ul>
AIDS	<ul style="list-style-type: none"> <li>Normal T-cell telomerase activity and up-regulation in human immunodeficiency virus-1 infection</li> <li>Telomerase activity of HIV-1-specific CD8 + T cells: constitutive up-regulation in controllers and selective increase by blockade of PD ligand 1 in progressors</li> </ul>
ATHEROSCLEROSIS	<ul style="list-style-type: none"> <li>Telomere shortening in atherosclerosis</li> <li>Short telomeres are associated with increased carotid atherosclerosis in hypertensive subjects</li> <li>Biological ageing and cardiovascular disease</li> </ul>
CANCER	<ul style="list-style-type: none"> <li>Are short telomeres predictive of advanced cancer?</li> <li>Telomere length and risk of incident cancer and cancer mortality</li> <li>Telomere shortening is an early somatic DNA alteration in human prostate tumorigenesis</li> </ul>
CARDIOVASCULAR	<ul style="list-style-type: none"> <li>Telomeres and cardiovascular disease risk: an update 2013</li> <li>The roles of senescence and telomere shortening in cardiovascular disease</li> </ul>
CYTOMEGALOVIRUS	<ul style="list-style-type: none"> <li>Cytomegalovirus infection reduces telomere length of the circulating T-cell pool</li> </ul>
DRUG CONSUMPTION	<ul style="list-style-type: none"> <li>Drug addiction is associated with leukocyte telomere length</li> </ul>

**FACTORS****CLICKABLE LINKS TO STUDIES****EXERCISE**

- Longer leukocyte telomeres are associated with ultra-endurance exercise independent of cardiovascular risk factors
- The power of exercise: buffering the effect of chronic stress on telomere length
- Telomeres and lifestyle factors: roles in cellular aging

**HEPATITIS**

- Telomere reduction in human liver tissues with age and chronic inflammation
- Telomere length in hepatitis C

**HIGH BLOOD PRESSURE**

- Association of leukocyte telomere length with circulating biomarkers of the renin-angiotensin-aldosterone system: the Framingham Heart Study
- Leukocyte telomere length, hypertension, and atherosclerosis: are there potential mechanistic explanations?
- Telomere length, risk of coronary heart disease, and statin treatment in the West of Scotland Primary Prevention Study: a nested case-control study

**HIGH GLUCOSE - DIABETES**

- White blood cells telomere length is shorter in males with type 2 diabetes and microalbuminuria
- Accelerated aging as evidenced by increased telomere shortening and mitochondrial DNA depletion in patients with type 2 diabetes
- Shortened telomere length in white blood cells of patients with IDDM

**INSOMNIA**

- Associations between rotating night shifts, sleep duration, and telomere length in women
- Short sleep duration is associated with shorter telomere length in healthy men: findings from the Whitehall II Cohort Study

**LUPUS ERYTHEMATOSUS**

- Shortened telomere length in patients with systemic lupus erythematosus

**NEURODEGENERATIVE DISORDERS**

- Accelerated cell aging in female APOE-e4 carriers: implications for hormone therapy use
- Association of shorter leukocyte telomere repeat length with dementia and mortality

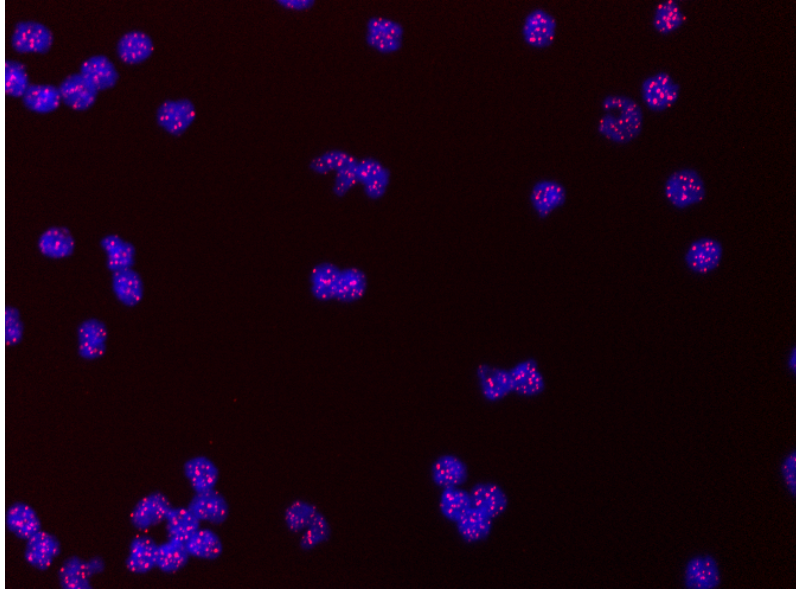
**OBESITY**

- Obesity, cigarette smoking, and telomere length in women
- Inverse association between adiposity and telomere length: the Fels Longitudinal Study
- Is obesity linked to aging?" Adipose tissue and the role of telomeres



FACTORS	CLICKABLE LINKS TO STUDIES
OSTEOPOROSIS	<ul style="list-style-type: none"> <li>Telomere length in leukocytes correlates with bone mineral density and is shorter in women with osteoporosis</li> <li>The effect of telomere length, a marker of biological aging, on bone mineral density in elderly population</li> </ul>
PULMONARY FIBROSIS	<ul style="list-style-type: none"> <li>Telomerase mutations in families with idiopathic pulmonary fibrosis</li> </ul>
RHEUMATOID ARTHRITIS	<ul style="list-style-type: none"> <li>Premature telomeric loss in rheumatoid arthritis is genetically determined and involves both myeloid and lymphoid cell lineages</li> <li>Reduced telomere length in rheumatoid arthritis is independent of disease activity and duration</li> <li>Defective proliferative capacity and accelerated telomeric loss of hematopoietic progenitor cells in rheumatoid arthritis</li> </ul>
SCHIZOPHRENIA	<ul style="list-style-type: none"> <li>Rapid telomere erosion in schizophrenia</li> </ul>
SMOKING	<ul style="list-style-type: none"> <li>Telomere shortening in smokers with and without COPD</li> <li>Obesity, cigarette smoking, and telomere length in women</li> </ul>
STRESS	<ul style="list-style-type: none"> <li>Accelerated telomere shortening in response to life stress</li> <li>Telomere length and early severe social deprivation: linking early adversity and cellular aging</li> </ul>
VITAMINS AND ANTIOXIDANTS	<ul style="list-style-type: none"> <li>Mediterranean diet, telomere maintenance and health status among elderly</li> <li>Higher serum vitamin D concentrations are associated with longer leukocyte telomere length in women</li> <li>Association of marine omega-3 fatty acid levels with telomeric aging in patients with coronary heart disease</li> </ul>

## Image capture taken from the HT Q-FISH analysis



This is an image of your own telomeres, unique to you. This comes from your blood sample, which was analyzed and measured using Life Length's state-of-the-art equipment, which allows us to take and process images on a sub-cellular level.

The image shows the nuclei of some of your cells from your blood samples (blue dots) and your telomeres (red dots). A higher intensity of fluorescence in the red dots indicates greater telomere length and a lower percentage of short telomeres.

# About telomeres in general

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## What are chromosomes?

Chromosomes are highly condensed rods of Deoxyribonucleic Acid (DNA), the genetic material which contains the building blocks of life. DNA carries a specific code that gives instructions to our body on how to grow, develop and function. The instructions are organized into units called genes. Chromosomes serve as the storage for this important material, periodically dividing along with cells and replicating to make copies of the DNA they contain. Chromosomes are also very important in sexual reproduction, as they allow an organism to pass genetic material on to its descendants. In organisms with cell nuclei, known as eukaryotes, chromosomes are found inside the nucleus. Most of these organisms have a set of chromosomes which come in pairs. In structural cells, each cell retains a complete set of chromosomes, in what is known as diploid form, referring to the fact the chromosomes contain two copies of each gene. In cells for sexual reproduction like eggs or sperm, each cell only has half of the parent organism's genetic material, stored in haploid form, ensuring that each parent passes down one copy of its genes.

## What are telomeres?

Telomeres are the ends of chromosomes, which have an essential role in protecting their integrity in the process of cellular replication. One common analogy is that they are like the plastic caps at the end of shoe laces which keep the laces from unraveling. Telomeres are formed by tandem repeats of a DNA sequence, which is highly conserved (TTAGGG in vertebrates) and associated proteins (the so-called telomere-binding proteins or "shelterins"). The function of telomeres is to protect chromosome ends from chromosome fusions and degradation, therefore, ensuring the proper functionality and viability of cells.

## What is telomerase?

Telomerase is an enzyme which is able to elongate telomeres and repair short telomeres by re-elongating them. To this end, telomerase adds telomeric repeats to the chromosome ends de novo. In non-pathological conditions telomerase is expressed in early stages of embryo development as well as in certain adult stem cell compartments. Telomerase is also highly expressed in pathological conditions, such as cancer, where it sustains the immortal growth of cancer cells. Healthy cells usually produce little or no telomerase and, as a consequence of this, they progressively shorten their telomeres associated with successive cycles of cell division, until they reach a critically short length which triggers cell death or an irreversible cell arrest known as replicative senescence (also known as the Hayflick limit).

## Why are telomeres important?

Cells stop duplicating when telomeres become too short. Therefore telomere length is considered to be an excellent biomarker of tissue renewal capacity and, consequently, of organismal aging. Telomeres progressively shorten with increasing age as a consequence of cumulative cycles of cell division that are required for tissue repair and regeneration. This occurs both in differentiated cells as well as in the stem cell compartments, and this shortening has been demonstrated to impair the ability of stem cells to regenerate tissues when needed. There is strong evidence from genetically modified mouse models demonstrating that accumulation of critically short telomeres is sufficient to cause organismal aging. Intervention that decrease the rate of telomere shortening with age, such as forced expression of the telomere-synthesizing enzyme telomerase, is also sufficient to delay aging and increase longevity. Thus, therapeutic strategies based on telomerase activation are envisioned as potentially important for intervening in age-related problems. Telomeres and telomerase are also relevant for cancer biology. More than 85% of all types of tumors activate telomerase during their formation in order to achieve immortality. Telomerase is, therefore, considered necessary to sustain cancer growth. Therapies aimed at inhibiting telomerase activity are currently tested in clinical trials of various types of human tumors.

## Why does Life Length inform the median telomere length rather than the mean value?

Telomere length is heterogeneous within each single cell, such that each chromosome end has a different length of telomeric repeats (there are 2 telomeres per chromosome and 23 pairs of chromosomes per cell). Average telomere length is the mean length of all telomeres considered together, usually within a population of cells (not even per individual cell). However, as the telomere length distribution of the cells is not symmetrical, the median telomere length is more representative of said distribution rather than the mean.

## What is the difference between median telomere length and the 20<sup>th</sup> percentile and why is this important?

The median telomere length represents the 50<sup>th</sup> percentile in the distribution of cell telomere lengths. In contrast, the 20<sup>th</sup> percentile indicates the telomere length below which 20% of the observed telomeres fall. As such it is an estimator of the percentage of short telomeres in the cells. This is important because mounting scientific evidence shows that it is the short telomeres that are responsible for causing aging and the collateral effects of aging. This is because critically short telomeres inflict permanent and deleterious damage to the cell, unless they are repaired by telomerase. Therefore, to be able to evaluate whether telomeres are prematurely short for a given chronological age it is necessary to use techniques that allow quantification of the abundance of short telomeres. Just measuring average or median telomere length of a population of cells is not sufficient to "identify" premature telomere shortening. The superiority of the technology commercialized by Life Length is based on our ability to precisely measure telomeres individually, allowing for the quantification of short telomeres.

## What is the relationship between biological age and chronological age that we can learn from our telomeres?

Not all individuals age at the same rate even though they may have the same chronological age. Therefore, it is important to identify molecular markers (other than chronological age) that can estimate the degree of aging of an organism. This information is useful for health professionals and individuals alike to anticipate premature development of age-related issues and to try to consider changes in life style (for instance, obesity and smoking have been shown to lead to accelerated telomere attrition while exercise and good nutrition slow it), to follow more closely our telomere dynamics over the years, or to benefit from potential telomerase activators. Mounting evidence suggests that the length of telomeres is a good indicator of the degree of aging of an organism.

## What are the factors that affect the length of my telomeres?

Genetics and lifestyle are fundamental factors that affect telomere length and the rate at which they shorten. Certain life habits have been associated to having longer or shorter telomeres in a significant manner. For example, smoking, obesity and psychological stress increase oxidative stress and inflammation which, in turn, contribute to higher rates of telomere attrition throughout life. Other factors such as diet, exercise, sleep are also believed to impact biological aging. Current therapies are being developed based on telomerase activation to rejuvenate telomeres. Measuring telomere length will be necessary to determine whether these therapies are effectively improving telomere length.

## Does a greater biological age compared to chronological age indicate that the individual has the risks and risk factors associated with their biological age?

There is increasing scientific evidence that shorter telomeres may be associated with higher risks of developing cardiovascular, neurodegenerative and many other age-related diseases.

## What is the relationship between telomeres and cancer?

It appears that longer telomeres may act as the defense mechanism to ward off the emergence of cancer and that when telomeres become short there is a greater chance of recombination which may give rise to cancer together with other factors. However, it is important to point out that these are currently only correlations and do not prove cause and effect relationships.

## Why do I need to know my biological age?

First, it is an excellent indicator of an individual overall general health status. Secondly, knowing our biological age permits us to obtain a better understanding of the life-style habits that impact aging and gives us the opportunity to make appropriate changes and by periodic re-testing, measure the results. Thirdly, as physicians and the medical community become more comfortable with Life Length's Telomere Analysis Technology (TAT), it will allow for more personalized medicine as doctors increasingly treat patients taking into consideration their biological age.

## How is this calculated?

Life Length calculates biological age using a mathematical formula that takes into consideration the individual's chronological age group which is then weighted by their telomere length results.

## How often should I get my telomeres measured?

We recommend that individuals interested in monitoring their telomere length repeat the measurement annually, although periods of six months may be considered for individuals making significant lifestyle changes.

## How do you measure telomeres?

We measure telomere length by quantitative FISH (Q-FISH or Quantitative Fluorescence In Situ Hybridization) on interphase nuclei both on tissue sections (Telomapping) and on blood cells or any other cell type that can be attached to a plate (High Throughput Q-FISH) where telomeres are hybridized with an anti-telomeric probe labeled with a fluorophore. Each anti-telomeric probe recognizes a fixed number of telomeric repeats (base pairs). For this reason, the intensity of the fluorescent signal from telomeric probes that hybridize to a given telomere is directly proportional to the telomere length. Fluorescence intensity signals are transformed into telomere length values for each individual telomere spot within a cell, allowing for the measurement of the whole telomere length distribution in a cell population.

## What other large scale techniques exist and why is Life Length's technology the most accurate among them?

Life Length's TAT is the only commercial telomere measurement technique that allows the quantification of all the telomeres in a cell population, providing the full histogram of telomere length distribution including the proportion of short telomeres. Alternative telomere length measurement techniques, such as Q-PCR (Quantitative Polymerase Chain Reaction) or flow cytometry based methods, can only determine the mean telomere length of a cell or a sample, but are unable to provide either the median value (a far better measure statistically) nor individual telomere measurements which are crucial to a clinical understanding of telomere attrition as a cause of aging and contributing factor to the development of age-related diseases.

## How precise is your measurement?

The mean variability of sample replicates has a coefficient of variation (C.V.) of approximately 5%. A human chromosome can contain 150 million pairs of nucleic acids or "base pairs" while the initial length of a telomere can be between 5,000 to 15,000 base pairs or less than 1/10,000 the length of the average chromosome. Life Length's TAT is so sensitive that it can measure down to 200 base pairs.

## Can you measure the telomeres in all 23 pairs of chromosomes in one cell? 92 measurements?

Yes, we can measure every single chromosome end by using quantitative telomeric FISH on metaphases. Typically for the HT Q-FISH, Life Length measures telomere spots in interphasic nuclei obtaining around of 25-30 telomeric spots per nuclei.

## How much blood is needed to measure the telomeres?

We typically use 8 - 12 ml (approx. 2 tablespoons) of blood for reproducibility and control purposes.

## What else can you measure (i.e. tissue)?

We can measure telomere length of any peripheral blood mononuclear cell type or any in vitro cultured cell line (normal or tumoral) by HT Q-FISH. Additionally the Telomapping method allows the quantification of telomere length in skin samples or biopsies (or any other available tissue), leading to the establishment of real telomere length maps. These maps can be used to localize stem cell niches or studying the biological age of a given tissue. This is important in pharmaceutical and skin care research where Life Length is providing its services to pharmaceutical, nutraceutical and other companies for product development as well as for clinical studies.

## How do I get my telomeres measured? Where is the technology offered?

Life Length offers the TAT test in more than 20 countries around the world through a growing network of major laboratory partners who work with us to commercialize the test and to assist in handling the logistics of collecting and preparing the needed blood sample.

## Are there any special requirements? Must I fast before the measurement?

No special preparation is required nor is it necessary to fast.

## How long does it take to get the results?

It takes approximately three to four weeks to deliver the results from the time that the sample is received and depending on the country where you live.



## What information do you require in the health questionnaire? Why is it so extensive?

In order to be able to provide individuals with increasingly robust information around how life-style habits and other factors influence the aging process, we require the completion of our anonymous online questionnaire ([www.lifelength-questionnaire.com](http://www.lifelength-questionnaire.com)) that is estimated to take less than 30 minutes to complete. It is important to have this information in order to be able to make statistical correlations with the questions asked and the results which, as our anonymous database grows, will allow us to provide physicians and individuals with more specific feedback and increasingly detailed statistical analysis about those aspects over which we can exercise at least some control and which impact on our rate of telomere loss and biological aging.

## How is my information kept anonymous and confidential?

Your blood sample is submitted using a numeric bar coded label and your questionnaire is completed using a corresponding and unique login and password provided by your physician. Life Length never receives your name. Reports are delivered back through our partner labs to your doctor, again using this identifying code.

## What if I get a "bad" result? What can I do?

Our report provides detailed information about your entire telomere length distribution including your 20<sup>th</sup> percentile as well as a statistically estimated biological age. Knowing that you have a lower than average 20<sup>th</sup> percentile is like knowing that you have high cholesterol or other conditions which are influenced by certain life-style choices. We always recommend you to follow professional medical advice to make those changes that may allow you to reduce your rate of telomere attrition and potentially even lengthen telomeres and thereby slow down biological aging. For individuals with unusually short telomeres, your result may have been influenced by a recent traumatic event, sickness or other stressful occurrence that could have temporarily affected the length of your telomeres. For this reason, we recommend that these individuals especially consider repeating the measurement in 6 months instead of annually.

## Want to continue to be informed about telomere biology and Life Length?

Please visit our website to see updated news and join us on:

