Telomeres and Ageing
What is Aging?

• Aging is associated with the gradual decline in performance and reserve capacity in organ systems

• Aging of organ systems is often associated with a decrease in the number and/or function of cells

• Old cells do not maintain and repair tissues as well as young cells, leading to decreased overall vitality
1930 - 1940: Beginning to Understand the End

Hermann J. Müller

X-ray mutagenesis experiments in Drosophila

Absence of terminal deletions or inversions after irradiation

Barbara McClintock

Cytogenetics of maize mutants

Chromosomes lacking telomeres form end-to-end fusions

Telomeres: special functional complexes at the end of eukaryotic chromosomes
1990’s: Discovery of enzyme “telomerase” which leads to Nobel Prize in Medicine 2009

“For the prediction and discovery of telomerase, a remarkable RNA-containing enzyme that synthesizes the ends of chromosomes, protecting them and maintaining the integrity of the genome.”

Elizabeth Blackburn
Jack Szostak
Carol Greider
Telomerase Reverse Transcriptase Delays Aging in Cancer-Resistant Mice
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Telomerase gene therapy in adult and old mice delays aging and increases longevity without increasing cancer
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Chromosomes are Capped by Telomeres

telo (end) mere (segment)

Why Should You Care About Telomeres?
What are telomeres?

Telomeres are structures on the ends of chromosomes which ensure their stability during the process of cellular replication.
Telomeres of a young or quiescent cell
Stop

Telomeres of a senescent (aging) cell or a cell with uncapped ends
Why are telomeres important?

- In any living organism, aging is the result of the cell replication process.
- As cells replicate, telomere length decreases to the point where they are no longer viable.
- Telomere length is the best-known indicator of the aging process.
- Telomere measurement facilitates personalized medicine and better preventative health care.
- The 2009 Nobel Prize was awarded for telomere and telomerase* research.

* Telomerase is the enzyme that regulates telomere length.
In Vitro: Replicative Senescence in Normal Cells

Short telomeres correlate with replicative senescence
In Vivo: Telomeres Shorten With Increased Age

Short telomeres correlate with increased age and disease risk.

Tissue Source

- Sperm
- Placenta
- Fetal brain
- Fetal kidney
- Colon mucosa (30-65 yrs)
- Colon mucosa (65-88 yrs)
- Blood (20-39 yrs)
- Blood (40-59 yrs)
- Blood (60-79 yrs)

Telomere Length (kb)

N. Hastie ....R. Allshire Nature, 346: 866
Adverse Consequences of Short Telomeres

- Loss of tissue renewal capacity
- Failure of stem cell niches
- Induction of metabolic dysfunction
- Senescence-associated secretory phenotype (SASP)
- Increased risk of cancer (genomic instability)
Short telomeres play a central role in the development of age-related diseases

Source: Recharge Biomedical Clinic & Dr. Ed Park
How is telomere length related to diseases and lifestyle?

**Cardiovascular diseases**
- Individuals with shorter leukocyte telomere length (LTL) present a higher prevalence of cardiovascular (CV) risk factors and coronary artery lesions, and a higher risk of CV mortality, in particular, of acute myocardial infarction (1)
- Telomere length is inversely associated with pulse pressure (2)
- Shorter than average leukocyte telomeres may mean 3-fold risk of myocardial infarction (3)

**Oxidative stress**
- Oxidative stress and inflammation are major factors that accelerate age-related telomere shortening, leading to the hypothesis that telomere attrition could serve as a biomarker of the cumulative burden of oxidative stress and inflammation (4)

**Depression and Stress**
- There is a correlation between depression and stress and shorter telomere length, therefore managing stress becomes a key component in prolonging telomeres' lifetime (5)

**Oncology**
- It is known that short telomeres and subsequent genomic instability contribute to malignant transformation, and it is therefore likely that people with shorter telomeres are at higher risk for different types of cancer (6)
- Telomere length as well as telomerase activity is involved in cancer progression and outcome (7)

**Neurology**
- Short telomeres are associated to mood disorders, depression in bipolar disorder, Alzheimer’s disease, dementia, etc. (8)

**Infertility**
- Telomere length predicts embryo fragmentation after in vitro fertilization (9)
- Short telomeres increase the risk of aneuploidy (10)

**Healthy lifestyle**
- Vigorous physical activity appears to protect those experiencing high stress by buffering its relationship with TL. Physical activity is related to longer telomeres (11)

**Nutraceuticals**
- Telomere length has been shown to be positively associated with nutritional status in human and animal studies. Various nutrients influence telomere length potentially through mechanisms that reflect their role in cellular functions including inflammation, oxidative stress, DNA integrity, DNA methylation and activity of telomerase, the enzyme that adds the telomeric repeats to the ends of the newly synthesized DNA (12)
Some nutritional factors that influence telomere length

- Diet and nutrition are among the most important factors influencing aging and health span and over 100 papers have been published demonstrating this.

- Therefore measuring telomeres as a biomarker for how these factors influence aging, and by extension, on the risk of developing age-related diseases, is highly relevant for physicians and individuals in preventive and personalized healthcare.
Influence of Telomeres on Cardiovascular Health

• Reduced telomere lengths are found in patients with cardiovascular risk factors such as atherosclerosis, hypertension, obesity, diabetes, smoking, physical inactivity, stress, and chronic infections.

• Shorter telomeres have been associated with increased incidence of diseases and poor survival.

• A positive effect on telomere length is found with increased physical activity, statins for treatment of high cholesterol and higher blood levels of omega-3 fatty acids.
Aging and Cancer: A Double-edged Sword

Cancer Rises with Increased Age
Telomeres and Aging Recent Headlines

• **Science Daily**, March 27, 2013. Short telomeres are not only a marker for higher risk of disease and mortality, but are a likely underlying cause of several age-related diseases—including heart disease and various cancers. The team measured telomere lengths in over 48,000 individuals and identified seven genetic variants that are associated with telomere length, and found that these genetic variants also affected risk of various diseases.

• **EurekAlert**, March 9, 2013. Scientists at the Intermountain Heart Institute Salt Lake City, showed that people with longer telomeres live longer. The study's lead researcher, Dr. John Carlquist, said of telomere testing "We can already test cholesterol and blood pressure of a patient to see how treatment is working, but telomere testing could give us a deeper view into how the treatment is affecting the body and whether or not the treatment is working.”
Telomeres and Aging Headlines


• **Genetic Engineering & Biotechnology News**, January 24, 2013. Research from the Spanish National Cancer Research Centre study shows caloric-restriction slows the rate of telomere shortening.

• **The New York Times**, January 27, 2010. German researchers find that middle-age people with more consistently active lifestyles had telomeres on average 40% longer than those who were primarily sedentary.

• **The Globe and Mail**, January 20, 2010. Researchers from the University of California, San Francisco, report that patients with coronary artery disease who had the highest blood levels of omega-3 fats had a slower rate of telomere shortening than those with less omega-3.
Telomere Length: Biomarker of Cellular Aging

- Telomere length
- Normal tissues and organs (stem cells)
- Telomeropathies
- Health
- Disease risk
- Age (years): 30-40, 70-80
Stress, Diet, Inflammation Leads to Oxidative DNA Damage and Can Accelerate Telomere Shortening

![Graph showing the relationship between telomere length and age. The graph illustrates that increased stress leads to a shorter telomere length, which correlates with an increased risk of disease, especially in older age ranges (50-80 years).]
Telomere Length Modification Delay Cellular Aging in Healthy Individuals

Reduced stress, better nutrition, exercise, reduced

Normal tissues and organs (stem cells)

Health

Disease risk

Age (years)

70-80
90-100
A New Biomarker for a New Age in Preventative and Personalized Medicine

• Life expectancy in the developed world has dramatically expanded to over 80 years.

• People routinely suffer from age-related diseases: cancer, cardiovascular diseases, and neurological diseases.

• At the core of all these diseases is the fundamental biology of telomeres.

• Genetic, epigenetic, environmental and life-style factors all influence in the rate of telomere loss in individuals.

• Telomere length has been established as the most accurate indicator of cellular aging, reflecting the influence of all these factors.

• Therefore, being able to measure and monitor the rate of telomere attrition and implied biological (vs. chronological) age is an incredibly important diagnostic tool for preventive and personalized medicine.
"If I'd known I was going to live this long, I'd have taken better care of myself."

• --Eubie Blake, age 100
The % of Short Telomeres, Not Average Telomere Length Determines the Onset of Disease

- Percent of short telomeres detect more differences between individuals than average length
- Percent of short telomeres show higher scattering as we age
- Percent of short telomeres reflect genetic, environmental and lifestyle habits
Conclusions

• The analysis of human telomere length has become a central validated biomarker that reflects biological (not chronological) human aging processes.

• There are many specific things that we can do that affect our level of cellular turnover, and hence telomere attrition and there rate of aging and risk of developing age-related diseases.
Introducing Telos95™ - an all-natural botanical extract that halts telomere shortening

Certified Nutraceuticals, the makers of Telos95™, have partnered with Life Length to study, test, and confirm that all-natural Telos95™ halts telomere shortening.

This means that Telos95™ can increase the healthy lifespan of your body’s cells, effectively delaying and slowing the ageing process at the DNA level.

Telos95™ is an affordable, all-natural product that:
- supports telomere health
- supports healthy longevity
- supports heart and cardiovascular health
- provides full-spectrum antioxidant activity