Telomeres and telomerase: source of eternal youth?

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Abstract
Telomeres of normal human somatic cells become shorter with each cell division as a result of end replication problem, so that they possess a limited replicative potential. Critically short telomeres can trigger a persistent DNA damage response that leads to the cell enters senescence and eventually apoptosis. This situation causes an accelerated-aging phenotype and decreased lifespan due to premature depletion of stem cells and subsequent organ/tissue failure. The rate of telomere shortening associated with normal aging can be modified by risk factors, such as psychological and oxidative stress, obesity and sedentary lifestyle, smoking, excess alcohol intake and cognitive impairment, that induce diseases and premature death.

Keywords: aging, leukocyte telomere length, lifespan, cell senescence, risk factors

Objective
Nowadays aging is one of the problems that more concern us. Hence, the aim of this work is to report on the factors that increase the rate of shortening telomere length and causes a premature-aging phenotype. Thus, we will can delay the telomere-based replicative senescence, and ultimately the onset of age-related diseases.

Methods
The materials required for the memory have been books, articles and reviews from Pubmed, articles whose corresponding author sent me, and videos. To choose them I considered the most outstanding authors in this field.

Results

1. Telomeres and telomerase

In mammals, telomeres are capped with shelterin complex. Some of these six core proteins influence the T-loop formation, which protects chromosome ends from degradation.

Telomere length is maintained by a balance between processes that lengthen telomeres, such as the activity of the telomerase, and processes that shorten them, as the end-replication problem.

2. Telomere length measurements

2.1. Telomere shortening

Telomeres are 15–20 kb but shorten gradually throughout the life.

2.2. Telomere length as a biomarker

• Biological ageing
• General health status and health span
• Chronic disease risk
• Progression and premature mortality for people aged >60 years

3. Replicative senescence promotes aging

Critical telomere shortening & loss of function of sheltering components
Single- and double-strand DNA breaks
Constitutive p53 maintains cellular senescence for years
Somatic mutations
Genomic instability
Cellular crisis
Reactivation of hTERT
Immortal growth state

Conclusions

1. Aging is dependent on number of cell divisions, not necessarily by chronological time, due to the end-replication problem provides a limited proliferative capacity
2. Telomere shortening in lymphocytes becomes faster in people >50 years of age. In the elderly, telomere shortening is strongly associated with age-related diseases and higher mortality rates.
3. The production of immortalized cells, using telomerase activators, may treat chronic and aged-related diseases that are due to telomere-based replicative senescence.
4. We have to adopt a healthy lifestyle, especially after age 30, when the low-risk factors most influence telomere length.

References

Table: Length telomere-related diseases

<table>
<thead>
<tr>
<th>Age-related diseases</th>
<th>Germine mutations in the Terc and Tert telomerase</th>
<th>Mutations in sheltering components</th>
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<tbody>
<tr>
<td>Type 2 diabetes</td>
<td>Dyskeratosis congental</td>
<td>Cancer</td>
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<td>Cardiovascular disease</td>
<td>Aplastic anaemia and leukaemia</td>
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<td>Vascular dementia</td>
<td>Idiopathic pulmonary fibrosis</td>
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Table: Factors that modulate aging

5.1. Genetics vs environment factors

Environment factors (healthy lifestyle behaviours) modulate inflammation and oxidative stress

5.2. Psychological stress

Difference in “biological age” between high- and low-stress groups: 9-17 years.

5.3. Physical activity, diet and body weight

Anti-aging effects
Pro-aging effects

Table: Smoking

5.5. Alcohol intake

The difference in leukocyte telomere length at old age between alcohol abstainers and heavy drinkers corresponds to a difference in “biological age” of 10 years.

5.6. Socio-economic status/education

Relative status reduces risk for multiple diseases of aging³ and better health.

Table: Conclusions

Age and telomere length: shorter length by race and education. From Adler N, et al. (2012) Brainbehaviorintrau. 87:11-21