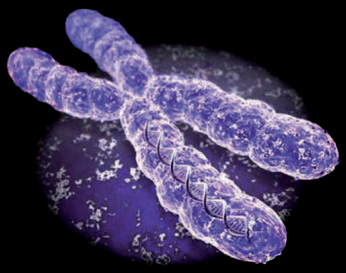
Telomeres:
cancer or eternal youth?



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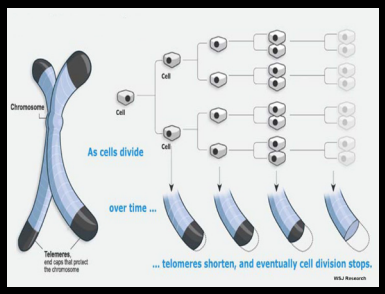
Introduction

Chromosomes cannot be completely replicated during DNA synthesis, a phenomenon termed the "end-replication problem". Telomeres are repetitive DNA sequences (GGGTTA) and specialized proteins at the end of linear chromosomes.
The end-replication problem can be overcome by telomeres and telomerase. Telomerase is an enzyme that can add telomeric DNA repeats to the chromosome ends the novo. However, most normal cells do not express telomerase and thus some telomeric sequences are lost in each cell division.
The telomeric structure prevents cellular DNA repair machineries from recognizing chromosome ends as broken DNA and thus prevents aberrant chromosome fusions and genomic instability.

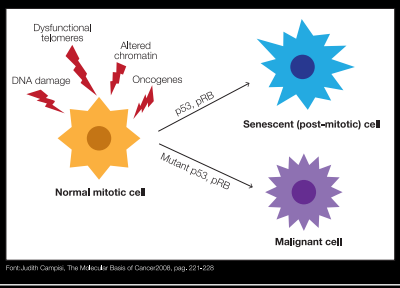
Senescence



Cellular senescence is an essentially irreversible arrest of cell proliferation. When telomeres become short, cells enter in this state. Telomerase is able to extend the lifespan of cells in culture by maintaining telomeres.

Cancer

Dysfunctional telomeres cause genomic instability, which in turn leads to malignant transformation because potentiate occurrence of mutations and reactivation of telomerase. This would provide to the mutated precancerous cell the capacity to divide indefinitely, impinging on tumorigenesis.



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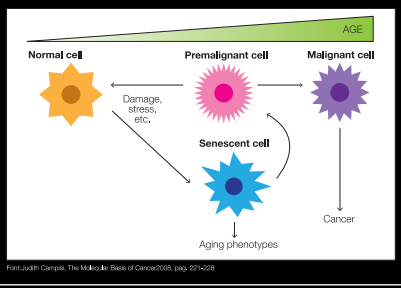
Aging

The accumulation of senescent cells can be attributed to an increase in the number of cells with dysfunctional telomeres. These cells might contribute to the age-related decline in tissue structure and function that is a hallmark of aging organisms. Telomerase exerts an anti-age activity.



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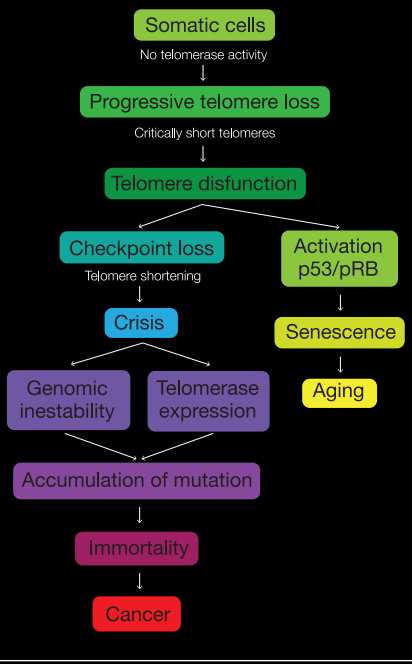
Risk factors of telomere shortening

There are some factors that seems to have influence on faster telomere shortening:

- Obesity
- Diet
- Smoking
- Stress
- Alcohol abuse
- Ultraviolet irradiation
- Low levels of education

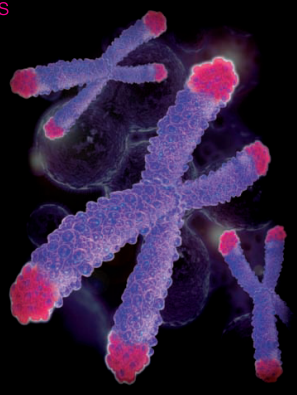
Most of them are associated with increased oxidative stress and inflammation. Both process lead to an increase in cell division.
There could be differences on telomere length between sexes or skin colour.

Summary



Conclusions

1. Senescent cells have two important roles:
   - Suppressing cancer development in young organisms
   - Facilitating cancer development (and other diseases) in ageing organisms
2. Balance between cell turnover and limited number of divisions.
3. Sufficient rate of cell division keep us relatively fit during the reproductive years, but not have an enormous reservoir of cell divisions
4. Telomerase:
   - Inhibition could be an effective anti-cancer therapy
   - Activators can be used for age-related diseases treatment



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