

# Abstract

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## Telomeres and aging.

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**BACKGROUND:** Telomeres play a central role in cell fate and aging by adjusting the cellular response to stress and growth stimulation on the basis of previous cell divisions and DNA damage. At least a few hundred nucleotides of telomere repeats must "cap" each chromosome end to avoid activation of DNA repair pathways. Repair of critically short or "uncapped" telomeres by telomerase or recombination is limited in most somatic cells and apoptosis or cellular senescence is triggered when too many "uncapped" telomeres accumulate. The chance of the latter increases as the average telomere length decreases.

**DISCUSSION:** The average telomere length is set and maintained in cells of the germline which typically express high levels of telomerase. In somatic cells, telomere length is very heterogeneous but typically declines with age, posing a barrier to tumor growth but also contributing to loss of cells with age. Loss of (stem) cells via telomere attrition provides strong selection for abnormal and malignant cells, a process facilitated by the genome instability and aneuploidy triggered by dysfunctional telomeres. The crucial role of telomeres in cell turnover and aging is highlighted by patients with 50% of normal telomerase levels resulting from a mutation in one of the telomerase genes. Short telomeres in such patients are implicated in a variety of disorders including dyskeratosis congenita, aplastic anemia, pulmonary fibrosis, and cancer.

**SUMMARY:** Here the role of telomeres and telomerase in human aging and aging-associated diseases is reviewed.

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