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# Longevity, telomeres and cancer

## Abstract

Telomeres are essential regulators of chromosomal integrity, cellular lifespan, and organismal aging. Progressive telomere shortening limits replicative capacity and functions as a tumor suppressor mechanism. However, critically short telomeres can induce genomic instability, facilitating carcinogenesis. In contrast, reactivation of telomerase in malignant cells restores replicative immortality. This dual and paradoxical role places telomeres at the center of the intersection between longevity and cancer. This editorial reviews the molecular mechanisms underlying telomere biology, its clinical implications, and emerging therapeutic strategies.

**Key words:** genomic instability, carcinogénesis, clinical implications, nucleotide sequences, malignant transformation

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## Introduction

Telomeres consist of repetitive nucleotide sequences (TTAGGG) and associated protein complexes that protect chromosomal ends from degradation and end-to-end fusion.[1] Their progressive shortening during cell division reflects the "end-replication problem," originally described in cellular aging models.[2]

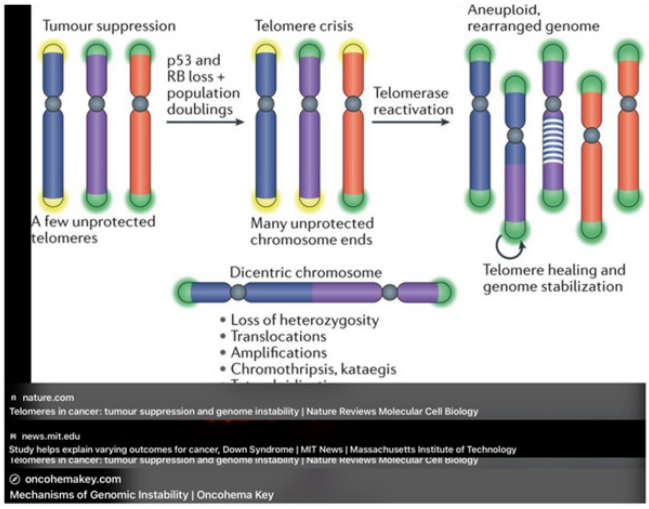
When telomeres reach a critical length, cells undergo senescence or apoptosis via activation of DNA damage pathways involving p53 and R.[3] This mechanism is a key barrier against malignant transformation.

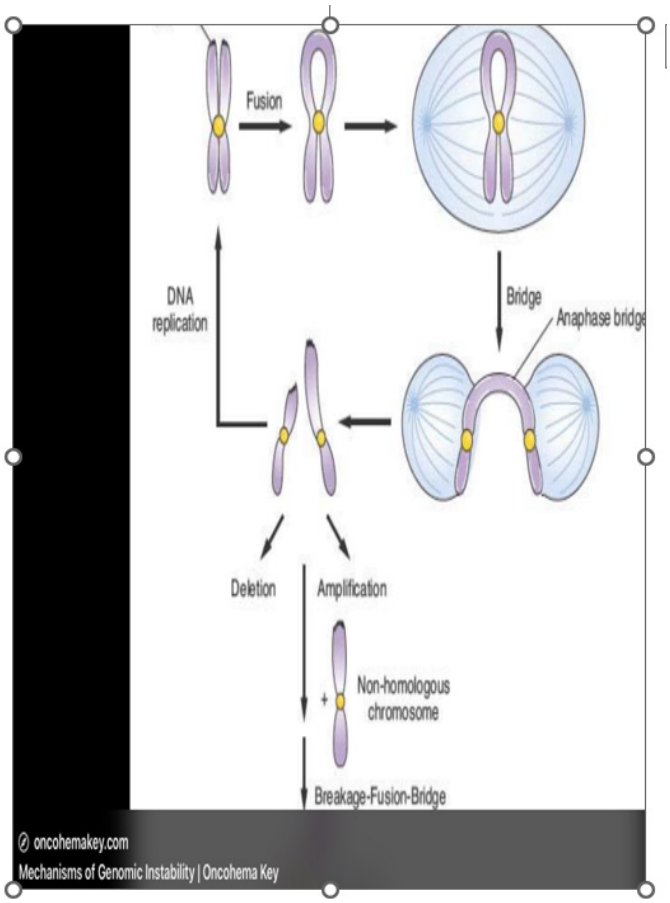
However, if these checkpoint pathways fail, telomere dysfunction leads to chromosomal instability—one of the defining features of cancer.[4]

## Development

### Telomeres and biological aging

Telomere shortening correlates strongly with biological aging. Epidemiological studies demonstrate that reduced telomere length is associated with increased mortality and age-related diseases (Figure 1).[5,6]



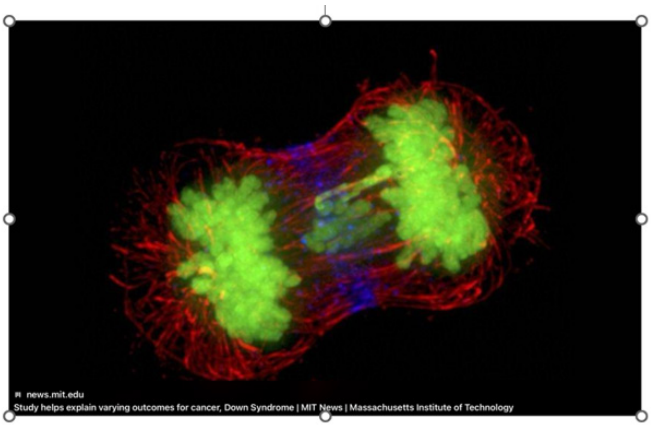



**Figure 1** Conceptual Model of Telomere Dynamics.

At the molecular level, critically short telomeres activate ATM/ATR-mediated DNA damage responses, leading to cellular senescence and the senescence-associated secretory phenotype (SASP), which contributes to chronic inflammation and tissue degeneration.[7]

### Telomere dysfunction and carcinogenesis

Telomere dysfunction has a dual role:

- Tumor suppression through replicative limits
- Tumor promotion via genomic instability

Critically short telomeres can trigger breakage–fusion–bridge cycles, generating:

- Chromosomal rearrangements
- Gene amplifications
- Aneuploidy

These alterations are central to early oncogénesis (Table 1) (Figure 2).[8]

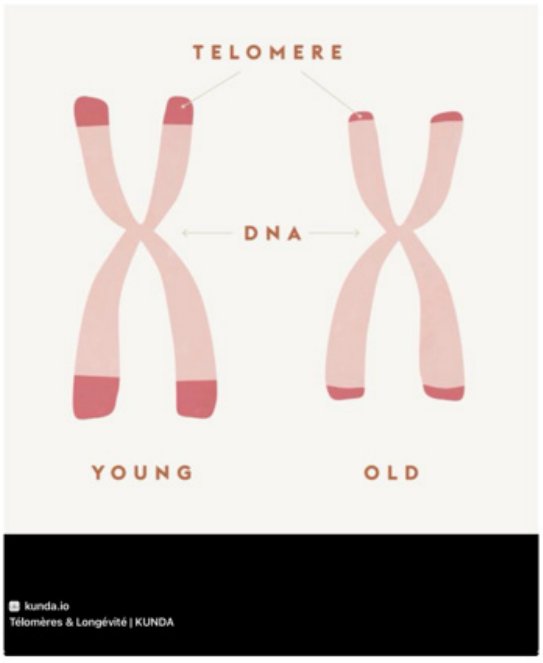



**Figure 2**

**Table 1** Dual role of telomeres

| Mechanism | Effect on aging | Effect on cancer |
|---|---|---|
| Telomere shortening | Cellular senescence | Tumor suppression |
| Critical shortening | Tissue degeneration | Genomic instability |
| Telomerase activation | Potential longevity | Cellular immortality |

### Telomerase reactivation and cellular immortality

Most cancers (≈85–90%) reactivate telomerase through upregulation of TERT.[9]

Foundational discoveries by Elizabeth Blackburn, Carol Greider, and Jack Szostak established telomerase as a central enzyme in chromosomal maintenance.[10]

Mechanisms include

- TERT promoter mutations
- Epigenetic reprogramming
- Alternative lengthening of telomeres (ALT)

This enables malignant cells to bypass senescence and achieve unlimited proliferation.[11]

### Clinical and therapeutic implications

Telomere biology is increasingly relevant in clinical oncology:

### Biomarkers

Telomere length has prognostic value in several malignancies.[12]

### Targeted therapies

Telomerase inhibitors (e.g., imetelstat) show activity in hematologic diseases.[13]

### Aging interventions

Strategies aimed at telomere preservation remain investigational and carry oncogenic risk.[14]

## Future Perspectives

Future directions include:

- Selective telomerase inhibition in cancer cells
- Integration of telomere profiling in precision oncology
- Gene-editing approaches targeting telomere dynamics
- Safer anti-aging strategies that minimize cancer risk

The key challenge is balancing longevity with oncologic safety.

## Conclusions

Telomeres represent a biological paradox: they suppress tumorigenesis by limiting cellular proliferation, yet their dysfunction promotes genomic instability and cancer development. Telomerase reactivation resolves this limitation in malignant cells, enabling immortality.

Understanding this duality is critical for advancing both oncology and longevity science. Future therapeutic strategies must carefully navigate this balance to avoid unintended consequences.

A biphasic model: progressive telomere shortening with age leads to a critical threshold (crisis). If checkpoint failure occurs,

genomic instability emerges. Subsequent telomerase activation allows malignant progression and immortalization.

## Acknowledgments

None.

## Conflict of Interest

None.

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