Telomeres and telomerase: Key players in the aging process and cancer progression.

Daisy Morgan*

Department of Human Genetics, University of Chicago, Chicago, USA

Received: *26-Apr-2024, Manuscript No. RNAI-24-137860;* **Editor assigned:** *29-Apr-2024, Pre QC No. RNAI-24-137860 (PQ);* **Reviewed:** *14-May-2024, QC No. RNAI-24-137860;* **Revised:** *20-May-2024, Manuscript No. RNAI-24-137860 (R);* **Published:** *27-May-2024, DOI: 10.35841/2591-7781.19.1000193.*

Description

Telomeres, repetitive nucleotide sequences located at the ends of chromosomes, play a critical role in maintaining chromosomal stability. Their primary function is to protect chromosome ends from deterioration and fusion with neighboring chromosomes. Telomerase, an enzyme complex that extends telomeres, is pivotal in preserving telomere length, particularly in stem cells and cancer cells. This manuscript explores the regulation of telomeres and telomerase activity, elucidating their implications for aging and cancer development.

Telomeres consist of repetitive DNA sequences (TTAGGG in vertebrates) and associated proteins forming a protective cap at the end of chromosomes. This structure prevents chromosome ends from being recognized as double-strand breaks by the DNA damage repair machinery. Each cell division results in the progressive shortening of telomeres due to the end-replication problem, wherein DNA polymerase cannot fully replicate the 3' end of the DNA strand. This attrition eventually leads to replicative senescence or apoptosis when telomeres become critically short, a process considered a hallmark of cellular aging.

Telomerase is a ribonucleoprotein enzyme composed of the catalytic subunit Telomerase Reverse Transcriptase (TERT) and an RNA Component (TERC) that serves as a template for adding telomeric repeats. Telomerase counteracts telomere shortening by elongating telomeres, thus extending the replicative lifespan of cells. While telomerase activity is prominent in embryonic stem cells, germ cells, and certain adult stem cell populations, it is absent or very low in most somatic cells.

The regulation of telomerase activity is multifaceted, involving transcriptional, post-transcriptional, and post-translational mechanisms. Key transcriptional regulators of TERT include the c-Myc oncogene, which activates TERT transcription, and the tumor suppressor p53, which represses it. Epigenetic modifications, such as DNA methylation and histone modifications, also influence TERT expression. Post-transcriptionally, alternative splicing of TERT mRNA can generate non-functional variants, modulating enzyme activity. Post-translational modifications, including phosphorylation and biquitination, further regulate telomerase assembly, localization, and function.

Telomere shortening is associated with cellular senescence, a state of irreversible growth arrest, and contributes to organismal aging. Senescent cells accumulate with age and secrete pro-inflammatory cytokines, growth factors, and proteases, collectively termed the Senescence-Associated Secretory Phenotype (SASP). This chronic inflammation can disrupt tissue homeostasis and function, promoting age-related diseases. Telomere length in leukocytes is commonly used as a biomarker of biological aging, with shorter telomeres correlating with increased morbidity and mortality. In contrast to somatic cells, most cancer cells activate telomerase, enabling limitless replicative potential, a hallmark of cancer. Approximately 85%-90% of cancers exhibit upregulated telomerase activity, while the remaining 10%-15% maintain telomere length through Alternative Lengthening of Telomeres (ALT) mechanisms. Telomerase activation in cancer cells is often due to mutations in the TERT promoter, leading to its upregulation. This reactivation of telomerase allows cancer cells to bypass senescence and evade apoptosis, contributing to tumorigenesis and progression.

Understanding the dual roles of telomeres and telomerase in aging and cancer opens avenues for potential therapeutic interventions. In the context of aging, strategies aimed at preserving telomere length, such as telomerase activation or telomere elongation therapies, hold promise for delaying aging and extending healthspan. However, these approaches must be cautiously developed to avoid increasing cancer risk.

In cancer therapy, telomerase inhibition represents a compelling target. Small-molecule inhibitors, antisense oligonucleotides, and immunotherapies targeting telomerase have shown preclinical efficacy in reducing tumor growth and inducing cancer cell death. For cancers utilizing ALT, targeting associated pathways and proteins involved in telomere maintenance presents an alternative therapeutic strategy.

Telomeres and telomerase are central to the regulation of cellular lifespan and genomic stability. Their roles in aging and cancer underscore the delicate balance between cell proliferation, senescence, and survival. Ongoing research into the molecular mechanisms governing telomere dynamics and telomerase activity will further elucidate their contributions to human health and disease, potentially leading to novel interventions for age-related diseases and cancer. Understanding and manipulating these processes could pave the way for advancements in regenerative medicine and

oncology, with the ultimate goal of improving human healthspan and lifespan.

***Correspondence to:**

Daisy Morgan

Department of Human Genetics, University of Chicago,

Chicago, USA

E-mail: m_daisy@uchicago.edu