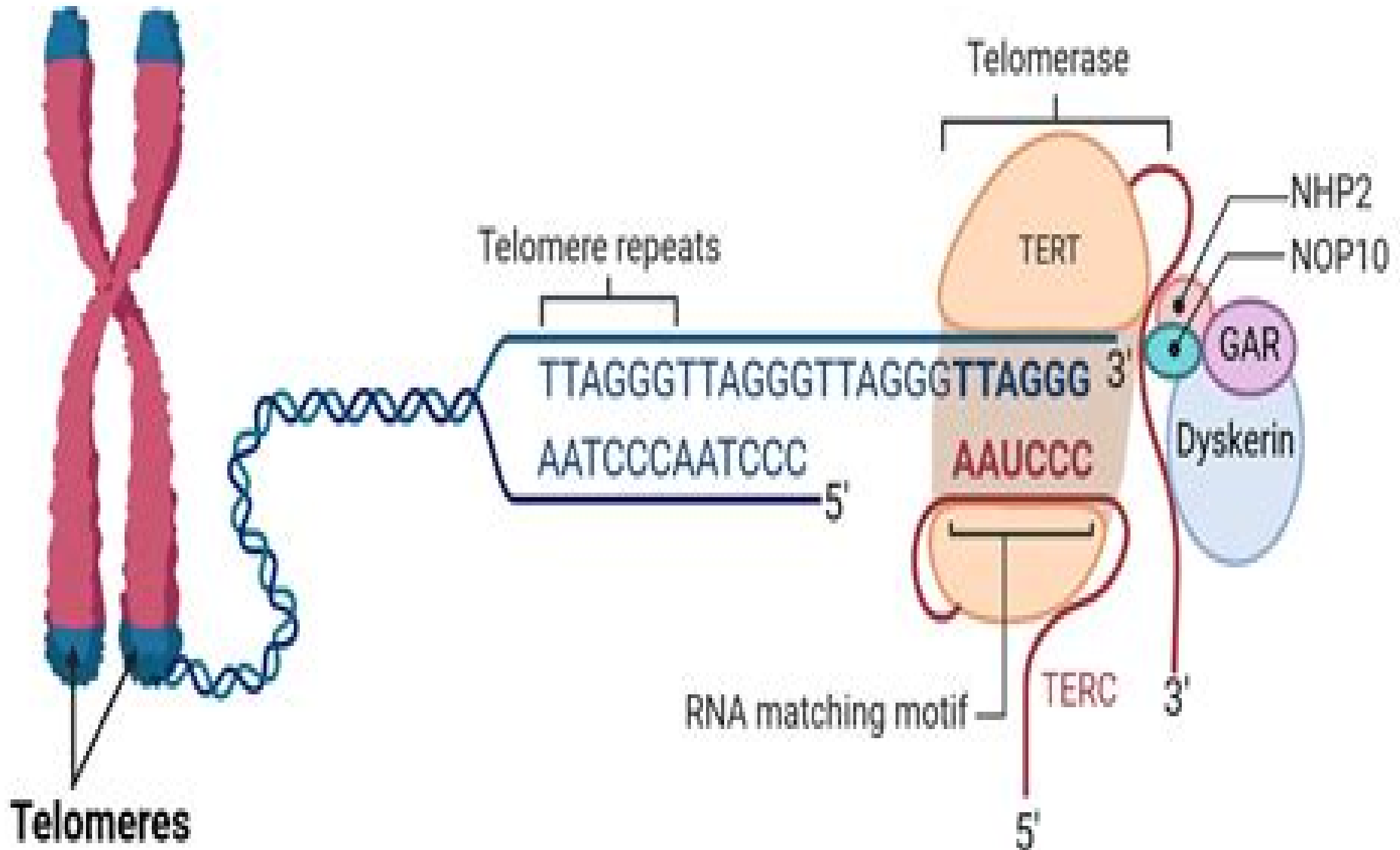


Telomeres and Telomerase

Chromosome



Telomeres

Telomeres And Telomerase

Carole Saintome



Telomeres And Telomerase:

Telomeres and Telomerase Derek J. Chadwick, Gail Cardew, 2008-04-30 Telomeres and Telomerase Chairman Sydney Brenner 1997 Telomeres are the protective genetic elements located at the ends of chromosomes and are essential for correct chromosomal structure and function They are not fully replicated by the conventional DNA polymerase system because DNA synthesis occurs only in the 5 to 3 direction and requires an RNA primer for initiation Consequently cells require a special enzyme to maintain the telomeric ends of chromosomes during each round of replication This enzyme telomerase is a ribonucleoprotein that extends chromosome ends by adding short stretches of nucleotide repeats using a portion of its integral RNA component as the template Recently much excitement has been generated by the suggestion that telomerase or rather the absence of telomerase and the resultant loss of terminal DNA is a cause of human ageing The evidence for this is twofold the telomeres of certain cells in culture shorten during their lifespan and immortalization of cells is associated at least in some cases with the maintenance of telomeres and telomerase activity The latter observation prompted the analysis of clinical samples from patients with cancer and the demonstration that in contrast to normal somatic cells malignant cells possess telomerase activity This is a unique book Not only does it contain the latest experimental results from an international group of experts but it also includes critical examinations of the current evidence and discussions that attempt to identify the central and underlying concepts of this rapidly expanding field **Telomeres and Telomerase** John A. Double, Michael J. Thompson, 2008-02-02 The fundamental problem that dividing cells have to overcome is that of end replication Chromosomes shorten by many bases during DNA replication and so this presents a major hurdle that a cell has to overcome both to enable it to proliferate and for the larger organism to survive and reproduce The enzyme telomerase provides a mechanism to ensure chromosome stability in both normal and neoplastic cells The demonstration of telomerase expression in a majority of tumors and the realization of the potential role of telomerase in aging has opened up the potential for telomerase to be used as a target for therapeutic intervention There is therefore great interest in the expression and activity of telomerase in a wide range of biological disciplines *Telomeres and Telomerase Methods and Protocols* has been produced as a tool for the many researchers in different areas of cell biology who are interested in following research in the area of telomerase and telomere maintenance either in the area of fundamental mechanisms or perhaps in the area of more applied drug discovery work *Telomeres and Telomerase in Aging, Disease, and Cancer* K. Lenhard Rudolph, 2007-11-07 Telomere shortening represents one of the basic aspects of ageing and telomere dysfunction could contribute to the accumulation of DNA damage during ageing This book summarizes evidence and data indicating that telomere dysfunction influences human ageing diseases and cancer The book describes our current knowledge on checkpoints that limit cellular lifespan and survival in response to telomere dysfunction There is special focus on adult stem cells **Telomeres and Telomerase in Cancer** Keiko Hiyama, 2009-03-18 Telomerase an enzyme that maintains telomeres and endows eukaryotic

cells with immortality was first discovered in tetrahymena in 1985 In 1990s it was proven that this enzyme also plays a key role in the infinite proliferation of human cancer cells Now telomere and telomerase are widely accepted as important factors involved in cancer biology and as promising diagnostic tools and therapeutic targets Recently role of telomerase in cancer stem cells has become another attractive story Until now there are several good books on telomere and telomerase focusing on biology in ciliates yeasts and mouse or basic sciences in human providing basic scientists or students with updated knowledge Telomerases, Telomeres and Cancer Guido Krupp, Reza Parwaresch, 2003-01-31 This volume provides broad insights to the most recent discoveries in telomere biology with current applications in tumor diagnostics and future potentials in therapy Special features of diverse organisms are presented with ciliates the telomerase discoverer organisms yeasts the molecular geneticists toy for eukaryotes including plants and insects as well 28 chapters were written by a group of leading research scientists working in the telomere telomerase fields today This book will be a core reference for any physician scientist or educated reader with an interest in the exciting developments in this research field **Telomerase and non-Telomerase Mechanisms of Telomere Maintenance** Tammy A. Morrish, 2020-04-01 This book Telomerase and non Telomerase Mechanisms of Telomere Maintenance is a collection of reviewed and relevant research chapters offering a comprehensive overview of recent developments in the field of biochemistry genetics and molecular biology The book comprises single chapters authored by various researchers and edited by an expert active in the molecular biology research area All chapters are individually complete but united under a common research topic This publication aims to provide a thorough overview of the latest research efforts by international authors on biochemistry genetics and molecular biology and open new possible research paths for further novel developments A note from the publisher It is with great sadness and regret that we inform the contributing authors and readers of this book that the Editor Dr Tammy A Morrish passed away during the publishing process of the book and before having a chance to see its publication The book Telomerase and non Telomerase Mechanisms of Telomere Maintenance was her first edited volume with us Fruitful collaboration continued until her final days We would like to acknowledge Dr Morrish s contribution to scientific publishing which she made during years of dedicated work and express our gratitude for her pleasant cooperation with us The Molecular Regulation of Telomeres and Telomerase Craig Daniel Nicholls, 2011 Telomeres are nucleoprotein caps present at each chromosomal end that play a key role in maintaining genomic stability Telomeres shorten with each cell division eventually reaching a critical length at which cellular senescence or death pathways are activated The enzyme telomerase overcomes this shortening through de novo synthesis of telomeric DNA and telomerase activity is present at high levels in cancer and stem cells Telomerase is highly regulated by extracellular and intracellular signals with this regulation having important consequences for telomere homeostasis This thesis primarily focuses on the novel role of the glycolytic enzyme glyceraldehyde 3 phosphate dehydrogenase GAPDH in the regulation of telomeres and telomerase Chapter 3 demonstrates an interaction between single

stranded 3' C rich telomeric overhangs and the N terminal Rossman fold containing NAD binding region of GAPDH. GAPDH is further revealed to inhibit telomerase activity in vitro and in cultured cells. This inhibition has been found to be dependent upon the C terminal catalytic region of GAPDH. Furthermore, this chapter also demonstrates that nitric oxide modification of GAPDH impairs telomerase inhibition. Chapter 4 examines the relationship between the telomeric DNA binding activity of GAPDH and its telomerase inhibitory function. Several residues critical for mediating telomeric DNA binding were identified by site directed mutagenesis and gel shift assays. Expression of these GAPDH mutants in MCF7 breast cancer cells revealed that they retained the ability to inhibit telomerase suggesting that telomeric DNA binding plays a role in positioning GAPDH on telomeres rather than inhibiting telomerase. However, the mutation K259N located in a known protein-protein interaction region abolishes telomerase inhibition and telomere shortening, demonstrating a critical role in telomerase inhibition for this region. This chapter also demonstrates for the first time an interaction between GAPDH and the telomerase RNA component hTERC, suggesting a switch between GAPDH binding of telomeric DNA and telomerase RNA. GAPDH specifically binds hTERC using identical components to those needed for the interaction with telomeric DNA. Furthermore, increased exogenous hTERC eliminates GAPDH mediated telomerase inhibition. Recent studies from our laboratory have demonstrated that exogenous provision of several TGF beta superfamily cytokines can inhibit hTERT expression and telomerase activity. Chapter 5 focuses on the role in telomerase regulation played by the TGF beta superfamily type II receptors by inhibiting their action with siRNA or expression of dominant negative DN proteins. Up regulation of hTERT and telomerase activity resulted from receptor knockdown, confirming the telomerase inhibitory role for these receptors. However, longterm disruption of receptor signalling by stable expression of DN receptors resulted in telomerase inhibition in three of the four receptors examined. This data clearly demonstrates a role for TGF beta superfamily receptor signalling in telomerase regulation, though this regulation is likely complex in nature. In summary, this thesis investigates a new mechanism of telomere and telomerase regulation in GAPDH while also furthering the understanding of the influence on telomerase activity by the TGF beta superfamily. The control of telomerase is important in the context of stem cell biology, cancer and aging research, and the findings from this thesis therefore have implications for all these fields.

Telomeres Carole Saintome, 2024-07-23. Telomeres are specialized DNA-protein structures that protect the ends of chromosomes to maintain their integrity. They are chromosome sentinels. This book, written by multiple authors, presents current knowledge and the most recent discoveries relating to telomeres. The first chapters describe telomere structures, DNA and proteins organization, dynamics and replication in a range of organisms including ciliates, yeast and mammals. The following chapters cover mechanisms that maintain telomere length involving telomerase and Alternative Lengthening Telomeres (ALT) mechanisms. Interestingly, telomeres are transcribed into repetitive RNA called TERRA. Telomeric repeat containing RNA: the state of the art regarding mammalian telomere transcripts is presented here. Two chapters are dedicated to the description of how telomere biology impacts the development of cancer.

and how their disfunctions induce telomeropathies telomere biology disorders Finally the book ends with a chapter presenting telomere and telomerase targeting agents as potential anticancer agents a promising therapeutic approach

Telomeres And Telomerase In Aging, Disease, And Cancer K. Lenhard Rudolph, 2009-08-01 *Telomeres* Leonardo Mancini, 2009 Telomeres are a region of repetitive DNA at the end of chromosomes which protects the end of the chromosome from destruction They protect chromosome ends from degradation and thus prevent chromosome end fusion This book describes the relevance of telomeres in the human ageing process and the telomere defects that play a role in the premature aging process Dysfunctional telomeres that can promote chromosome instability leading to DNA amplifications and terminal deletions cell cycle arrest and cell death are also described The biology and function of both telomeres and telomerase are described in this book The possible connection between telomeres ageing and senescence as well as the many disorders and chronic diseases where telomere biology seems to be important are addressed as well as future therapeutic perspectives The importance of this enzyme in cancer is reviewed in this book The data of various kind of cancers are discussed in addition to the clinical application of telomere and telomerase in human cancer The role of telomere dysfunction in apoptosis and senescence as well as its role in newly proposed models that link telomere loss to chromosome missegregation in mitosis are explained Characteristic differences of telomere lengthening during oocyte and spermatozoa growth during embryo development is also reviewed as well as the transcriptional activity at the telomeres of *Chironomus* *Diptera* and its possible role in the lengthening of the telomeres Telomere shortening in Diabetes Mellitus is also described as well as its association with hypertension diabetes mellitus insulin resistance obesity and cardiovascular mortality The notion that alterations in the three dimensional organisation of telomeres may cause malignant transformation is also addressed

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