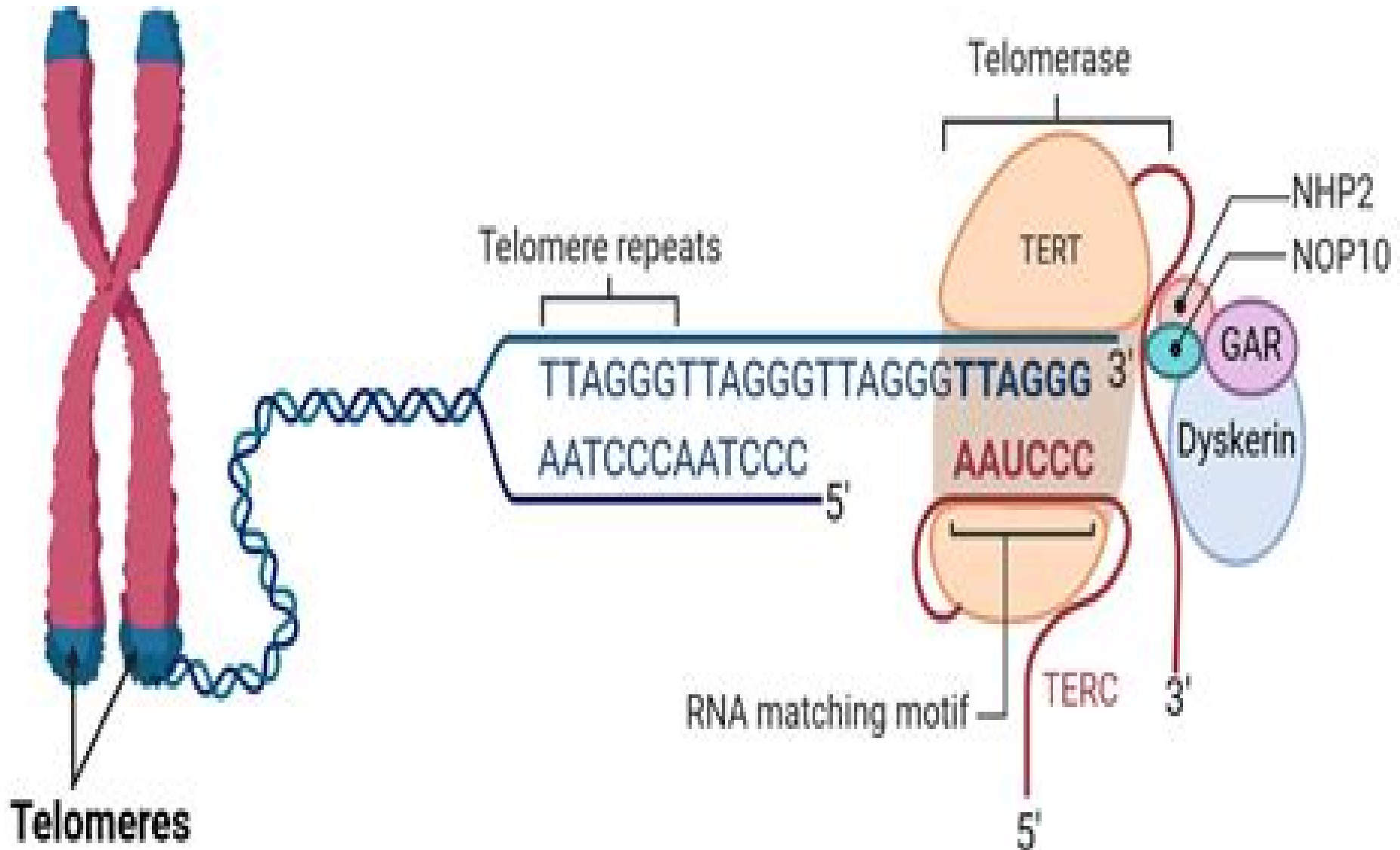


Telomeres and Telomerase

Chromosome



Telomeres And Telomerase

Joëlle El Hajj



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 genetisists 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 Rossmann 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, 2024-06-12 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 dysfunctions 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 Telomerases Neal F. Lue,Chantal Autexier,2012-05-22 This book is a comprehensive and up to date review and evaluation of the contemporary status of telomerase research Chapters in this volume cover the basic structure mechanisms and diversity of the essential and regulatory subunits of telomerase Other topics include telomerase biogenesis transcriptional and post translational regulation off telomere functions of telomerase and the role of telomerase in cellular senescence aging and cancer Its relationship to retrotransposons a class of mobile genetic elements that shares similarities with telomerase and serves as telomeres in selected organisms are also reviewed Telomeres and Telomerase Marie Eve Brault,2013 Telomeres and telomerase stand at a junction of cellular processes that govern aging cancer and disease Premature aging syndromes and age related diseases are characterized by short telomeres which compromise cell function and viability whereas cancer cells are able to reactivate telomerase or alternative lengthening of telomeres ALT mechanisms to maintain their telomeres and become immortal Telomeres and telomerase represent very attractive targets for the development of anticancer therapies However there is concern that these therapies may lead to cell resistance including the

reactivation of telomerase or ALT in telomerase positive cells Here we show that telomeric recombination can be promoted by telomere induced dysfunction an anticancer strategy currently in development despite the presence of an active telomerase Our results highlight an important potential mechanism of cancer cell resistance but might also help to understand the interplay between telomerase and the ALT pathway in the cell Defective telomere maintenance is associated with premature or accelerated aging disease Mutations in almost every component of the telomerase holoenzyme have been found to be implicated in Dyskeratosis congenita DC revealing the importance of a functional telomerase for stem cell maintenance and cell proliferative potential We found that the telomerase component dyskerin is sumoylated on highly conserved lysines and that lysine to arginine dyskerin mutants reproduce the phenotype observed in DC Our findings identify that impaired post translational modifications can lead to DC and importantly point to new possibilities in the treatment of DC Finally we investigated the complex relationship between telomere maintenance frailty and cardiovascular disease We examined the feasibility of measuring telomere length as a predictor of morbidity in elderly patients undergoing cardiac surgery Our preliminary data do not identify telomere length as a predictor of surgery outcomes Our findings also suggest that telomere length measurement in an epidemiological clinical context must be interpreted with great caution

Telomeres, Diet and Human Disease Amelia Marti,Guillermo Zalba,2017-08-30 The maintenance of telomeres repetitive sequences at the end of chromosome is essential to health Dysfunction in telomere maintenance pathways plays a role in aging cancer atherosclerosis and other diseases This has led to telomere maintenance as a prime target for patient therapies This book describes the advances in telomere research as it applies to human health and especially how lifestyle and dietary factors could modify the telomerase maintenance process The book examines the mechanisms involved the primary of which are oxidative stress and the role of sirtuins and how they can be modified by dietary patterns such as Mediterranean diet

Telomeres in Health and Disease ,2014-06-26 This special volume of Progress in Molecular Biology and Translational Science focuses on telomeres in health and disease This volume covers a variety of topics with reviews written by experts in the field Contributions from specialists in telomere diseases Informs and updates on how telomere dysfunction may cause disease in humans *Telomeres* Titia De Lange,Vicki Lundblad,Elizabeth Helen Blackburn,2006 An up to date survey of the current exciting state of telomere biology Telomeres specialized structures found at the ends of chromosomes are essential for maintaining the integrity of chromosomes and their faithful duplication during cell division Chapters in this volume cover telomere structure and function in a range of organisms focusing on how they are maintained their roles in cell division and gene expression and how deficiencies in these structures contribute to cancers and other diseases and even aging

Elizabeth Blackburn and the Story of Telomeres Catherine Brady,2009-02-13 The story of molecular biologist Elizabeth Blackburn and her groundbreaking research on telomeres and what it reveals about the resourceful opportunism that characterizes the best scientific thinking Molecular biologist Elizabeth Blackburn one of Time magazine s 100 Most

Influential People in the World in 2007 made headlines in 2004 when she was dismissed from the President's Council on Bioethics after objecting to the council's call for a moratorium on stem cell research and protesting the suppression of relevant scientific evidence in its final report. But it is Blackburn's groundbreaking work on telomeric DNA which launched the field of telomere research that will have the more profound and long-lasting effect on science and society. In this compelling biography Catherine Brady tells the story of Elizabeth Blackburn's life and work and the emergence of a new field of scientific research on the specialized ends of chromosomes and the enzyme telomerase that extends them. In the early stages of telomere research telomerase heralded as a potential cure for cancer and diseases related to aging attracted the voracious interest of biotech companies. The surrounding hype succeeded in confusing the role of telomerase in extending the life of a cell with a mechanism that might extend the lifespan of an entire organism. In Brady's hands Blackburn's story reveals much about the tension between pure and applied science, the politicking that makes research science such a competitive field and the resourceful opportunism that characterizes the best scientific thinking. Brady describes the science accessibly and compellingly. She explores Blackburn's struggle to break down barriers in an elite male-dominated profession, her role as a mentor to other women scientists, many of whom have made their mark in telomere research and the collaborative nature of scientific work. This book gives us a vivid portrait of an exceptional woman and a new understanding of the combination of curiosity, imaginative speculation and aesthetic delight that powers scientific discovery.

Telomeres and Telomerase in Neuroblastoma Joëlle El Hajj, 2017 Telomeres are nucleoprotein structures located at the ends of linear chromosomes. In most human adult normal somatic cells telomeres shorten after each cellular division. This shortening ultimately leads to senescence and/or apoptosis. By contrast, in most cancer cells telomerase activation compensates this loss and confers to these cells their infinite cell proliferation potential. Neuroblastoma (NBL) is a malignant tumor of the peripheral sympathetic nervous system and the most frequent extracranial solid tumor of childhood. NBLs are remarkably heterogeneous both at the levels of biology, genetic and clinical courses. Indeed, some of NBLs can regress spontaneously or after a mild treatment while others are in the high-risk category with poor prognosis. The molecular bases underlying this heterogeneity are poorly understood. MYCN V-Myc Avian Myelocytomatosis Viral Oncogene Neuroblastoma derived Homolog amplification, recognized as strongly associated with unfavorable patient outcome, is found in only 40% of the high-risk disease, indicating the involvement of other mechanisms. Recent observations suggest that telomerase expression and telomere dysfunctions may be one critical step in NBL development. This review provides recent insights on telomeres, telomerase regulation in NBL. Because of their involvement in the tumor cell biology, telomere and telomerase are currently at the core of new drug development.

Telomeres and Telomerase in Human Diseases Bea Wisman, 2000 *Origin and Evolution of Telomeres* Jozef Nosek, Lubomir Tomaska, 2008-05-26 Linear chromosomes represent an evolutionary innovation associated with the origin of eukaryotic cells. This book describes how linear chromosomes and primordial

pathways for maintaining their terminal structures telomeres emerged in early eukaryotes Telomeres derived from the Greek meaning terminal part were first described by Hermann Muller i

The Evolving Telomeres Arthur J. Lustig, Kurt Runge, 2016-07-19

What controls the different rates of evolution to give rise to conserved and divergent proteins and RNAs How many trials until evolution can adapt to physiological changes Every organism has arisen through multiple molecular changes and the mechanisms that are employed mutagenesis recombination transposition have been an issue left to the elegant discipline of evolutionary biology But behind the theory are realities that we have yet to ascertain How does an evolving cell accommodate its requirements for both conserving its essential functions while also providing a selective advantage In this volume we focus on the evolution of the eukaryotic telomere the ribo nuclear protein complex at the end of a linear chromosome The telomere is an example of a single chromosomal element that must function to maintain genomic stability The telomeres of all species must provide a means to avoid the attrition from semi conservative DNA replication and a means of telomere elongation the telomere replication problem For example telomerase is the most well studied mechanism to circumvent telomere attrition by adding the short repeats that constitutes most telomeres The telomere must also guard against the multiple activities that can act on an unprotected double strand break requiring a window or checkpoint to compensate for telomere sequence loss as well as protection against non specific processes the telomere protection problem This volume describes a range of methodologies including mechanistic studies phylogenetic comparisons and data based theoretical approaches to study telomere evolution over a broad spectrum of organisms that includes plants animals and fungi In telomeres that are elongated by telomerases different components have widely different rates of evolution Telomerases evolved from roots in archaebacteria including splicing factors and LTR transposition At the conserved level the telomere is a rebel among double strand breaks DSBs and has altered the function of the highly conserved proteins of the ATM pathway into an elegant means of protecting the chromosome end and maintaining telomere size homeostasis through a competition of positive and negative factors This homeostasis coupled with highly conserved capping proteins is sufficient for protection However far more proteins are present at the telomere to provide additional species specific functions Do these proteins provide insight into how the cell allows for rapid change without self destruction

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