International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Telomeres-The Protective Caps of Chromosomes

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Abstract: ***Telomeres are repetitive nucleotide sequences present at each end of the chromatids of the chromosomes.Telomeres have been compared with the "Plastic tips on the sholaces" because they prevent the chromosome ends from fraying and sticking to each other, which would scramble an organism's genetic information to cause cancer, other diseases or death. Yet each time a cell divides the telomeres get shorter. When they get too short, the cell no longer can divide and become inactive or senescent or dies. This process is associated with ageing, cancer and higher risk of death. So telomeres have been compared with a "Bomb Fuse". The telomere length is considered as a "Biomarker In Cellular Ageing". Here in this article the structure, function of telomeres and its importance in cellular ageing and human-ageing related disease is reviewed.***

Keywords: Immunosenescence, Role in Ageing, Shortening, Telomeres, Telomerase

1. Introduction

Telomeres are one of the most important element present in the chromosome of this dynamic system that plays an important role in ageing .Here studies about telomeres on ageing have been demonstrated and other human-ageing related disease is also discussed.

2. Headings

2.1 Historic Background

(From cytogenetics to replicative ageing)[1]. Chromosome ends play an important role in ensuring chromosome stability was first proposed by Barbara McClintock[2] working with maize and Herman Muller with fruit flies[3]in the 1930s.Muller coined the term "telomere" from the Greek word for "end"(telos) and "part"(meros)

The correlation between telomere length and replicative potential became a mechanistic link when it was demonstrated that the replicative potential of primary human fibroblasts can be extended indefinitely by artificially elongating telomeres [1]

2.2 Regulation of the Telomere Length in Ageing Process

2.2.1 Genetic Factors

Telomere length was measured in whole White Blood Cells (WBC) isolated from monozygotic and dizygotic twin pairs. It was found that monozygotic twins had very similar mean telomere length whereas dizygotic twins differed in this aspect [5]

Single nucleotide polymorphisms (SNPs) regarded to be the most common germ line genetic variants in the human genome, were thought to play a role in telomere length regulation [6]

2.2.2 Sex Hormones in the Control of Telomere Length

Hormonal regulation of telomere length best described for Estrogen-influence the attrition of telomeres based on protection of DNA from ROS induced damage. They exert an antioxidant effect by scavenging free radicals, inhibiting free radical formation and stimulating enzymes engaged in radical detoxification [7]

Findings of equivalent telomere length in newborn [8] boys and girls and occurrence of longer telomeres in women than men strongly support links between oestogen and telomere biology

3. Why This Shortening of Telomeres Occur?

3.1 DNA Can Be Made Only in One Direction!!

Telomeres shorten in part because of the end replication problem that is exhibited during DNA replication in eukaryotes only. On the leading strand, DNA polymerase can make a complementary DNA strand without any difficulty because it runs from 5' to 3'.There is problem going in the direction in the lagging strand. A section of the telomere is lost during each cycle of replication at the 5' end of the lagging strand.

4. Dr. Ricahrd Cawthon-Prospect of Telomeres-"Key to Ageing"

Geneticist Richard Cawthon and colleagues at the University of Utah found shorter telomeres are associated with shorter lives .Among people older than 60,those with shorter telomeres were three times more likely to die from heart disease and eight times more likely to die from infectious disease.

Cawthon's study found that when people are divided into two groups based on telomere lengths, the half with longer telomere lengths lived five years longer than those with shorter telomere. This suggests that lifespan could be increased five years by increasing the length of telomeres in people with shorter ones.

People with longer telomeres still experience telomere shortening as they age.

Once a person is older than 60, their risk of death doubles every eight years of age. So a 68-year old has twice the chance of dying compared with a 60-year old. Cawthon's

study found that the differences in telomere length accounted only for 4% of that difference.

5. Telomerase

Telomere length is maintained by a balance between processes that lengthen telomeres such as activity of the cellular ribonucleoprotein enzyme complex termed telomerase and processes that shorten telomeres such as lack of complete lagging DNA strand etc., Telomerase stabilizes telomere length by adding TTAGGG repeats onto the telomeric ends of the chromosomes, thus compensating for continued erosion of telomeres that occur in its absence. Telomerase contains two essential components: TELOMERASE REVERSE TRANSCRIPTASE CATALYTIC SUBUNIT (TERT), FUNCTIONAL TELOMERASE RNA (TR/TERC).Telomerase is expressed in embryonic cells and in adult male germ line cells but is undetectable in normal somatic cells except for proliferative cells of renewal tissues. Thus telomeres are the molecular clock, that counts the number of times a cell has divided, and telomeres determine when cellular senescence and crisis occurs

6. Telomere length in Hutchinson-Gilford Progeria Syndrome

Hutchinson-Gilford Progeria Syndrome (HGPS) is a rare premature aging disorder caused by mutations in the gene *LMNA*, which encodes the nuclear matrix protein lamin A. Previous research has shown that the average telomere length in fibroblasts from HGPS patients is shorter than in age-matched controls. How mutations in lamin A lead to shortened telomere lengths is not known nor is the contribution of individual chromosome ends to the low average length understood. To measure the telomere length of individual chromosomes, Quantitative Fluorescence in situ Hybridization (Q-FISH) was used. In agreement with previous studies, it was found that the average telomere length in HPGS fibroblasts was greatly reduced; however, the telomere length at chromosome ends was variable. In contrast, the telomere length in hematopoietic cells which typically do not express lamin A, was within the normal range for three out of four HGPS patient samples. Results suggested that mutant lamin A decreases telomere length via a direct effect and that expression of mutant *LMNA* is necessary for telomere loss in HGPS.[9]

The repeated injury of the endothelium and subsequent turnover of intimal and medial cells have been implicated in atherosclerosis, we examined telomere length, a marker of somatic cell turnover, in cells from these tissues. Telomere lengths were assessed by Southern analysis of terminal restriction fragments (TRFs) generated by HinfI/Rsa I digestion of human genomic DNA. Mean TRF length decreased as a function of population doublings in human endothelial cell cultures from umbilical veins, iliac arteries, and iliac veins.[10]

7. Telomere Length Inversely Correlates with Pulse Pressure and is Highly Familial

There was evidence that telomeres the ends of chromosomes serve as clocks that pace cellular ageing both in vivo and in vitro. A twin study was conducted to investigate the relation between telomere length in white blood cells and pulse pressure where simultaneously assessing the role of genetic factors in determining the telomere length. A Southern blot analysis was conducted to measure the mean length of the Terminal Restriction Fragments (TRF) in white blood cells of 49 twin pairs from Danish twin Register and assessed the relations of blood pressure parameters with TRF.TRF length showed an inverse relation with pulse pressure. A conclusion was made that the telomere length, which is under genetic control, might play a role in mechanisms that regulate pulse pressure, including vascular ageing.[11]

8. Conclusion

Accumulated data support the notion that the loss of telomere repeats in (stem) cells and lymphocytes contributes to human ageing. This notion is not widely supported primarily because the gradual loss of telomere repeats with age in cells of various tissues and is not easily measured and because the average telomere length shows a lot of variation between species and between individuals of the same age. However, studies of model organisms as well as patients with telomere mutations have shown that short telomeres result in dire consequences .The telomere gene will likely to have many important applications in future of medicine and cellular engineering.

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