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Telomerase enzyme in aging and cancer

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Abbreviations
DNA, deoxyribonucleic acid; A, adenine; G, guanine; C, cytosine; T, thymine.
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Abstract
Telomerase is an enzyme that maintains the length of telomeres at the ends of chromosomes. Telomeres are protective caps at the ends of chromosomes that keep genetic information intact, enable cells to multiply and provide insight into some of the mysteries of ageing and cancer. Telomerase activity affects ageing and cancer development in humans by preventing telomeres from becoming too short, which can lead to cellular senescence and death. When telomerase is suppressed, cancer cells die, and telomerase inhibitors can be used to kill human breast and prostate cancer cells grown in the laboratory. Studies have also found an association between shorter telomeres, a decreased overall lifespan, and an increased risk of cardiovascular disease and infectious illness. Despite research linking telomere shortening to the ageing process, additional research is needed to fully understand the role of telomerase in the ageing process, including whether or not it is the cause of these changes. Other variables, such as oxidative stress, glycation, and inflammation, also contribute to the ageing process and may explain the remaining 33 percent of the variance in the probability of passing away. The authors of this paper discuss the current understanding of telomerase enzyme activity and its effects on ageing and cancer, as well as the implications of telomerase research and the potential for developing innovative drugs and gene therapies.

Keywords: telomerase; ageing; cancer; telomeres; chromosomes, DNA; oxidants; glycation

Background

Telomeres are essential structures that exist at the ends of chromosomes in the nucleus of a cell. This helps to keep genetic information intact, enabling cells to replicate and providing insight into some of the mysteries of aging and cancer. The telomeres at the end of the chromosomes are protective caps that are similar to the plastic points on shoelaces, and over time, as cells divide, the telomeres shrink. An enzyme known as telomerase is responsible for re-adding the TTAGGG repeat sequence to the ends of chromosomes in younger cells. This helps to prevent the telomeres from becoming overly short, which can result in the cell becoming senescent or dying. In addition, telomerase has been linked to the development of cancer, as it can speed up the aging process in cancer cells and ultimately cause them to die. In this paper, we will discuss the effects of telomerase enzyme activity on aging and cancer development in humans.

Discussion

Telomerase enzyme in aging and cancer

Chromosomes, or twisted, double-stranded DNA strands, are found in the nucleus of a cell. Telomeres at the ends of the chromosomes keep genetic information intact, enable cells to multiply and provide light on some of the mysteries of ageing and cancer [1]. Telomeres are protective caps at the ends of chromosomes and have been likened to the plastic points on shoelaces. Because telomeres maintain an organism's genetic information intact, this is the reason why this is so. In contrast, telomeres shrink when cells divide. If a cell becomes too short, it loses its ability to divide and is deemed "senescent" or dead. Ageing, cancer, and a higher mortality rate are linked to this accelerated ageing process [2]. Telomeres have been likened to bomb fuses for this reason. The paper, therefore, elaborates on how telomerase enzyme activity affects ageing and cancer development in human beings.

Chemical coding chains are used to construct both genes and chromosomal regions. However, telomeres stand out from other parts of the genome because they also contain DNA sequences. DNA is composed of four nucleic acid bases: guanine, adenine, thymine, and cytosine. TTAGGG and AAT CCC sequences are consistent throughout telomeres [1]. There are six "base pairs" in each telomere region, which defines it as a "repeat". Telomeres on white blood cells may be as long as 8,000 base pairs in newborns or as short as 1,500 base pairs in older adults. Telomeres can also vary in length depending on age. A single chromosome is composed of around 150 million nucleotide pairs. Every time a cell divides, it sheds between 30 and 200 base pairs off the very end of its telomeres. A cell has the potential to divide between fifty and seventy times before either becoming senescent or passing away [3]. The telomeres of cells that do not divide very often, such as those found in the heart muscle, are not lost over time.

If telomeres did not exist, the key chromosomal section that contains genes necessary for maintaining life would become smaller with each cell division. Telomeres make it possible for cells to divide without losing their genes in the process. The production of new cells for skin, blood, bone and other tissues depends on a process called cell division. If chromosomal ends join, a loss of telomeres might result in malfunction in the cell, cancer, or even death of the cell. The damage done to a cell's chromosomes may be identified and corrected because damaged DNA is dangerous. Because the caps of the chromosomes would seem to be damaged DNA during the time when the telomeres were not there, the cell would seek to repair something that wasn't broken. They would ultimately cease reproducing as a direct result of this, resulting in their death [4].

Their telomeres get very shorter when cancer cells divide an excessively high number of times, which is one of the characteristics of cancer. There is a possibility that the cell may perish if the telomeres on its chromosomes are too short. Because the telomeres of this cell have already shrunk to their smallest feasible length, the cell must keep producing telomerase enzymes to ensure that it does not perish [5]. The telomeres of cancerous cells in many different kinds, including those of the pancreas, bones, prostate, bladder, lungs, kidneys, head and shoulders, and others, are abnormally short. In diagnosing cancer, telomerase measurements could be useful [6]. It is feasible that scientists may be able to treat cancer by blocking the function of the enzyme telomerase, which speeds up the ageing process in cancer cells and ultimately causes them to die [7]. Inhibitors of the enzyme telomerase can kill human breast and prostate cancer cells grown in the laboratory. There are certain dangers associated with it. There is a possibility that suppressing telomerase will have a negative effect on fertility, the healing of wounds, the production of blood cells, and the development of immune cells.

Researchers at the University of Utah led by geneticist Richard Cawthon and his colleagues discovered an association between having shorter telomeres and a reduced overall lifespan. The University of Utah conducted this research. People over the age of 60 who had shorter telomeres had a risk of cardiovascular disease that was three times greater and an increased risk of infectious illness that was eight times higher, respectively. Even though a shorter length of telomeres has been associated with becoming older, it is still not apparent whether this happens due to age-related changes or whether or not it is the cause of these changes [5]. If telomerase can make cancer cells live forever, then there is a possibility that it might also slow down the ageing process in healthy cells. Is it feasible to make individuals live longer by preventing their telomeres from shortening or restoring their telomeres' length via telomerase? Does the fact that this is the case imply an increased risk of us getting cancer?

Even at this late date, there is still a lack of consensus among academics. However, telomerase has been found to be successful in preventing cancer from growing in human cells even after the cells have multiplied much beyond their usual capacity to divide. This is the case even after the cells have been cultured for a long period. This has been achieved due to its use in the laboratory [2]. The enzyme telomerase makes it possible to "immortalize" cells responsible for producing insulin, muscle, cartilage, and skin. This would make it possible for us to access a vast quantity of cells suitable for transplantation, including cells that can treat wounds and burns [2]. Having access to an unending supply of healthy human cells created in a laboratory might be beneficial for developing innovative drugs and gene therapies. These fields could profit from the availability of these cells.

Compared to the telomeres of shorter-lived mice that only live a few years, the telomeres of longer-living animals such as humans and mice, like mice, are discernibly shorter. Long-living animals include mice. Nobody can explain why this is the case. On the other hand, research does show that the length of a person's telomeres is not the most crucial determinant in predicting how long they will live. According to the findings of the study that Cawthon carried out, if you divide individuals into two groups based on the length of their telomeres, those people who have telomeres that are longer have an average lifetime that is five years longer than those people whose telomeres are shorter [8]. Individuals with shorter telomeres than average can add five years to their life expectancy if they can lengthen their telomeres. Even though we have longer telomeres than younger people, the telomeres in our cells become shorter as we get older. Younger folks have longer telomeres. If our telomeres did not progressively become shorter as we got older, how much longer could we realistically expect to live? Cawthon can see anywhere from 10 to thirty years into the foreseeable future.

After the age of 60, a person's risk of dying increases by a factor of two every eight years. Compared to those who are 68 years old, those who are 60 years old have a mortality rate that is two times higher than those who are 68 years old. According to Cawthon's study, telomere length variations accounted for just 4% of the total variance. Although it seems intuitive to assume that as we age, our chance of death would also grow, statistics show that this is only the case for around 6 percent of the population. The length of an individual's

telomeres, in addition to their chronological age and gender, may explain 37% of the variance in the probability of disappearing beyond the age of 60. The question now is, what variables account for the remaining 33 percent of the total contribution? The term "oxidative stress" significantly contributes to the ageing process. Damage to DNA, proteins, and lipids (also known as fats) is caused by oxidants, highly reactive molecules that contain oxygen in their composition and are to blame for this damage. Inflammation, infection, and the use of cigarettes and alcohol are all factors contributing to these oxidants' creation. In one experiment, the lifespan of worms was shown to be increased by an average of 44% when oxidant-neutralizing compounds were used.

The term "glycation" refers to yet another component of the ageing process. Because glucose binds to our DNA, proteins, and lipids, these macromolecules become disabled and can no longer carry out the processes necessary for survival. As we get older, the disease worsens, leading to illness and mortality due to tissues in the body that aren't working properly [9]. It's possible that glycation is to blame for the improved lifespan seen in animals when their caloric intake is restricted. There is a significant link between becoming older and reaching a certain chronological age, telomere shortening, glycation, oxidative stress, and the expression of a large number of genes.

Those born with dyskeratosis congenita have considerably shorter telomeres, much more quickly than what is typical for people born with this illness. They have a higher risk of developing leukaemia and other blood malignancies, intestinal problems, liver cirrhosis, and pulmonary fibrosis, which is a potentially fatal hardening of the lung tissue. These people face an early demise and accelerated ageing. They also have a higher risk of developing pulmonary fibrosis, a potentially fatal lung tissue hardening [10]. Grey hair, balding, slow wound healing, skin blemishes, digestive problems, bone deterioration, and cognitive disabilities are also more frequent among this population. Since these conditions have a commonality in the often dividing tissues they affect, telomeres may have a role in them [8]. There is preliminary evidence that Alzheimer's disease is associated with telomere shortening, arterial hardness, high blood pressure, and type 2 diabetes; however, further study is required to confirm these associations.

Telomere shortening and aging

Telomeres play a role in the ageing process of our cells. After a particular threshold has been reached and they have shrunk to an insufficient size, the cell will no longer be able to divide or duplicate itself. This state of inactivity, known as senescence, ultimately results in the death of cells via a process known as apoptosis. The shortening of telomeres has been linked to ageing, cancer, and an increased risk of passing away. Telomeres play a crucial role in maintaining life and health since cells make up every organ and tissue in the body [11].

Telomere shortening is an excellent predictor of biological age as opposed to chronological age since it is linked to all aspects of the ageing process. Scientists made the first observation that there was a correlation between the shortening of telomeres and the ageing process almost 40 years ago. To this day, scientists are hard at researching telomeres and the positive effects that could result from potentially reversing the shortening of telomeres as people age [11].

An enzyme known as telomerase is responsible for re-adding the TTAGGG repeat sequence to the ends of chromosomes in younger cells. This protects the telomeres from losing an excessive number of bases. The telomeres, on the other hand, begin to shorten as the cell ages because telomerase loses its ability to keep up with the increasing number of bases that need to be added as the cell divides more and more.

Rapidly dividing cells, such as stem cells and germ cells, have a high concentration of telomerase. In these cells, telomerase protects the length of telomeres, resulting in DNA following replication. This is why their telomere length is stable or even increases with time, suggesting that these cells do not experience cellular senescence. On the other hand, somatic cells have only trace amounts of telomerase, which implies that they degenerate and lose function with time. According to Stellos & Spyridopoulos (2019), somatic cells are the cells that make up the remainder of our body. Cancer cells have telomerase in high concentrations, which is one reason why these cells can maintain their viability and continue to replicate. If the telomerase activity in these cells could be blocked, the telomeres on their chromosomes would become too short to allow for effective cell division and the formation of tumours [12].

There is some evidence that the length of an individual's telomeres may be used as a predictor of their lifetime. In neonates, telomeres on white blood cells may be anywhere from 7,000 to 13,500 base pairs in length. However, in adults, they are only 3,000 base pairs long; in older adults, they are only 1,500 base pairs long. The average annual loss of base pairs after the neonatal period is between 19 and 41. This pattern usually emerges sometime after the newborn stage. A person's telomeres may have shrunk by as much as 1,500 base pairs by the time they reach the age of 40. While ageing is a major contributor to telomere shortening, other variables, including smoking and obesity, may also have an impact [13].

Telomerase and stem cells

Undifferentiated cells that have the potential to develop into any form of somatic cell may be referred to as stem cells. In addition, stem cells can maintain their viability by dividing themselves to produce additional cells of the same kind [14]. Bone marrow and the heart are two organs that divide quickly to repair an injury. However, some organs like bone marrow and liver only divide under very particular conditions.

When a person becomes older, the number of stem cells in their body declines, and they also create fewer new somatic cells. This results in the organs being less functional over time. Stem cells can extend their lifetime by preserving the length of their telomeres in several different ways. Among them are telomerase, DNA duplicase, and telomere-binding proteins, which regulate telomere length. Pierre Jerome et al. (2018) states that telomerase is the crucial regulator of telomere length since it prevents or postpones the spontaneous shortening of telomeres that happens during cell division, thereby preserving the integrity of the genome. Except for stem cells and quickly renewing cells like platelets and lymphocytes, telomerase expression is high throughout embryonic development and declines a few weeks after birth. Telomerase expression is high in cells throughout embryonic development.

Replication, self-renewal, and proliferation of stem cells are hampered in vitro mostly due to the loss of telomerase and subsequent changes in the expression of the enzyme. The ability to generate or boost telomerase expression is crucial for the work being done in the rapidly expanding field of tissue engineering, where researchers are focusing on stimulating stem cells to differentiate into a wide variety of unique cell lines [15].

Telomere lengthening in cancer

Telomerase is extremely active in cancer cells, repairing and extending broken or short telomeres, enabling the cells to divide rapidly and uncontrollably, a hallmark of the disease. Highly active telomerase contributes to cancer cells' fast and uncontrolled cell division. The enzyme telomerase is responsible for cancer cells' fast and seemingly endless proliferation by elongating their telomeres.

Without telomerase, cancer cells would not be able to increase, and they would ultimately die through a process known as apoptosis. Therefore, telomeres and telomerase are of major interest to researchers working to discover novel cancer treatments. Inhibitors of telomerase or agents that might cause the death of cells that generate the enzyme can deactivate cancer cells and halt the development of cancer. Inhibiting telomerase activity, on the other hand, might have a detrimental effect on cells dependent on the enzyme, such as sperm, eggs, and immune cells. This could lead to issues with fertility and the immune system's ability to fight off infections [16].

However, telomerase activity is only present in somatic cells at very low levels or not at all, meaning that these cells should be mainly

unaffected by the treatments being used. The researchers are hoping that this may result in cancer patients suffering fewer adverse effects with this sort of treatment in comparison to the medications that are now accessible. In cancer research, the biology of telomeres is of special significance, and researchers are eager to understand better how these structures might be used to develop treatment options [16].

Professor Sandy Chang of the Yale School of Medicine's Departments of Laboratory Medicine, Pathology, and Molecular Biophysics and Biochemistry studies telomeres to learn more about their function in ageing and cancer. Studies conducted by Chang have demonstrated how shelterin proteins bind to telomeres to protect them. These studies also demonstrated that telomeres become unstable when shelterin components are mutated or removed, which in turn induces genome changes that can potentially cause cancer. Additionally, he discovered that when a certain shelterin protein was removed from a mouse model, the stem cells in the animal lost their capacity to perform their normal functions. Chang believes that correcting these mutations in afflicted people might one day extend the amount of time a patient lives and postpone the beginning of cancer [16].

Telomeres and other diseases

The presence of telomeres that shorten considerably faster than is typical in people with dyskeratosis is one of the defining characteristics of this disorder. People who suffer from dyskeratosis have skin that keratinizes earlier than normal, and the disorder may have symptoms similar to premature ageing (progeria). These people have a much greater likelihood of developing life-threatening infections, blood malignancies, liver cirrhosis, gastrointestinal problems, and pulmonary fibrosis.

They are also more prone to suffer from learning impairments, balding, grey hair, spots, bone softening, and poor wound healing. Additionally, they are more likely to develop bone softening. This supports the hypothesis that telomeres play a role in the disorders in question, all of which involve tissues that undergo rapid division. The shortening of telomeres has been linked to several diseases, including hypertension, type 2 diabetes, and Alzheimer's disease, according to some studies [16].

One of the questions that scientists have is whether or if the enzyme telomerase may be employed to lengthen telomeres to boost the chances of survival. Scientists may be able to create cells that might be used for transplantation if human cells could be "immortalized" in this way. These cells could be utilized to treat a variety of conditions, including diabetes, arthritis, muscular dystrophy, and wound healing, among others. Experiments designed to find new drugs and genes would benefit from having access to an unending supply of the cells.

Conclusion

In conclusion, telomerase enzyme activity plays an important role in ageing and cancer. Telomeres, which are protective caps at the ends of chromosomes, can influence the ageing process and the development of cancer. Telomeres become shorter with each cell division; when they become too short, the cell can no longer divide and is deemed "senescent" or dead. Telomerase enzyme activity can prevent cancer from growing in human cells and may even slow down the ageing process in healthy cells. Telomere length is a good predictor of biological age as opposed to chronological age since it is linked to all aspects of the ageing process. While ageing is the major contributor to telomere shortening, other factors, such as smoking and obesity, could also have an impact. Further research into telomerase enzyme activity and its effects on ageing and cancer is needed.

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