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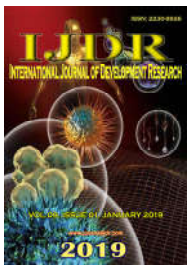

ORIGINAL RESEARCH ARTICLE OPEN ACCESS

TELOMERS AND THE EFFECT OF THE PRACTICE OF PHYSICAL EXERCISES IN THEIR COURSE

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ABSTRACT

This article aims to explore the effect of telomerases on the shortening of telomeres in people who perform physical activities in high, medium and low intensities and to diagnose what would be the best results obtained in them. It is known that the telomeres are the ends of the cellular structure of the DNA that, as its aging, its ends are shortening and degenerating, causing in the senescence of the cell. The telomerase - DNA reverse transcriptase enzyme - acts on shortening the telomeres and protects them from degeneration, replicating pairs of their ends and thus ensuring a longer shelf life. In practitioners of moderate physical activity, the effect of telomerase significantly improves its function, thus ensuring its prolongation and avoiding its senescence. Through a bibliographical review - which basically presents numerous laboratory researches with both guinea pigs / mice and experiments on human observations - we will explore some of the structure and composition of telomeres and telomerase, their action and how they work, so that we can enter the heart of the work that is how the practice of physical exercises acts in the shortening of the telomeres and how to delay it. In conclusion, we will see that not only sedentariness and morbid idleness are great cause of shortening of telomeres, but that both the excessive practice of physical exercises - as athletes and athletes - as the normal practice of activity also influence their cellular senescence.

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INTRODUCTION

For years, studies have sought measures that aim at improving quality of life, especially in the elderly. It is consensual in countless literatures, researches, experiences and works that there is in fact a direct relation between the organic process of aging to the health, to the lifestyle and the sedentarism or pro activity of each individual. One of the most complete studies that work on senescence and physical exercise is perhaps the theory of telomeres shortening and the action of the enzyme telomerase on the genetic code of the individual. Based on the hypothesis that telomeres (which are complexes of DNA, found within the chromosomes) are related to several basic biological functions of the organism and that their motor functions are based on the renewal of the chromosome but, over time, In the natural way, this action is diminished, and as a result, it loses its force, the cells are not renewing and the telomeres are shortening causing cell senescence (or aging of the cell), which can cause in genetic diseases, such as cardiovascular diseases, diabetes mellitus, obesity and lack of reflexive reaction, both muscular and cognitive, etc. Such shortening of the telomeres and consequent cellular senescence can be "controlled" with a moderately active life. Current studies show that moderate but frequent physical exercises have the power to generate an enzyme that creates molecular bases around the telomeres, with an unlimited proliferative potential, which consists of two basic components: the functional ribonucleic acid (RNA), which will work as a telomeric synthesis of DNA, and also the catalytic protein, which has reverse transcriptase activity (LIBERTINI; FERREIRA, 2016). Such components add specific and repetitive sequences to the DNA in senescence, particular extremities - already affected by the telomeric shortening. The purpose of this study is to explore the functioning of telomeres, its composition, action on the body, effect on senescence and the telomerase reaction in this organism, especially when the routine of the individual is involved in sports and physical activities. your body. Based on the premise that this article aims to prove how the body reacts beneficially

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when it follows a routine of activities, to improve the quality of life and deny the idleness of habit, the main focus of it, not to extend into technical terminologies , nor to escape the proposal, we will focus on the cellular part of the context, only to explain how its operation occurs and the reactions of the same in the organism, and we will give prominence to the chemical reagents that the sport practice brings beneficial to the subject. For this, we will use scientific articles and journals that corroborate with the biological theme of our approach and we will seek in the literature focused on physical practice the key component for a good quality of life. In order to add value to the cellular theme, with a focus on physical education, we seek to contribute with a theme that has not been explored in the middle of physical education, but which has proved to be as pertinent as necessary to its study and understanding. Soon, this article will explore how telomeres work within the living cell and how the practice of physical activities in moderate but routine doses helps in the molecular reconstruction of the DNA in a state of degeneration, controlling its shortening and expanding its "useful life." We will discuss and punctuate the points of agreement and disagreement of the different authors, to conclude what is the most appropriate measure, and the exercises that most contribute beneficially to the living organism, especially when they are more advanced.

Literature review

Conceptions of Telomeres: In the design of Romano *et al.* (2013), Telomeres are repeated sequences of DNA (5'TTAGGGn - 3 'composition), which protect the chromosome tips in partnership with protective proteins called shelterin. Shammas (2011) states that these protein complexes prevent shortening and fusion between the strands of the DNA strand, in their final portions soon, are of utmost importance for the replication, stability and protection of the genetic material.

According to Ferrer (2017): "Telomeres are involved in a number of biological functions of paramount importance, including protecting the chromosomes from recombination and fusion of the final sequences with other chromosomes; recognize DNA damage; establish mechanisms for chromosome replication; contribute to the chromosomal functional organization within the nucleus; to participate in the regulation of genetic expression, and to serve the molecular machinery as a "clock" that controls the replicative capacity of human cells and the entry of them into cellular senescence "(FERRER *et al.,* 2017). Muller and McClitock were in 1938-42 the first to suggest the existence of telomeres when studying the breakage and fusion of chromosomes as well as their cellular remodeling. Hayflick (1961), following this line of thought, hypothesized that the molecular cells were limited in their cell divisions, not being immortal and suggesting the possible existence of some sort of mechanism that divided them internally. However, it was only Olovnikov in 1973 that he could actually connect both theories, associating the final fragment of the chromosomes with this internal mechanism of division. Only ten years later, Robert Moyazis and a group of researchers were able to prove theories about these cell divisions and that the sequence of these human telomeres was actually the replications of the TTAGGG nitrogen bases, thus serving as the basis for future studies on the telomeric sequences (Blackburn *et al.,* 2006). In addition, it is possible to show that the species is still well preserved during the evolutionary process. Considering its structure, for Gao *et al.* (2015) telomeres are composed of short, repetitive and sequential series. They are, as said before, comprised of variable-length nucleoproteins, normally formed heterochromatin, formed by repetitive extensions of 5'-TTAGGG-3 'hetero-chains, a double chain and a very specific protein complex, aforementioned, called shelterin. In humans, its size varies from 9 to 15 Kb. According to Lemos (2015), the exonucleares, in the case of telomeres, form a repeated frame of simple chains, with guanine richness at their ends, curving to their backs along the entire DNA structure, leading in a loop formation (T-Loop) with the help of Telomericrepeatbinding Factor 2 (TRF2) or Telomeric Repetitive Bonding Factor which play the role of protecting against the reaction of molecular repair machinery and DNA damage monitoring, the action of proteins at the tips of the telomeres, barring the fusion of telomeric ends and serving as protection to the chromosomes.

According to Libertini and Ferrara (2016) there are six proteins that are part of the protein complex that connects to the telomeric DNA, being:

- Telomericrepeatbinding Factor 1 (TRF1) or Telomeric Repetitive Binding Factor1;
- Telomericrepeatbinding Factor 2 (TRF2) or Telomeric Repetitive Binding Factor2;
- Repressor / Activatorprotein 1 (RAP1);
- TRF1 Interactingprotein 2 (TIN2);
- TTP1 or POT1, also known as po interacting protein 1 (TINT1 / PIP1 / PTOP1) and;
- Protectionoftelomeresprotein 1 (POT1).

Libertini and Ferrara (2016) state that in addition to replication, there is a gradual perception of a partial loss of DNA from the ends of the chromosomes, since conventional DNA polymerase cannot reproduce the 3 'ends of the linear molecule, a problem of its replication Last. According to Martinez and Blasco (2017) it is during this period that the progressive shortening of the chromosome ligaments occurs, along the dividing lines of a cell line, with loss of replication capacity and increased senescence. When the last primer is removed at the end of the telomere, the DNA polymerase cannot synthesize its own segment - that is what causes the substitution - since it requires a 3 'tip by which this segment could grow, thus causing telomere continuity failure. Thus, in consecutive cell fragments, with each extraction of the primer, a segment of the DNA is lost which, consequently, causes the progressive shortening of the telomere. Carcano (2016) points out that with the passage of time and the aging of the individual, the length of the telomeres in humans suffers a fall to be considered. When the chromosomes are partitioned, telomeres are automatically diminished, indirectly inducing, in the cell cycle and repair, even before the cell is able to continue its cell division and its own cycle of replication. There is also the factor of apparent stability at the chromosomal tips of whole-cell telomeres, protected by them from fusion and nuclear degradation when in contact with other broken chromosomes, while maintaining their genetic stability. Therefore, both actions of this structure are correlated to their capacity for cell proliferation, which is substantially important in lineages with a high doubling rate. Knowing that the machinery of replicating the DNA of a cell cannot completely replicate the ends of the chromosomes, the telomeres are subject to nuclease action, and chromosomal shortening may occur in each division of the cell and

occasionally lead to senescence and end of the cell. In order for these actions not to spread to each cell division and not lose all genetic information, a ribonucleoprotectic enzyme component, called telomerase, recovers them in their critical states and periodically prolongs in the lost DNA segments, in order to preserve the durability and of his life (HEIDEREICH; KUMAR, 2017). Carol Greider, a laboratory student, discovered this enzyme in 1985, noting that, unlike DNA polymerase, telomerase was able to lengthen telomeres in cell units with high proliferative potential (Blackburn, 2010; Blackburn *et al.,* 2006). The elongation elicited from the 3 'end of the chromosome is completed by the repetitive action of telomeric DNA in most living organisms, and telomerase adds constant repeats of telomeric DNA, providing a molecular basis for performing the missing production of this DNA sequence (GAO *et al.,* 2015). The protein base or molecular structure of telomerase is composed of a ribonucleoprotein, called RNA telomerase where there is a catalytic subunit within it, which performs reverse transcriptase activity - or an "inverted copy" in a way contrary to the cellular pattern, called TERT or Telomerase reverse transcriptase - and RNA or TERC - Telomerase RNA componet, which is the model sequence for elongation of telomeric DNA. TERT is a sequence of amino acids equal to other reverse transcriptases, where all are equally responsible for the recognition of nucleotides, binding to DNA and catalytic action. To date, more than 40 other proteins within TERT have been discovered in eukaryotes, which share a great deal of similarity in their structural organization (LIU; XING, 2016).

Martinez and Blasco (2017) say that when mature, TER is a small, simple RNA molecule of 451 nucleotides and its structure is formed by a central domain, where the conserved Region 4 and 5 - or CR4 / CR5 are known such as STE -, the TBE or Template Boundary Elemen, and the domain formed by the H / ACA boxes that have the Conservation Region 7 or CR7. The TER makes two direct contacts with the TERT through its center domain and the RC4 / RC5, and this interaction is what allows the reconstitution of the telomerase in vitro. Therefore, it may be said that this enzymatic complex is a DNA / RNA dependent polymerase that performs synthesis of telomeric DNA repeats. Telomerase binds molecular bases to an unlimited proliferative potential, and consists of two essential complexes: the functional RNA (in humans, called hTERC) and which functions as a model for the telomeric synthesis of DNA as well as the catalytic protein (hTERT) with reverse transcriptase activity (LIBERTINI; FERREIRA, 2016). However, Heinderech and Kumar (2017) state that telomerase performs very low activity when in mature cells or in differentiation, such as blood. Already in stem cells, which are examples of immortalized cells - just like the cancerous ones - there is a great evidence of actions of this enzyme. We can observe that a large part of the embryonic stem cells or the tumor, the replicative aging is blocked by means of the constant increase of the activities of the actions of the telomerase, that induces the stabilization of the telomeres and, if further investigated, could even aid in the possession of some kind of "immortal phenotype." Lemos (2015) believes that the telomerase enzyme works in a manner inverse to the size of the telomer, that is, if the telomer is shorter than normal, it will open space for telomerase action. This theory of Lemos (2015) is based on the observation of human cells and on how limited the telomerase replications are, and also seeing that this action occurs only when telomeres are really short, so we can see that telomeres can substitute between a state open to the replicative action of telomerase that will allow the telomerase to elongate or, in a closed state, that will not allow the junction of telomeric repeats bound to the enzyme telomerase. Therefore, we can state that replicative senescence or human cell aging is directly associated with this loss of replications and telomerase non-replication, or the absence of telomerase action on telomere shortening. Ironically, the same enzyme that allows the prolongation of human cell life is also present, on a frighteningly large scale, in human cancer cells, making it an essential marker for diagnoses and prognostic proposals (GAO *et al.,* 2015).

Lima and Simões (2014) summarize the action of telomerase well

Telomerase is able to synthesize telomeric DNA by reverse transcription, adding base pair sequences to the ends of the chromosomes. In this way, it can maintain or increase the telomere length, delaying cellular senescence. In addition to telomere length maintenance, 31 evidence suggests that telomerase improves repair of DNA damage, increases resistance to apoptosis, promotes changes in chromatin structure, and therefore gene expression, and protects mitochondrial function under oxidative stress. Thus, telomerase function appears to be critical for organ homeostasis, by maintaining the structure of telomeres and preventing senescence. It is important to note, however, that postmitotic cells such as skeletal muscle and cardiac muscle generally have low telomerase activity, so that these tissues are preferentially prone to telomeric DNA damage and the deleterious effects of aging. Despite this, transfer of the TERT gene appears to reduce replicative senescence and extend the life span of various cell types, including cardiomyocytes. In addition, not only the reduction in telomere length, but also changes in structure and function may result in senescence or cellular apoptosis, with consequent organ dysfunction.

Physical exercise and aging: For Spirduso (1995) the natural action of aging is the sum of the natural processes, alterations and adaptations that happen with the passage of the years in the organism of the human beings. Aging is a natural consequence of every living organism, from its creation to the end of its cycle and is characterized by a torrent of chemical-biological changes, inherent in the process of aging, especially after a certain age group. Carvalho (2003) exemplifies one of these changes as the diminution of the functional capacity of the individual, because of the diminution and restriction of the physical capacities, as the coordination or the muscular force, the resistance and diminished visual acuity, as well as the own immunological system that begins to weaken causing the possibility of the person acquiring many more diseases, mainly cardiac. For CHAIMOWICZ (1997), technological advances, especially in the area of medicine, brought the prospect of a significant improvement in quality of life, mortality rate and pharmaceutical advances, but on the contrary, these advances have also caused catastrophic changes in demographic frames of the world, leading to an exponential increase in the incidence of new and stronger diseases that, not only being increasingly decreasing the life expectancy of the human being, has generated a condition of chemical-pharmaceutical dependence, psychological traumas and of course, the idle sedentarism coming from the lack of energy given the age. Veras (2009) relates the proportionality between the advancement of the age group and the constant increase in the

prevalence of chronic diseases, showing that in the majority of the population, in every three subjects, at least one of them has some chronic disease and, if we are treating the elderly, eight out of ten, too. Silvestre (1999) states that in addition to the commitment that these problems cause in people of more advanced ages, such events affect other sectors of public life, such as the increase in health expenses. In his theory, Silvestre (1999) subdivides the population into three age groups - from zero to fourteen, fifteen to fifty-nine and over sixty - and analyzes the variables that exist among them, such as mortality, (for consultations or ailments), hospitalizations, surgeries, expenses, etc., and concludes that the highest percentage of medical incidents occurs in the elderly group.

Bolkovoy and Blair (1994), in a study on age and physical exercises, found that most health problems, especially in the elderly, are sedentary lifestyle and lack of regular physical activity. Both for cardiovascular problems - as is the evil of the vast majority - and for problems of genetic degeneration of cells. Bolkovoy and Blair (1994) argue that an improvement in the quality of life of these people could represent a 54% decrease in their mortality rate due to coronary diseases, not to mention that it could still extend about 30% of their cell life. Indeed, what their arguments suggest is that the adoption of a more active and less idle life, with a more adequate diet and a routine of moderate exercise, would contribute greatly to reducing the incidence of numerous diseases and, consequently, age group of the elderly population. Reinforcing this hypothesis, we have Gobbi, Villar and Zago (2005) who confirm that any individual - even in advanced ages - who implement a more active routine, tends to have a 40% decrease in death from heart problems. Trombetta (2006) investigated that 60-70% of the Brazilian population does not perform any physical activity, and Spirdurso (1995) claims that 50% of the biological decline is caused by the atrophy caused by lack of use and non-physical exercise, whatever it may be. With this, we can have an idea of the reason for the high incidence of elderly people with so many diseases in the country. Therefore, acquiring a healthier routine and inserting more physical activities in it is an act that will benefit the health-disease relationship, altering not only the current epidemiological data but also, realizing even a cellular improvement in the individual. Blair and Morris (2009) reinforce this theory and affirm that physical exercise can directly affect cell senescence. As we know, the shortening of the telomeres is directly linked to the cellular aging process and consequently physical, so it can be assumed that a healthier life practice also affects them.

Ludlow and Roth (2011) suggest that, just as a life of physical idleness negatively affects the dynamism of telomeres in their actions, studies suggest that the practice of physical activities, on a moderate scale and intensity, creates chemical enzymes telomerase) that decrease the accumulation of harmful cells, which preserves the telomeres. With this proposal, several studies are being carried out today to reinforce the claim regarding the length of the telomeres and how moderate physical activity can interfere in its decrease and degeneration. A study by Du *et al.* (2012) has shown that a routine of moderate or more vigorous physical activities directly assists the length of the telomeres in leukocytes (this research was performed with about 7,000 women in ages ranging from forty to seventy years, since I find that the length of telomeres in women is higher than men's, possibly due to the extra amount of estrogen hormones). The same study also found that there is an average of 4.4 years more in people who exercise, than in people who lead a sedentary life. Cherkas *et al.* (2008) also associates physical leisure activities (such as cycling, skates, skates, etc.) and their action on the length of telomeres, suggesting a natural anti-aging effect in the subjects. According to Werner *et al.* (2009), athletes of advanced ages also present a greater length of their telomeres in relation to other individuals of their age groups and similar to that of young people. Song *et al.* (2010) goes further in his research and points to an adverse relationship between exercise volume and DNA damage, in order to confirm that regularity of physical activity, in a moderate and constant way, actually minimizes the loss of function cell - a natural factor in aging - and further accelerate the creation of telomerase that protects the length of telomeres. But what would be the ideal average in the definition of "regular physical activity"? Kim *et al.* (2012) conducted a survey of women with a weekly average of three times a week for nineteen months, and found that the gradual regression of the telomere length of these women (in 73.17% of the participants) and that this variable was really caused by the physical exercises they performed, since even the longest telomeres lengths of sedentary women were still lower than those who actively participated in the research. These numbers could also be associated with an observation at higher levels of adponectin and HDL cholesterol. Corroborating this research, Woo *et al.* (2008) carried out an observation in a Chinese cohort, only with the elderly, and he was surprised to find no significant difference between the telomere length of the same ones, even in those who had an active life and who practiced exercises regularly. These results were interpreted as a sign that there is difference, mainly in the tissue analyzed as to the degree of the exercise that is practiced.

When the "moderate" factor is mentioned in the practice of physical exercise, it is necessary to be clear why this expression. According to Collins *et al.* (2003) the constant practice of exercise releases numerous chemicals in the body. When it comes to cellular effects, the body needs an average treatment, not so much above its capacity, not so low that it makes no difference. When an individual forces beyond their limits, he is wearing out and stressing not only his body but his mind, thus causing a kind of chronic fatigue. This fact was observed when studying the telomeres of athletes who, although healthy and without any damages or cellular diseases, have their telomeres shorter than normal - not to mention the biopsies performed on the muscles that showed exhaustive signs of almost forced regeneration. Ludlow *et al.* (2008) agree with this statement, and report that the link between the telomeres leucocytes length and the intensity of physical exercises, is represented by a U-inverted curvature. For this assertion, they performed experiments with a group that was divided according to the weekly energy expenditure of calories being: a) less than 990 kcal; b) between 991 and 2340 kcal; (c) 2341 and 3540 kcal and; d) more than 3541 kcal. In summary, the best results were observed from group B, where telomeres were better preserved. Those in group C had minimal preservation and both groups A and D had telomeres shorter than the others. Savela *et al.* (2012) corroborates with such data, presenting a survey of approximately 780 men of average ages of 47 years, who practiced physical activities at low, medium and high levels. The results showed that the groups where the physical activities were performed in an average but frequent manner had the lengths of their telomeres larger than the others, also showing that the few shortened telomeres found in all men in the study were in greater presence in those

who practiced activity at low and high intensities. There was also an indication that the life-span of the cells of both groups was four to six years lower than the average activity group life-time. Therefore, we can observe that physical exercise, even if it brings the well-being that it wishes to the practitioner, in a cellular sphere, both in great intensity and small, can actually contribute to the shortening of telomeres and accelerate cellular senescence. Making it clear that there is, in fact, an average value / amount of intensity that must be realized so that there can be the protective effect of your cells.

Conclusion

Considering everything we have seen so far, we could have a clearer notion of telomeres, their composition, function, and structure. When in development, the normal telomere length basically consists of the cell structure of the DNA strand. With the advancing age, these tips will shorten and degenerate, causing consequently the senescence of that cell. There are other factors that contribute to the shortening of the telomeres, and these are both the sedentary lifestyle and the extreme practice of physical activities. Factors such as smoking, alcoholism, the use of narcotics and any other chemicals that degenerate the organism also influence its shortening, and invariably, in the early aging of the subject. For the retardation of this effect - natural or induced - there is the enzyme called telomerase, which acts as a protection against the shortening of the telomeres and replicate them to delay the senescence of the cell. Synthesizing the telomeric DNA by reverse transcription, it is able to recreate pairs of the bases of the telomeres at the tips of the chromosomes, thus, it stabilizes the telomer in some cases, helps in its regeneration. In addition, telomerase also helps in the repair of DNA damage, strengthening apoptosis, generating a change in its chromatin structure and, consequently, in gene expression, protecting the mitochondrial action that undergoes oxidative stress. Making telomerase a valuable tool for homeostasis of the internal organs, since it stabilizes the cellular structure of the telomeres and thus, prevents cell aging and, therefore, physical. The practice of physical activities should be part of the human daily life, whether in function or vanity, well being, health or even their work. But there must be parsimony in what will be accomplished. Not demanding more than the body supports and maintaining a routine in which, externally as much can be supported, as internally does not harm. Daily walks and races are great for the body, do not require too much of the cells and do not affect the metabolism aggressively, which is not, as we have already studied, a marathon all week. Performing activities such as bodybuilding, functional training, crossfit, etc., may seem aggressive to the body but, depending on the intensity, are not and bring both the calorie burning that the individual wants consciously, as the release of endorphins and dopamine, aiding in the well being and rooting the brain with "good" enzymes. That is, any constant but moderate physical activity will not only benefit the subject as he desires - the perfect body, a better physical condition, a better quality of life, etc. - how much it will help in a micro cellular way, in a way that this operation will bring you an even greater benefit than expected, because the genetic changes that the same adopt in your body will guarantee you a life as much longer as much healthier and satisfactory.

REFERENCES

AUBERT, G., LANSDORP, P.M. 2008. Telômeros e Envelhecimento. *Physiol Rev.,* 88(2):557-79.

BLACKBURN, E.H. 2010. Telomeres and telomerase: the means to the end (Nobel lecture). Angewandte Chemie (International ed English), 49, 7405–7421.

BLACKBURN, E.H., GREIDER, C.W., SZOSTAK, J.W. 2006. Telomeres and telomerase: the path from maize, Tetrahymena and yeast to human cancer and aging. *Nature Medicine,* 12:1133 -1138.

BLAIR, S.N., MORRIS, J.N. 2009. Healthyhearts--andthe universalbenefits of being physicallyactive: physical activityandhealth. *Ann Epidemiol.,* 19(4):253-6.

BOLKOVOY, J.L., BLAIR, S.N. 1994. Aging and exercise: a health perspective. *J Aging Phys Act.,* 2(3): 243-60. 15.

CÁRCANO, FM. 2016. Study of clinicopathological associations with molecular and genetic alterations in testicular germ cell tumors. Thesis (Doctorate's degree).Barretos: Barretos Cancer Hospital.

CARVALHO J.A.M., GARCIA R.A. 2003. O envelhecimento da população brasileira: um enfoque demográfico. Caderno de Saúde Pública, Mai./Jun; 19(3): 725-33.

CAWTHON, R.M., SMITH, K.R., O'BRIEN, E., SIVATCHENKO, A., KERBER, R.A. 2003. Association between telomere length in blood and mortality in people aged 60 years or older. *Lancet*, 361(9355):393-5.

CHAIMOWICZ F. A saúde dos idosos brasileiros às vésperas do século XXI: problemas, projeções e alternativas. Rev Saúde Pública 1997 abr; 31(2): 184-200.

DU, M., PRESCOTT, J., KRAFT, P., HAN, J., *et al.* 2012 Physical activity, sedentary behavior, andleukocyte telomere lengthin women. *Am J Epidemiol.,* 175:414–22.

FERRER, D.M.P., *et al.* 2017. Contribuição dos telômeros e da telomerase no surgimento de neoplasias e no processo de envelhecimento. Universidade Federal do Piauí, Coordenação do Mestrado em Ciências e Saúde. Revista Interdisciplinar Ciência e Saude. V.4, N.2 – Edição.

GAO, K. *et al.* 2015. Can Genomic Amplification of human telomerase gene and C-MYC in Liquid-Based Cytological Specimens be use as a method for opportunistic cervical cancer screening? *Gynecol Obstet Invest,* v.80, p.153-163, Disponível em:<https://www.karger.com/Article/ Abstract/ 371760#>. Acessoem 26/05/17.

GAVA, A.A., ZANONI, J.N. 2005. Envelhecimento celular. Arq. Ciênc. Saúde Unipar, Umuarama, 9(1), jan./abr. p.41-46.

GOBBI, S., VILLAR. R., ZAGO, A.S. 2005. Bases teórico-práticas do condicionamento físico. Rio de Janeiro: Guanabara Koogan, Educação Física no Ensino Superior. 284 p.

HAYFLICK, L., MOORHEAD, P.S. 1961. The serial cultivation of human diploid cell strains. *Experimental Cell Research,* 25:585–621.

HEIDENREICH, B., KUMAR, R. 2017. TERT promoter mutations in telomere biology. MutationResearch, v.771, p. 15-31, Disponível em: <http://www.sciencedirect.com/ science/article/pii/S1383574216301016>. Acesso em 14/05/18.

HIRAI, A.E. 1982. Envelhecimento celular. [Especialização]. Maringá: UEM.

IBGE, 2004. Pesquisa sobre o padrão de vida brasileiro. Rio de Janeiro: IBGE, Disponível em: URL: www.ibge.gov.br/ imprensa/ notícias/ppv11.html

KIM, J.H., KO, J.H., LEE, D.C., LIM, I., BANG, H. 2012. Habitual physical exercise has beneficial effects on telomere length in postmenopausal women. *Menopause*, 19(10):1109-15.

LEMOS, C.A.R.C. 2015. Aspectos estruturais e funcionais do complexo telômero/telomerase. 2015. 60f. Dissertação (Mestrado em Ciências Farmacêuticas) - Universidade Fernando Pessoa, Porto, Disponível em :<http://bdigital. ufp.pt/bitstream/10284/5320/1/PPG_28168.pdf>. Acesso em 16/05/18.

LIBERTINI, G., FERRARA, N. 2016. Possible interventions to modify aging. Biochemistry, Moscow, v. 81, n. 12, pp. 1413-1428.

LIMA, L.C.J., SIMÕES, H.G. 2014. Telômeros: estrutura, função e relação com o exercício físico. R. bras. Ci. e Mov., 22(4):185-201.

LIU, R., XING, M. 2016. TERT promoter mutations in thyroid cancer. Endocr Relat Cancer, v.24, n.2, p.97-106, Disponível em: <http://erc.endocrinology-journals. org/ content/ 23/3/R143>. Acesso em 26/05/18.

LUDLOW, A.T., ROTH, S.M. 2011. Physical activity and telomere biology: exploring the link with aging-related disease prevention. *J Aging Res.,* id 790378.

MAGALHÃES, J.P. 2004. From cells to ageing: a review of models and mechanisms of cellular senescence and their impact on human ageing. *Experimental Cell Research*, 300 (1): 1–10.

MARTINEZ, P.; BLASCO, M.A. Telomere-driven diseases and telomere-targeting therapies.The JournalofCellBiology. Mar. 2017.

MCCLINTOCK, B. 1941. The stability of broken ends of chromosomes in Zea mays. *Genetics*, 26 (2): 234–282.

MEDICINE, 1998. American College of Sports. Atividade física, aptidão física e hipertensão arterial. Revista Brasileira de Medicina do Esporte, 4(5): 160-7.

MULLER, H.J. 1938. The remaking of chromosomes. *Collecting Net,* 13: 182–198.

O'SULLIVAN, R.J., KARLSEDER, J. 2010. Telomeres: protecting chromosomes against genome instability. *Nature Reviews Molecular Cell Biology,* 11, (3):171-181.

OLOVNIKOV, A.M. 1973. A theory of marginotomy. The incomplete copying of template margin in enzymic synthesis of polynucleotides and biological significance of the phenomenon. *Journal of Theoretical Biology*, 41(1): 181–190.

Romano, G.H., Harari, Y., Yehuda, T., Podhorzer, A., Rubinstein, L., *et al.* (2013) Environmental Stresses Disrupt Telomere Length Homeostasis. PLOS Genetics, 9(9):1-9.

SAVELA, S., SAIJONMAA, O., STRANDBERG, T.E., KOISTINEN, P., STRANDBERG, A.Y., TILVIS, R.S. *et al.* 2012. Physicalactivity in midlife andtelomere lengthmeasuredin oldage. *Exp Gerontol.,* 48:81–84

Shammas, M.A. 2011. Telomeres, lifestyle, cancer, and aging. *Current Opinion in Clinical Nutrition and Metabolic Care,* 14(1): 28–34.

SILVESTRE, J.A. 1999. Área técnica da saúde do idoso. Ministério da Saúde. Brasília,

SPIRDUSO, W.W. 1995. Physical dimensions of aging. Champaign: Human Kinetics, 432 p.

TROMBETTA, I.C., *et al.* 2006. Sedentarismo e risco cardiovascular. Hipertensão, 9(2): 65-71.

VERAS R. 2009. Envelhecimento populacional contemporâneo: demandas, desafios e inovações. *Rev Saúde Pública,* 43(3): 548-54.

WERNER, C., FÜRSTER T., WIDMANN, T., PÖSS J., ROGGIA, C., HANHON, M., SCHARHAG, J., *et al.* 2009. Physical exercise prevents cellular senescence in circulating leukocytes na in the vessel whal. Circulation, 120(24): 2438-47.

WOO, J., TANG, N., LEUNG, J. 2008. No association between physical activity and telomere length in an elderly Chinese population65 years and older. *Arch Intern Med.,* 168(19):2163.

_____ (1942). The fusion of broken ends of chromosomes following nuclear fusion. Proceedings of the National Academy of Sciences of the United States of America. 28 (11): 458–463.

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