International Research Journal of Pharmacy and Medical Sciences
ISSN (Online): 2581-3277

Discussion About Correlation Between Telomere and Heart Disease

Jian Gao[1]
[1]International Education School, China Medical University, Shenyang, Liaoning, P. R. China-110122

***Abstract*—** *This paper introduces research on telomere and heart disease. Extended knowledge of telomere, such as telomerase, chromosome, telomere length, telomerase activity and its correlation with heart disease, were introduced theoretically and proved by clinical results. In addition to its correlation with heart disease, telomere also has important research value in tumors and other cardiovascular diseases. It is also closely related to the occurrence of human diseases and the length of life. This paper mainly focuses on research related to telomere and heart disease. In the part of theoretical basis, its derived knowledge and other related diseases are also introduced, which helpful to better understanding the pathogenesis, clinical manifestations and condition research of telomere and heart disease. The content mainly comes from literature reviews and clinical reports in different databases, quotation, analysis discussion, introduction and comprehensive discussion of research in recent years.*

***Keywords*—** *Telomere, heart disease, telomerase, chromosome, telomere length, telomerase activity.*

I. INTRODUCTION

Telomere and telomerase are the most curious part of human mystery, because they regulate our life activities and healthy life span to a certain extent. This paper introduces and discusses telomere, telomere length, telomerase, telomerase activity, chromosome, heart disease and their related links. Investigation and research are carried out based on theoretical basis and correlation discussion, mainly existing literature database, comprehensive review. All of about if telomere is related to heart disease, if it has the value of research relevance, etc., to be learned and discussed.

II. THEORETICAL FRAME

Telomere is the centromere on the end of cell chromosome, every time a human cell divides, the telomere will be shortened [2]. The cell can no longer divide and die when the telomere is too short [2]. During cell division, the degree of telomere depletion varies from person to person; the telomere length of the elderly is shorter than that of the child, this is because the cells of the elderly undergo multiple divisions, and telomere depletion is more frequent [2]. Telomeres are composed of simple DNA (deoxyribonucleic acid) highly tandem repeats TTAGGG, which is located at the end of chromosomes, telomere DNA and telomere related proteins play an important role in telomere function [23]. Telomere is a special cap like structure at the end of cell chromosome, like a plastic cap at the ends of a shoelace, telomere is the "cap" at both ends of chromosome, chromosome is a linear substance in the nucleus [21]. There are 23 pairs of chromosomes in the somatic cells of normal people, chromosomes carry genetic information, which is of great significance to human life, X and Y chromosomes are sex chromosomes that determine the gender of men and women; telomere is the "protective cap" at the end of chromosomes in cells, it can maintain the stability of chromosomes, just like a loyal "life guard", it not only protects the chromosome DNA from being eroded by external adverse factors, but also wraps the genome sequence inside to avoid the destruction of the chromosome structure gene at the expense of itself in the process of replication, thus preventing the loss of genetic information and maintaining the integrity of the chromosome structure and function [21]. Elizabeth Blackburn, one of the Nobel laureates in physiology or medicine, said: “with the growth of human beings, the telomeres are gradually worn [21].”

The main function of telomere is to maintain the integrity of chromosome ends during cell division and DNA replication, which is essential to maintain the integrity of genome [23].

The length of telomere gradually shortens with the growth of individuals, some endogenous and exogenous factors may cause or accelerate this process, including inflammatory reaction, oxidative stress, smoking, obesity, stress, etc. [23].

In the special telomere structure, telomerase is also called telomerase reverse transcriptase (TERT), which plays an active role in maintaining telomere length [23].

Telomerase containing two main components can prevent telomere shortening by increasing the sequence of DNA at the end of chromosome, one of which is the RNA component hTERC (telomerase RNA template), and the other is the hTERT component with reverse transcriptase activity [23].

Telomerase can promote telomere growth, reverse cell aging, restore human internal circulation function, maintain vascular elasticity and cell activity, thus treating various diseases caused by aging [21]. However, telomerase is like a double-edged sword, properly handled, it can reverse transcribe telomere sequences, lengthen telomeres, and become an "elixir of life". Improperly handled, it will cause cells to proliferate crazily, if cells are dominated by oncogenes at this time, cancer may also occur when cells can live forever [21].

The telomere protein complex contains six core components, as shown in Figure 1:

Jian Gao, “Discussion about correlation between telomere and heart disease,” *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 5, Issue 6, pp. 59-63, 2022.

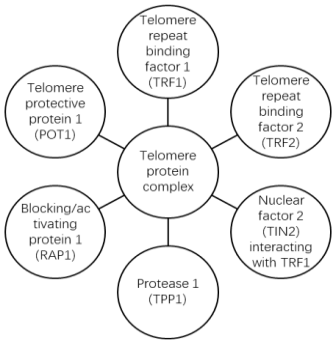

Figure 1 [23]

These components play a key role in telomere protection and telomerase regulation [23] [29].

III. Clinical Study on the Correlation Between Them

British scientists found that the gradual depletion of chromosome telomeres may play a key role in the pathogenesis of heart disease, a new study they carried out showed that the chromosome telomeres of people with frequent heart disease are much shorter than those of healthy people [2]. Researchers from the University of Leicester and the University of Glasgow in the United Kingdom used five years to track 1542 men aged between 45 and 64, during the five years, 484 people suffered from heart disease, a comparative study found that people with shorter telomeres were twice as likely as others to suffer from heart disease [2].

The discovery of telomere, like the biological clock, may one day find that it will affect the treatment of atherosclerosis, heart failure and other cardiovascular diseases [3].

Telomeres are considered to be one of the molecular bases for the occurrence of degenerative diseases [18]. Thoracic aortic aneurysm (TAA), influencing factors of telomere length and telomerase activity change in development (Figure 2):

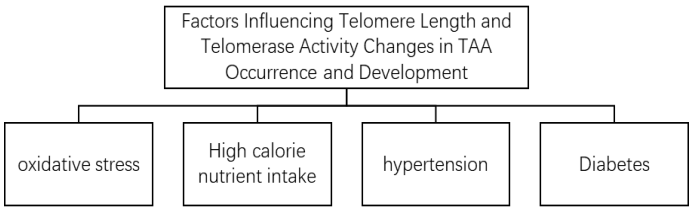

Figure 2 [18]

Several research groups have shown that telomeres at the end of chromosomes of patients with coronary artery blocked by cholesterol, victims of heart attacks, and patients with heart and circulatory system failure are shorter than those of healthy people [3].

Congenital heart disease is a complex disease, which is difficult to prevent and prognosis [1]. Therefore, the study of early diagnosis and preventive measures of congenital heart disease is of great significance to reduce the incidence of perinatal malformations [1]. Telomeres close the ends of chromosomes and maintain the stability of chromosomes; cell replication is accompanied by telomere depletion; telomere deletion will cause chromosome fusion and lead to cell aging and death [1]. The impact of telomeres and telomerase on congenital heart disease has not been studied yet [1].

It can be seen from the research that the length of telomere decreases with age, and there is no obvious correlation with the incidence of congenital heart disease [1]. Although it is directly related to the incidence of other cardiovascular diseases and tumors, and has a significant impact on the proliferation and apoptosis of myocardial cells and tumor cells, this study did not find that congenital heart disease is directly related to telomere and telomerase, and further research is needed [1].

IV. Discussions

Even before the causal relationship is established, it is possible to find a drug therapy that can protect telomeres, so that heart and vascular cells can remain young and strong for a long time [3]. One of the studies shows that statins may be able to do this, and other drugs or gene therapies being considered to increase telomerase activity, thereby protecting the structure of chromosomes [3].

Stanford University School of Medicine has developed a technology to extend the length of human DNA telomeres, this technology can increase the number of cell divisions and make cells younger and more durable, which provides ideas for the treatment of premature senility, Duchenne muscular dystrophy and even heart disease [5].

The average age of Chinese people has reached 72 years, which is close to the level of developed countries [14]. The aging phenomenon is increasingly emerging, the age of people can be divided into legal age, physical age, psychological age, and social age, the key lies in the mentality and correct treatment [14]. The world has continued to explore the mechanism of longevity, and there have been breakthroughs in recent years; the discovery of telomerase has led to new ideas on how to live a long and healthy life and fight cancer, exercise is conducive to the up regulation of telomerase activity, which provides a more scientific basis for the idea that exercise is beneficial to health [14].

Telomere is the DNA repeat sequence at the end of chromosome, which is used to maintain the integrity of chromosome, every time a cell divides, the length of telomere will be shortened a little [5]. At a certain key point, the cell will not divide anymore and will die, the telomere of young people has 8000-100000 nucleotides, this technology developed by researchers has extended the length of telomere by 1000 nucleotides [5]. The proliferation mode of treated cells is very similar to that of many younger cells, which is very different from that of cells of the same age but not treated, the new technology uses improved RNA, which contains a coding sequence called TERT that activates telomerase synthesis, telomerase is an enzyme that reconstructs telomeres and stem cells, the experiment found that the number of divisions of treated epidermal cells increased by 28 times compared with ordinary cells, the number of muscle cell divisions increased three times [5]. Although this RNA did extend the telomere length at the beginning, the telomere began to shorten within 48 hours of

Jian Gao, "Discussion about correlation between telomere and heart disease," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 5, Issue 6, pp. 59-63, 2022.

cell division, in fact, this is not a bad thing, because endless division will increase the risk of cancer [5].

Spanish scientists recently published a new research achievement online in the Journal of the Federation of American Societies of Experimental Biology (FASEB J), they found that statins can not only play a role in lowering blood lipids and reducing the incidence of heart disease and moderate wind by blocking the activity of cholesterol synthase in the liver, but also slow down the rate of telomere shortening, indicating that they may have an anti-aging effect [6]. Statins are a new kind of molecular switch, which can slow down cell senescence by activating telomerase, thus prolonging the life span of the body [6].

Because telomere shortening is the result of many factors, and is first manifested in diseases, it is not so much that telomere measurement can predict a person's life span as telomere measurement can obtain some methods to prevent and treat diseases, especially some chronic diseases, such as cardiovascular disease and diabetes [9]. For example, research has found that exercise can not only relieve people's tension and depression, but also maintain telomere length, it can also reduce the risk of illness [9]. In fact, it also advocates and requires people to have a healthy lifestyle, so as to maintain telomere length and prevent many diseases [9].

The researchers investigated men at risk of heart disease in Scotland, and measured their telomere length, then they gave them either statin (a drug to prevent heart disease) or placebo, and later checked the preventive effect of statin [9]. The results showed that those with the first third of telomere length could not be protected by statin, in other words, people with short telomeres are indeed more likely to suffer from heart disease than those with long telomeres, and preventive drugs do not work [9]. In addition, researchers have also found that telomerase activity is positively related to whether people take antidepressants [9].

Telomere biology plays an important role in the regulation of myocardial regeneration ability and participates in the pathophysiological process of heart failure [1].

In a clinical study of 803 patients, it was found that the telomere length of white blood cells in patients with heart failure was reduced by about 40%, indicating that the telomere length of patients with heart failure was related to the severity of the disease [1]. A study investigated the correlation between left ventricular ejection fraction and telomere length shortening, and the results showed that a standard deviation of telomere length was shortened and the ejection fraction was reduced by 5% [1].

V. Conclusions

In theory, if we can keep telomeres intact, our cells can live forever, so far, scientists have developed genetic detection methods that can detect more than 10 diseases, human genes play a great role in the formation of diabetes, heart disease and other diseases [10]. Therefore, doctors using genetic detection will be able to take timely measures for those who are in danger in the future, for example, people who are likely to suffer from heart disease are advised to exercise more and eat less cholesterol containing food to prevent the onset of the disease [10].

The Nobel expert review team believes that telomerase has a decisive effect on human longevity and the treatment of various diseases caused by aging and functional degradation, the rational use of the technology of extracting biological telomerase will enable the global physiological age of human beings to increase inversely, and many chronic diseases that puzzle the medical community will be treated [21].

Acknowledgment

I really appreciated lecturers of Cell Biology Teaching and Research Group in China Medical University. Especially, Mr Xiaodong Li, a professor in the Cell Biology Teaching and Research Group in China Medical University, for his patience and meticulous explanation and video demonstration in class.

References

[1] Shi Y G, et al., "Correlation between telomere length and telomerase activity and the pathogenesis of congenital heart disease in children." (in Chinese), *modern biomedical progress*, 13 (05): 872-875 + 985, 2013.

[2] "Research shows that heart disease is related to chromosome telomere loss." (in Chinese), *China practical medicine*, (09): 88, 2006.

[3] Xiao M Y, "targets for the development of new drugs for heart disease." (in Chinese), *knowledge of cardiovascular disease prevention and treatment*, (02): 58, 2010.

[4] Wang X R, Concept of health preservation and health based on traditional medicine and modern technology. (in Chinese), *2017 annual meeting of China Society of integrated traditional Chinese and Western medicine anesthesia [CSIA], the Fourth National Symposium on Integrated Traditional Chinese and Western medicine anesthesia and the inaugural meeting of the anesthesia Professional Committee of Shaanxi society of integrated traditional Chinese and Western medicine*, Xi'an, Shaanxi, China, 2017.

[5] "The United States prolongs cell life through telomere prolongation technology." (in Chinese), *Chinese Journal of bioengineering*, 35 (01): 120, 2015.

[6] Fan M, "Scientists found that statins may have anti-aging effect." (in Chinese), *pharmaceutical progress*, 37 (08): 389, 2013.

[7] "18 globally recognized life prolonging secrets." (in Chinese), *work of Shandong National People's Congress*, (12): 64, 2012.

[8] Zhang T K, "Uncover the truth behind scientific fortune telling: the relationship between telomere and life span." (in Chinese), *today Keyuan*, (15): 128-129, 2012.

[9] Zhang T K, unravels the truth of "scientific fortune telling" (in Chinese), popular science and technology news: B05.

[10] Liu L S, "Life science breeds a big market." (in Chinese), *world science*, (10): 12-13, 2002.

[11] "Window of medical garden." (in Chinese), *Zhejiang Journal of traditional Chinese medicine*, (09): 430-431, 1997.

[12] LJ, W., et al., "Association between telomere length and heart disease in a narrow age cohort of older people." *Experimental Gerontology* 42(6): 571-573, 2010.

[13] Li Y Q and Ma H Y, "Telomere and atherosclerosis and their risk factors." (in Chinese), *new medicine*, 41 (12): 832-835, 2010.

[14] Zhou Sh F, Review and Prospect of geriatric heart disease rehabilitation (outline). (in Chinese), *Proceedings of the sixth geriatric rehabilitation academic conference of China Rehabilitation Medical Association*, Beijing: 1-2, 2010.

[15] Ye X, et al., "Effect of Wenxin Granule on serum N-terminal pro brain natriuretic peptide in patients with permanent atrial fibrillation." (in Chinese), *Chinese medical guide*, 08 (23): 93-94, 2010.

[16] "Refuse death." (in Chinese), *nature exploration*, (5): 17-20, 2000.

[17] Liang L Q, "Overview of telomerase and its relationship with diseases." (in Chinese), *biology teaching*, 0 (3), 2019.

[18] Xu H J, "Research progress on Influencing Factors of telomere length and telomerase activity during the occurrence and development of

thoracic aortic aneurysm." (in Chinese), *Shandong medicine*, 59 (6), 2019.
[19] Liu Y Y, "Effects of Tiaozhi Recipe on arterial plaque and telomerase telomere system in ApoE - / - mice." (in Chinese), *medical theory and practice*, 32 (16), 2019.
[20] Wu Q, "Correlation between relative telomere length of leukocyte DNA in peripheral blood and risk of progressive cerebral infarction." (in Chinese), *southeast national defense medicine*, 0 (2), 2019.
[21] Yuan P G, "Magic telomere and telomerase." (in Chinese), *Dr. liver*, 0 (1), 2018.
[22] Lei J, "Relationship between telomere and cardiovascular disease." (in Chinese), *modern medicine and health research*, 0 (15), 2018.
[23] Sun J, "Telomere and its effect on related diseases." (in Chinese), *Journal of Luoyang Normal University*, 37 (5), 2018.
[24] Lv T, "Research progress on the relationship between telomere length and cardiovascular disease risk factors." (in Chinese), *Journal of heart*, 30 (5), 2018.
[25] Ye X, "distribution characteristics and changes of human telomere length" (in Chinese), *Journal of Central South University: Medical Edition*, 43 (9), 2018.
[26] Zhao L Z, "research progress on telomere length and risk factors of coronary heart disease" (in Chinese), *Chinese Journal of circulation*, 33 (5), 2018.
[27] Han X L, "Telomere length of peripheral blood leukocytes in patients with hypertension and prediabetes." (in Chinese), *China clinical research*, 31 (6), 2018.
[28] Zhuang Y, et al., "A case of circular chromosome 10." (in Chinese), *National Medical Journal of China*, 94 (2): 160-160, 2014.
[29] Choi K H, et al., "Characterization of the DNA binding specificity of Shelterin complexes." *Nucleic Acids Res*, 39: 9206-9223, 2011.
[30] Ji, T., et al., "Diagnosis and fine location of deletion region in Jacobsen syndrome patients." *Chinese Journal of Practical Pediatrics*, 25(08): 602-606, 2010.
[31] Ma, L.-y., et al., "Tumorigenicity of human bone marrow mesenchymal stem cells during proliferation in vitro and following differentiation into cardiomyocytes." *Journal of Clinical Rehabilitative Tissue Engineering Research*, 13(14): 2661-2666, 2009.
[32] Zhao X H, et al., "Telomere and telomerase and coronary heart disease." (in Chinese), *Chinese Journal of arteriosclerosis*, 14 (10): 917-918, 2006.
[33] Maeda, M., et al. "An Inhibitor of Activated Blood Coagulation Factor X Shows Anti-Endothelial Senescence and Anti-Atherosclerotic Effects." *Journal of Vascular Research*, 56(4): 181-190, 2019.
[34] Marin-Aguilar, F., et al., "NLRP3 inflammasome suppression improves longevity and prevents cardiac aging in male mice." *Aging Cell*, 2019.
[35] Pintado-Berninches, L., et al., "GSE4 peptide suppresses oxidative and telomere deficiencies in ataxia telangiectasia patient cells." *Cell Death and Differentiation*, 26(10): 1998-2014, 2019.
[36] Pusceddu, I., et al., "Telomere length, vitamin B12 and mortality in persons undergoing coronary angiography: the Ludwigshafen risk and cardiovascular health study." *Aging-Us*, 11(17): 7083-7097, 2019.
[37] Shadyab, A. H., et al., "Associations of parental ages at childbirth with healthy aging among women." *Maturitas*, 129: 6-11.
[38] Shimizu, I. and T. Minamino, "Cellular senescence in cardiac diseases." *Journal of Cardiology*, 74(3-4): 313-319, 2019.
[39] Smith, J. A., et al., "Intrinsic and extrinsic epigenetic age acceleration are associated with hypertensive target organ damage in older African Americans." *Bmc Medical Genomics*, 12(1), 2019.
[40] Teo, J. X., et al., "Digital phenotyping by consumer wearables identifies sleep-associated markers of cardiovascular disease risk and biological aging." *Communications Biology*, 2, 2019.
[41] Wahlberg, K., et al., "Filaggrin variations are associated with PAH metabolites in urine and DNA alterations in blood." *Environmental Research*, 177, 2019.
[42] Zhu, X., et al., "Fine-Tuning of PGC1 alpha Expression Regulates Cardiac Function and Longevity." *Circulation Research*, 125(7): 707-719, 2019.
[43] Dai, Z., et al., "Systematic biomedical research of the NASA Twins Study facilitates the hazard risk assessment of long-term spaceflight missions." *Protein & Cell*, 10(9): 628-630, 2019.
[44] Dlouha, D., et al., "Association between aortic telomere length and cardiac post-transplant allograft function." *International Journal of Cardiology*, 290: 129-133, 2019.
[45] Ghimire, S., et al., "Decline in telomere length by age and effect modification by gender, allostatic load and comorbidities in National Health and Nutrition Examination Survey (1999-2002)." *Plos One*, 14(8), 2019.
[46] Hamad, R., et al., "Quality and quantity: The association of state-level educational policies with later life cardiovascular disease." *Preventive Medicine*, 126, 2019.
[47] Kuo, C.-L., et al., "Telomere length and aging-related outcomes in humans: A Mendelian randomization study in 261,000 older participants." *Aging Cell*, 2019.
[48] Lee, Y., et al., "Epigenome-wide association study of leukocyte telomere length." *Aging-Us*, 11(16): 5876-5894, 2019.
[49] Lu, A. T., et al., "DNA methylation-based estimator of telomere length." *Aging-Us*, 11(16): 5895-5923, 2019.
[50] Matrone, G., et al., "Dysfunction of iPSC-derived endothelial cells in human Hutchinson-Gilford progeria syndrome." *Cell Cycle*, 18(19): 2495-2508, 2019.
[51] Yamamoto-Shimojima, K., et al., "Natural histories of patients with Wolf-Hirschhorn syndrome derived from variable chromosomal abnormalities." *Congenital Anomalies*, 59(5): 169-173, 2019.
[52] Yorichika, N., et al., "The effects of Tel2 on cardiomyocyte survival." *Life Sciences*, 232, 2019.
[53] Anonymous. "*87th Congress of the European-Atherosclerosis-Society (EAS), Maastricht, NETHERLANDS, May 26 -29, 2019.*" Atherosclerosis 287: E1-7, 2019.
[54] Chen, W., et al., "Novel homozygous ataxia-telangiectasia (A-T) mutated gene mutation identified in a Chinese pedigree with A-T." *Molecular Medicine Reports*, 20(2): 1655-1662, 2019.
[55] Chiriaco, M., et al., "Inflammation and Vascular Ageing: From Telomeres to Novel Emerging Mechanisms." *High blood pressure & cardiovascular prevention: the official journal of the Italian Society of Hypertension*, 26(4): 321-329, 2019.
[56] Dato, S., et al., "Untangling the Genetics of Human Longevity-A Challenging Quest." *Genes*, 10(8), 2019.
[57] McIntyre, R. L., et al., "From molecular promise to preclinical results: HDAC inhibitors in the race for healthy aging drugs." *Embo Molecular Medicine*, 11(9), 2019.
[58] Monroe, D. M., et al., "Clinical associations with telomere length in chronic spinal cord injury." *Spinal cord*, 2019.
[59] Saucourt, C., et al., "Design and Validation of an Automated Process for the Expansion of Peripheral Blood-Derived CD34(+) Cells for Clinical Use After Myocardial Infarction." *Stem Cells Translational Medicine*, 8(8): 822-832, 2019.
[60] Tian, H., et al., "Physical exercise, autophagy and cardiometabolic stress in aging." *Aging-Us*, 11(15): 5287-5288, 2019.
[61] van der Spek, A., et al., "Metabolomics reveals a link between homocysteine and lipid metabolism and leukocyte telomere length: the ENGAGE consortium." *Scientific Reports*, 9, 2019.
[62] Wade, T. J., et al., "Adverse childhood experiences (ACEs) and cardiovascular development from childhood to early adulthood: study protocol of the Niagara Longitudinal Heart Study." *BMJ open*, 9(7), 2019.
[63] Jones, C. W., et al., "The transgenerational transmission of maternal adverse childhood experiences (ACEs): Insights from placental aging and infant autonomic nervous system reactivity." *Psychoneuroendocrinology*, 106: 20-27, 2019.
[64] Kachuri, L., et al., "Investigation of Leukocyte Telomere Length and Genetic Variants in Chromosome 5p15.33 as Prognostic Markers in Lung Cancer." *Cancer Epidemiology Biomarkers & Prevention*, 28(7): 1228-1237, 2019.
[65] Le, T. L., et al., "Enhanced cardiac repair by telomerase reverse transcriptase over-expression in human cardiac mesenchymal stromal cells." *Scientific Reports*, 9, 2019.
[66] Lee, G., et al., "PGC-1 alpha, a potential therapeutic target against kidney aging." *Aging Cell*, 18(5), 2019.
[67] Myers, K. O., et al., "The effect of maternal vitamin C intake on fetal telomere length." *Journal of Maternal-Fetal & Neonatal Medicine*, 2019.
[68] Su, C., et al., "Study on the relationship between telomere length changes and recurrence of atrial fibrillation after radiofrequency catheter ablation." *Journal of Cardiovascular Electrophysiology*, 30(7): 1117-1124, 2019.
[69] Sullivan, S., et al., "An investigation of racial/ethnic and sex differences

in the association between experiences of everyday discrimination and leukocyte telomere length among patients with coronary artery disease." *Psychoneuroendocrinology*, 106: 122-128, 2019.
[70] Yang, T. O., et al., "T-cell aging in end-stage renal disease: an evolving story with CMV." *Medical Microbiology and Immunology*, 208(3-4): 281-287, 2019.
[71] Yu, P. L. I., et al., "Distinct Nuclear Organization of Telomeres and Centromeres in Monoclonal Gammopathy of Undetermined Significance and Multiple Myeloma." *Cells*, 8(7), 2019.
[72] Zhang, L., et al., "Association between leukocyte telomere length and hostility in US army service members." *Neuroscience Letters*, 706: 24-29, 2019.
[73] Casselli, T., et al., "A small intergenic region of lp17 is required for evasion of adaptive immunity and induction of pathology by the Lyme disease spirochete." *Cellular Microbiology*, 21(7), 2019.
[74] Chi, C., et al., "Vascular smooth muscle cell senescence and age-related diseases: State of the art." *Biochimica Et Biophysica Acta-Molecular Basis of Disease*, 1865(7): 1810-1821, 2019.
[75] Elena Gomez-Gomez, M. and S. C. Zapico, "Frailty, Cognitive Decline, Neurodegenerative Diseases and Nutrition Interventions." *International Journal of Molecular Sciences*, 20(11), 2019.
[76] Hayashi, T., "Vascular Senescense and Endothelial Function - Can We Apply It to Atrial Fibrillation?" *Circulation Journal*, 83(7): 1439-1440, 2019.
[77] Jia, G., et al., "Endothelial cell senescence in aging-related vascular dysfunction." *Biochimica Et Biophysica Acta-Molecular Basis of Disease*, 1865(7): 1802-1809, 2019.
[78] Lawes, S., et al. (2019). "Combined influence of depressive symptoms and systemic inflammation on all-cause and cardiovascular mortality: evidence for differential effects by gender in the English Longitudinal Study of Ageing." *Psychological Medicine*, 49(9): 1521-1531, 2019.
[79] Pan, K.-L., et al., "Shorter Leukocyte Telomere Length Is Associated with Atrial Remodeling and Predicts Recurrence in Younger Patients With Paroxysmal Atrial Fibrillation After Radiofrequency Ablation." *Circulation Journal*, 83(7): 1449-1455, 2019.
[80] Subedi, P., et al., "Telomere length and cancer mortality in American Indians: The Strong Heart Study." *Geroscience*, 41(3): 351-361, 2019.
[81] Than, Y., et al., "Telomere Length: A Potential Biomarker for the Risk and Prognosis of Stroke." *Frontiers in Neurology*, 10, 2019.
[82] Wu, Q., et al., "Expression of telomere repeat binding factor 1 and TRF2 in Alzheimer's disease and correlation with clinical parameters." *Neurological Research*, 41(6): 504-509, 2019.
[83] Reischauer, S., et al., "Cloche is a bHLH-PAS transcription factor that drives haemato-vascular specification." *Nature*, 535(7611): 294-298, 2016.
[84] Birch, J., et al., "Mitochondria, telomeres and cell senescence: Implications for lung ageing and disease." *Pharmacol Ther*, 183: 34-49, 2018.
[85] Booth, L. N. and A. Brunet, "The Aging Epigenome." *Mol Cell*, 62(5): 728-744, 2016.
[86] Everaerts, S., et al., "The aging lung: tissue telomere shortening in health and disease." *Respir Res*, 19(1): 95, 2018.
[87] Fyhrquist, F., et al., "The roles of senescence and telomere shortening in cardiovascular disease." *Nat Rev Cardiol*, 10(5): 274-283, 2013.
[88] Han, H., et al., "Association of TERT polymorphisms and risk of coronary heart disease in a Chinese Han population." *Oncotarget*, 8(40): 67519-67525, 2017.
[89] Marin-Aguilar, F., et al., "NLRP3 inflammasome suppression improves longevity and prevents cardiac aging in male mice." *Aging Cell: e*, 13050, 2019.
[90] Martinez, P. and M. A. Blasco, "Heart-Breaking Telomeres." *Circ Res*, 123(7): 787-802, 2018.
[91] Mwasongwe, S., et al., "Leukocyte telomere length and cardiovascular disease in African Americans: The Jackson Heart Study." *Atherosclerosis*, 266: 41-47, 2017.
[92] Peng, H., et al., "Leukocyte telomere length and ideal cardiovascular health in American Indians: The Strong Heart Family Study." *Eur J Epidemiol*, 32(1): 67-75, 2017.
[93] Sahin, E., et al., "Telomere dysfunction induces metabolic and mitochondrial compromise." *Nature*, 470(7334): 359-365, 2011.
[94] Staerk, L., et al., "Association Between Leukocyte Telomere Length and the Risk of Incident Atrial Fibrillation: The Framingham Heart Study." *J Am Heart Assoc*, 6(11), 2017.
[95] Sung, Y. J., et al., "A Large-Scale Multi-Ancestry Genome-wide Study Accounting for Smoking Behavior Identifies Multiple Significant Loci for Blood Pressure." *Am J Hum Genet*, 102(3): 375-400, 2018.
[96] Terai, M., et al., "Association of telomere shortening in myocardium with heart weight gain and cause of death." *Sci Rep*, 3: 2401, 2013.
[97] Townsley, D. M., et al., "Bone marrow failure and the telomeropathies." *Blood*, 124(18): 2775-2783, 2014.
[98] Woody, A., et al., "Buccal telomere length and its associations with cortisol, heart rate variability, heart rate, and blood pressure responses to an acute social evaluative stressor in college students." *Stress*, 20(3): 249-257, 2017.