The Pharma Innovation Journal 2024; 13(3): 27-31

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
TPI 2024; 13(3): 27-31

www.thepharmajournal.com
Received: 16-01-2024
Accepted: 20-02-2024

Deepthi Chandaka
Department of Livestock Farm Complex, School of Veterinary and Animal Sciences, Centurion University of Technology and Management, Paralakhemundi, Odisha, India

Robin Tiwari
Department of Livestock Farm Complex, School of Veterinary and Animal Sciences, Centurion University of Technology and Management, Paralakhemundi, Odisha, India

Prem Kumar Regulagadda
Department of Livestock Farm Complex, School of Veterinary and Animal Sciences, Centurion University of Technology and Management, Paralakhemundi, Odisha, India

Upendra Chandaka
Senior Medical Officer, NHPC Ltd (A Government of India Enterprise), Baira Siul Power Station, Surangani, Himachal Pradesh, India

BVS Bhavya Charitha
Department of Livestock Farm Complex, School of Veterinary and Animal Sciences, Centurion University of Technology and Management, Paralakhemundi, Odisha, India

Chaitanya Gollu
Department of Veterinary Physiology, School of Veterinary and Animal Sciences, Centurion University of Technology and Management, Paralakhemundi, Odisha, India

Devshri Pajai
Department of Veterinary Public Health and Epidemiology, Nagpur Veterinary College, MAFSU, Maharashtra, India

Corresponding Author:
Deepthi Chandaka
Department of Livestock Farm Complex, School of Veterinary and Animal Sciences, Centurion University of Technology and Management, Paralakhemundi, Odisha, India

Exploring dynamics and functional significance of telomeres in livestock

Deepthi Chandaka, Robin Tiwari, Prem Kumar Regulagadda, Upendra Chandaka, BVS Bhavya Charitha, Chaitanya Gollu and Devshri Pajai

Abstract
Telomeres, the protective caps at the ends of chromosomes, play crucial roles in maintaining genomic stability, regulating cellular proliferation, and impacting various physiological processes. This review delves into the intricate biology, dynamic nature, and multifaceted functions of telomeres in livestock species. The telomere dynamics, encompassing processes of shortening and lengthening, are examined in the context of cellular aging, disease susceptibility, and reproductive outcomes. Functionally, telomeres are integral to cellular homeostasis, immune function, and developmental processes, with implications extending to livestock productivity, aging, and disease susceptibility. Drawing from recent studies in diverse livestock species, including cattle, pigs, horses, and poultry, we examine the implications of telomeres in cancer research, assisted reproductive technologies, and breed-specific differences. Through a comprehensive synthesis of existing literature and recent findings, this review underscores the importance of telomeres in livestock biology and highlights avenues for future research in this vital area of study.

Keywords: Telomeres, genetics, chromosomes, DNA and livestock

1. Introduction
Across diverse organisms, from plants to animals, telomeres serve as guardians of genomic integrity, safeguarding chromosomes from degradation, fusion, and aberrant recombination events. Understanding the biology, dynamics, and functions of telomeres is essential not only for unraveling fundamental cellular processes but also for elucidating their implications in various physiological and pathological conditions. Chromosomes, comprising DNA wrapped around histone proteins, harbor the genetic information essential for cellular functioning. Yet, with each round of cell division, chromosomes face the challenge of incomplete replication at their ends, a phenomenon known as the "end replication problem." Telomeres, composed of repetitive nucleotide sequences and associated proteins, provide a solution to this problem by preventing the loss of critical genetic material and maintaining chromosomal stability. The discovery of telomeres by pioneering geneticists such as Hermann Muller and Barbara McClintock marked a significant milestone in understanding chromosome biology, highlighting the distinct structures and functions of chromosomal ends. Drawing from a plethora of studies conducted in diverse livestock species, we highlight the relevance of telomere research in enhancing animal health, productivity, and welfare.

2. History of Telomeres
The discovery and elucidation of telomeres represent key milestones in the understanding of chromosomal biology and cellular senescence. Telomeres, first identified in 1938 by Hermann Muller in fruit fly (Drosophila) cells and later in 1939 by Barbara McClintock in corn (Zea mays) cells, emerged as distinct structures located at the ends of natural chromosomes (Varela and Blasco, 2010) [34]. Muller's and McClintock's observations highlighted the unique nature of these chromosomal ends compared to broken chromosomes, prompting Muller to introduce the term "telomeres," derived from the Greek words "Telos" meaning "End" and "Meros" meaning "Part." (Muller, 1938) [23].
Anatomist Leonard Hayflick's seminal work in 1961 demonstrated the finite replicative capacity of normal fetal cells, revealing a phenomenon later termed the "Hayflick limit." This limit was attributed to the gradual shortening of telomeres with each cell division, as observed by Alexey Olovnikov in 1971 [26].

Olovnikov's research proposed a link between telomere shortening and cellular senescence, laying the groundwork for understanding the role of telomeres in cellular aging. In the late 1970s, Elizabeth Blackburn and Jack Szostak embarked on investigations to unravel the molecular mechanisms underlying telomere function. Blackburn focused on uncovering telomere end sequences in the unicellular ciliate Tetrahymena, while Szostak explored DNA recombination mechanisms in yeast cells (Shampay *et al*., 1984) [31]. Their collaborative efforts culminated in the landmark discovery in 1982, demonstrating the stabilizing role of repeat telomere sequences in replication. This groundbreaking work laid the foundation for understanding telomere biology across species. The pivotal discovery of telomerase, elucidated by Blackburn and Carol Greider in 1989, marked a significant advancement in telomere research (Greider, 1990) [11]. Telomerase, identified as a reverse transcriptase enzyme, was found to replenish telomeric DNA by adding repeat sequences to chromosome ends, thus counteracting telomere shortening and cellular aging. This discovery not only shed light on the mechanisms underlying telomere maintenance but also opened new avenues for studying telomerase's implications in aging, cancer, and cellular longevity.

3. Biology of Telomeres

3.1 Structure and maintenance

Vertebrate telomeres, characterized by highly conserved repetitive sequences, feature a distinctive 5′-TTAGGG-3′ pattern with a long double-stranded AGGGTT region and a shorter G-tail, varying in length across species. Critical to telomere function is the shelterin complex, composed of various proteins including TRF1, TRF2, TIN2, RAP1, TPP1, and POT1 (Fig 1). Among these, TRF2 plays a significant role in orchestrating the formation of a specialized structure known as the 't-loop' or telomeric loop. This loop, situated at the distal end of the telomere, comprises a 300 base pair single-stranded segment. Functioning akin to a knot, the t-loop stabilizes the telomere structure, preventing the chromosome ends from being mistaken as DNA damage sites by the cellular repair machinery. Moreover, components of the shelterin complex, particularly TRF2 and POT1, provide protection to both the double-stranded and single-stranded regions of telomeric DNA, inhibiting the activation of DNA damage response kinases such as ATM and ATR. In addition to the t-loop, telomeres can adopt other secondary structures, including G-quadruplexes, which further contribute to their stability. However, these structures can also pose challenges during DNA replication by stalling the replication fork and inhibiting telomere elongation by telomerase and associated proteins. At the very end of the T-loop, the single-stranded telomere DNA is held onto a region of double-stranded DNA by the telomere strand disrupting the double-helical DNA, and base pairing to one of the two strands. This triple-stranded structure is called a displacement loop or D-loop. Emerging proteins like CST and HOT1 regulate telomere replication and telomerase activity, while Telomeric RNA (TERRA) modulates telomere dynamics. Telomerase, a specialized enzyme, counteracts telomere shortening by adding telomeric repeats to the G-tail. This process helps to offset the gradual loss of telomeric DNA that occurs during each round of DNA replication, a phenomenon known as the end replication problem. In cells lacking sufficient telomerase activity, progressive telomere shortening eventually leads to cellular senescence, highlighting the importance of telomere maintenance mechanisms in preserving cellular viability and lifespan (Lu *et al*., 2013) [21].

3.2 Length and Dynamics

Telomere length, regulated by two opposing mechanisms—erosion and telomerase-dependent lengthening—dictates cellular lifespan. While telomere length varies greatly among species, its dynamics influence aging and disease susceptibility. Shortened telomeres induce replicative senescence, impacting immune function and promoting diseases like cancer and progeria syndrome. Conversely, longer telomeres may extend lifespan but could increase cancer risk (Weinstein and Ciszek, 2002) [36]. Researches on mammalian and avian species have established that telomere loss is greatest during early life, which may be due to the rapid growth and cell division during early life (Zeichner *et al*., 1999; Baerlocher *et al*., 2007; Salomons *et al*., 2009) [38, 2, 28]. Telomere manipulation offers promise in aging research, with studies suggesting potential rejuvenation effects. However, the intricacies of telomere dynamics, observed even in long-lived species like seabirds (Juola *et al*., 2006), highlight the complexity of telomere biology and its role in longevity.

3.3 Cloning- Telomere Shortening

Somatic cell nuclear transfer in livestock allows cloning for genetic superiority and transgenic traits. However, offspring may start life with shortened telomeres, leading to premature aging and disease susceptibility, particularly cancer. Cloned animals often exhibit shorter telomeres, but results vary across species and cell types used (Table 1) (Burgstaller and Brem, 2017) [5]. Telomere length discrepancy can arise from cell type variations in somatic cell nuclear transfer. Telomerase activity during embryo development influences Telomere length restoration, with tissue-to-tissue Telomere length variations observed. Species and sex differences also impact Telomere length in cloned animals. Trichostatin A treatment has shown promise in lengthening telomeres in cloned offspring. Comprehensive research with larger sample sizes is vital for understanding TL dynamics in cloned livestock and ensuring their health and longevity (Zhang *et al*., 2023) [39].

4. Implications of Telomeres in Livestock

Telomeres play diverse roles in livestock, including cancer and disease research, assisted reproductive technologies, developmental biology, epigenetic regulation of telomere length, productive lifespan, aging, and breeds variations. The subsequent sections delve into the outcomes of different telomere investigations conducted in livestock.

4.1 Age and Longetivity

Research findings indicate that as livestock age, their average telomere length diminishes, as evidenced in studies involving cattle (Brown *et al*., 2012; Seeker *et al*., 2018; Haagen *et al*., 2022; Muratori *et al*., 2022) [4, 29, 12, 24]. Whittemore *et al*. (2019) [27] highlighted a correlation between the rate of telomere attrition and species lifespan. However, the breeding value for telomere length did not correlate with cow longevity or other fitness measures (Muratori *et al*., 2022) [24]. Froy *et al*. (2021) [10] established an association between average telomere length and individual lifespan in Soay sheep. In pigs,

Jin *et al*. (2014) [19] observed that older pigs had relatively shorter telomeres compared to younger ones. Additionally, Denham *et al*. (2019) [8] reported an average annual telomere shortening of 134 base pairs per year in thoroughbred horses. These findings underscore a strong inverse correlation between age and telomere length across livestock species. However, the correlation between longevity and telomere length remains inconclusive due to limited and inconsistent reports.

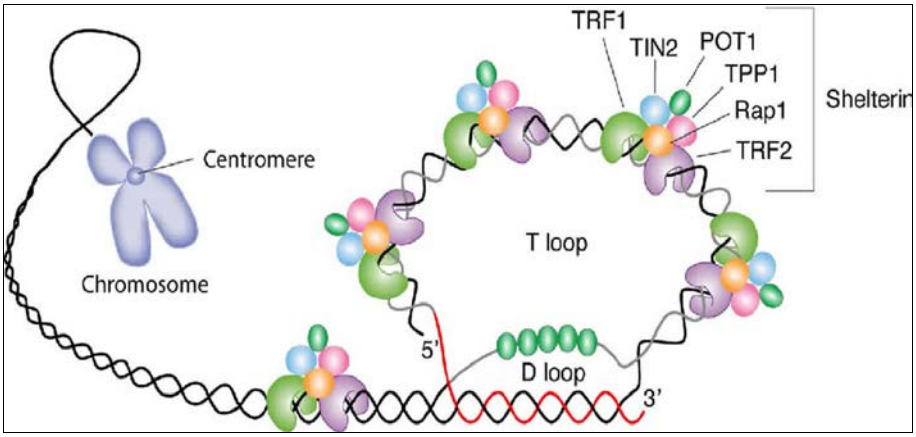

Fig 1: Structure of Telomere (Cesare and Reddel, 2010-13) [6]

Table 1: Telomere Length (TL) in Cloned animals (Burgstaller and Brem, 2017) [5]

Cloned Species	Breed	Donor cell type	TL in relation with control
Cattle (64.6% normal/ longer TL)	Holstein	Somatic	Longer
	Brahman	Fibroblast	Same
	Holstein	Oviduct	Shorter
	Holstein	Ear	Shorter
	Jersey	Oviduct	Shorter
Swine (69.6%)	Landrace	Ear fibroblast	Shorter
	Yorkshire	Ear fibroblast	Same
	Crossbred	Skin fibroblast	Same
Sheep (37.5%)	Black Welsh	Fetal fibroblast	Shorter
	Dorset Cross	Fetal fibroblast	Same
	Poll Dorset	Embryonic cells	Shorter
Goat (36.4%)	Boer	Skin fibroblast	Same
	Nigerian	Adult Granulosa	Shorter

4.2 Production

Seeker *et al*. (2018) [29] noted a negative correlation between the birth weight of calves and telomere length. Muratori *et al*. (2022) [24] observed that breeding values linked to telomere length were correlated with enhanced productive life. Additionally, lameness (Ilska-Warner *et al*., 2019) [18] and heat stress (Seeker *et al*., 2021) [30] in cows were found to reduce the telomere length of their offspring. The age of the cow also plays a role in offspring telomere length, with older cows tending to produce calves with shorter telomeres (O'Daniel *et al*., 2023; Meesters *et al*., 2023) [25, 22]. O'Daniel *et al*. (2023) [25] found a positive correlation between parturition duration and cow telomere length. Moreover, as temperature and humidity increase during the third trimester of gestation, the telomere length of calves decreases (Meesters *et al*., 2023) [22]. In bulls, higher semen quality-characterized by factors like sperm volume, motility, viability, and low abnormalities-correlates with longer telomeres (Meesters *et al*., 2023) [22]. In pigs, sperm telomeres were found to be longer than somatic cells (Fradiani *et al*., 2004) [9], and no significant association was observed between telomere length and semen quality (Ribas-Maynou *et al*., 2022) [27]. Denham and Denham (2019) [8] reported that telomere length and performance traits in horses were not significantly associated.

4.3 Disease Resistance

Szczotka *et al*. (2019) [32] observed that telomeres in diseased or infected cattle were notably shorter compared to those in healthier counterparts. Furthermore, breeding values linked to telomere length correlated with enhanced resistance to diseases such as mastitis, metritis, and displaced abomasum (Muratori *et al*., 2022) [24]. Hanis *et al*. (2022) [13] suggested that telomere length might serve as an indicator of health, particularly in relation to abnormal oral behavior in horses. However, their subsequent study (Hanis *et al*., 2023) [14] did not reveal any significant difference in telomere length before and after dietary changes.

4.4 Economical traits

According to Watson *et al*. (2017) [35], mature ewes aged over 3 years generally exhibit longer telomeres compared to rams. However, in horses, Muratori *et al*. (2022) [24] found no significant variation in telomere length concerning sex or coat color.

4.5 Other Studies

Tilesi *et al*. (2010) [33] assessed telomere length in two Italian cattle breeds, Chianina and Maremmana, finding that telomere length variation was minimal among individuals in Chianina but more pronounced in Maremmana. They

proposed that telomere length is influenced by breed characteristics. Fradiani *et al*. (2004) [9] investigated telomere and telomerase activity in pig tissue, determining that telomerase activity is absent in maturing spermatozoa. This suggests that sperm telomere elongation is constrained during spermatogenesis. Argyle *et al*. (2003) [1] concluded that telomerase does not significantly contribute to the development of the most common equine tumors.

In summary, telomeres play pivotal roles in various aspects of livestock biology, including aging, production, disease resistance, and economical traits. Studies have consistently shown an inverse correlation between age and telomere length across different livestock species, highlighting telomeres' importance in the aging process. Moreover, telomere length has been associated with productive traits such as birth weight in calves and semen quality in bulls. Additionally, telomeres may serve as indicators of disease resistance, as evidenced by shorter telomeres observed in diseased cattle. However, the relationship between telomere length and longevity remains inconclusive, necessitating further investigation. Furthermore, breed variations and sex-specific differences in telomere length underscore the complexity of telomere biology in livestock.

5. Conclusion

Telomeres emerge as crucial players in the biology of livestock, influencing various aspects such as aging, productivity, disease resistance, and economic traits. Through a thorough exploration of telomere dynamics and functions, this review sheds light on their multifaceted roles in maintaining genomic stability, regulating cellular proliferation, and impacting physiological processes in livestock species. The findings underscore the significance of telomeres in diverse areas of livestock research, including cancer studies, assisted reproductive technologies, and breed-specific differences. While significant strides have been made in understanding the implications of telomeres in livestock biology, several avenues for future research remain. The inconclusive nature of the relationship between telomere length and longevity necessitates further investigation, particularly with larger sample sizes and longitudinal studies. Additionally, exploring the underlying mechanisms driving telomere dynamics and their impact on disease susceptibility and productivity traits could provide valuable insights for livestock management and breeding programs. Overall, this review emphasizes the importance of telomeres in livestock biology and highlights the need for continued research to unravel their intricate roles and potential applications in improving animal health, welfare, and productivity.

6. Acknowledgments

We express our gratitude to Centurion University of Technology and Management for their valuable support. Additionally, we acknowledge ChatGPT, an AI-powered chatbot developed by OpenAI (https://www.openai.com/chatgpt), for its assistance in language modulation.

7. References

1. Argyle D, Ellsmore V, Gault EA, Munro AF, Nasir L. Equine telomeres and telomerase in cellular immortalisation and ageing. Mech Ageing Dev. 2003;124(6):759-764.
2. Baerlocher GM, Rice K, Vulto I, Lansdorp PM. Longitudinal data on telomere length in leukocytes from newborn baboons support a marked drop in stem cell turnover around 1 year of age. Aging Cell. 2007;6(1):121-123.
3. Blackburn EH, Gall JG. A tandemly repeated sequence at the termini of the extrachromosomal ribosomal RNA genes in Tetrahymena. J Mol Biol. 1978;120(1):33-53.
4. Brown DE, Dechow CD, Liu WS, Harvatine KJ, Ott TL. Association of telomere length with age, herd, and culling in lactating Holsteins. J Dairy Sci. 2012;95:6384-6387.
5. Burgstaller JP, Brem G. Aging of cloned animals: A mini-review. Gerontology. 2017;63(5):417-425.
6. Cesare AJ, Reddel RR. Alternative Lengthening of Telomeres in Mammalian Cells. In: Madame Curie Bioscience Database [Internet]. Austin (TX): Landes Bioscience; c2000-2013. Available from: https://www.ncbi.nlm.nih.gov/books/NBK6486.
7. Denham J, Denham MM. Leukocyte telomere length in the Thoroughbred racehorse. Anim Genet. 2018;49:452-456.
8. Denham J, Stevenson K, Denham MM. Age-associated telomere shortening in Thoroughbred horses. Exp Gerontol. 2019;127:110718.
9. Fradiani PA, Ascenzioni F, Lavitrano M, Donini P. Telomeres and telomerase activity in pig tissues. Biochimie. 2004;86(1):7-12.
10. Froy H, Underwood SL, Dorrens J, Seeker LA, Watt K, Wilbourn RV, *et al*. Heritable variation in telomere length predicts mortality in Soay sheep. Proc Natl Acad Sci USA. 2021;118:e2020563118.
11. Greider CW. Telomeres, telomerase and senescence. BioEssays. 1990;12(8):363-9.
12. Haagen I, Muratori T, Dechow C. Breed differences between Montbeliardes, Holsteins, and their crosses for production, body condition score, stature, and telomere length. J Dairy Sci. 2022;105:239.
13. Hanis F, Chung ELT, Kamalludin MH, Idrus Z. Blood profile, hormones, and telomere responses: Potential biomarkers in horses exhibiting abnormal oral behaviour. J Equine Vet Sci. 2022;118:104130.
14. Hanis F, Chung ELT, Kamalludin MH, Idrus Z. Effect of feed modification on the behavior, blood profile, and telomere in horses exhibiting abnormal oral behaviours. J Vet Behav. 2023;60:28-36.
15. Hayflick L, Moorhead PS. The serial cultivation of human diploid cell strains. Exp Cell Res. 1961;25(3):585-621.
16. Iannuzzi A, Albarella S, Parma P, Galdiero G, D'Anza E, Pistucci R, *et al*. Characterization of telomere length in Agerolese cattle breed, correlating blood and milk samples. Anim Genet. 2022;53:676-679.
17. Iannuzzi A, Iannuzzi L, Parma P. Molecular cytogenetics in domestic Bovids: A Review. Animals. 2023;13:944.
18. Ilska-Warner JJ, Psifidi A, Seeker LA, Wilbourn RV, Underwood SL, Fairlie J, *et al*. The genetic architecture of bovine telomere length in early life and association with animal fitness. Front Genet. 2019;10:1048.
19. Jin L, Jiang Z, Xia Y, Lou P, Chen L, Wang H, *et al*. Genome-wide DNA methylation changes in skeletal muscle between young and middle-aged pigs. BMC Genomics. 2014;15:653.

20. Juola FA, Haussmann MF, Dearborn DC, Vleck CM. Telomere shortening in a long-lived marine bird: cross-sectional analysis and test of an aging tool. The Auk. 2006;123(3):775-783.
21. Lu W, Zhang Y, Liu D, Songyang Z, Wan M. Telomeres-structure, function, and regulation. Exp Cell Res. 2013;319(2):133-141.
22. Meesters M, Van Eetvelde M, Martens DS, Nawrot TS, Dewulf M, Govaere J, *et al*. Prenatal environment impacts telomere length in newborn dairy heifers. Sci Rep. 2023;13:4672.
23. Muller HJ. The Remaking of Chromosomes. Woods Hole. 1938;pp181-198.
24. Muratori T, Haagen IW, Shabtay A, Cohen-Zinder M, Dechow CD. Association of telomere length with genetic merit for fitness in Holsteins of different ages. J Dairy Sci. 2022;105:238-239.
25. O'Daniel SE, Kochan KJ, Long CR, Riley DG, Randel RD, Welsh TH. Comparison of telomere length in age-matched primiparous and multiparous Brahman cows. Animals. 2023;13:2325.
26. Olovnikov AM. Principle of marginotomy in template synthesis of polynucleotides. Doklady Akademii Nauk. 1971;201(6):1496-1499.
27. Ribas-Maynou J, Llavanera M, Mateo-Otero Y, Ruiz N, Muino R, Bonet S, *et al*. Telomere length in bovine sperm is related to the production of reactive oxygen species but not to reproductive performance. Theriogenology. 2022;189:290-300.
28. Salomons HM, Mulder GV, Van de Zande L, Haussmann MF, Linskens MH, Verhulst S. Telomere shortening and survival in free-living corvids. Proc Biol Sci. 2009;276(1670):3157-3165.
29. Seeker LA, Ilska JJ, Psifidi A, Wilbourn RV, Dorrens J, Froy H, *et al*. Longitudinal changes in telomere length and associated genetic parameters in dairy cattle analysed using random regression models. PLoS ONE. 2018;13:e0192864.
30. Seeker LA, Underwood SL, Wilbourn RV, Dorrens J, Froy H, Holland R, *et al*. Telomere attrition rates are associated with weather conditions and predict productive lifespan in dairy cattle. Sci Rep. 2021;11:5589.
31. Shampay J, Szostak JW, Blackburn EH. DNA sequences of telomeres maintained in yeast. Nature. 1984;310(5973):154-7.
32. Szczotka M, Kocki J, Iwan E, Pluta A. Determination of telomere length and telomerase activity in cattle infected with bovine leukaemia virus (BLV). Pol J Vet Sci. 2019;22:391-403.
33. Tilesi F, Domenico EGD, Pariset L, Bosco L, Willems D, Valentini A, *et al*. Telomere length diversity in cattle breeds. Diversity. 2010;2(9):1118-1129.
34. Varela E, Blasco MA. 2009 Nobel Prize in Physiology or Medicine: telomeres and telomerase. Oncogene. 2010;29(11):1561-1565.
35. Watson RL, Bird EJ, Underwood S, Wilbourn RV, Fairlie J, Watt K, *et al*. Sex differences in leucocyte telomere length in a free-living mammal. Mol Ecol. 2017;26:3230-3240.
36. Weinstein BS, Ciszek D. The reserve-capacity hypothesis: evolutionary origins and modern implications of the trade-off between tumor-suppression and tissue-repair. Exp Gerontol. 2002;37(5):615-627.
37. Whittemore K, Vera E, Martínez-Nevado E, Sanpera C, Blasco MA. Telomere shortening rate predicts species lifespan. Proc Natl Acad Sci USA. 2019;116:15122-15127.
38. Zeichner SL, Palumbo P, Feng Y, Xiao X, Gee D, Sleasman J, *et al*. Rapid telomere shortening in children. Blood. 1999;93(9):2824-2830.
39. Zhang N, Baker EC, Welsh Jr T H, Riley DG. Telomere Dynamics in Livestock. Biology. 2023;12(11):1389.