EDITORIAL

Unlocking the connection: Aging as a lens to examine the effects of climate warming

Miaomiao Wang[1] **and Baojun Sun**[2,*]

[1]College of Life Sciences, Zhejiang Normal University, Jinhua 321004, China

[2]Key Laboratory of Animal Ecology and Conservation Biology, Institute of Zoology, Chinese Academy of Sciences, Beijing 100101, China

*Correspondence: sunbaojun@ioz.ac.cn (B.S.)

Received: June 2, 2023; Accepted: June 12, 2023; Published Online: June 20, 2023; https://doi.org/10.59717/j.xinn-life.2023.100003

Citation: Wang M. and Sun B. (2023). Unlocking the connection: Aging as a lens to examine the effects of climate warming. The Innovation Life **1(1)**, 100003.

Biodiversity plays a critical role in maintaining the stability of the ecosystem. However, global climate warming has caused species extinction on a global scale and threatened biodiversity. It is of utmost importance to gain a comprehensive understanding of the mechanisms that drive biological extinction and range contraction due to global climate warming. This understanding can contribute to mitigating the loss of biodiversity driven by the climate warming in the 21st century and beyond.

Climate warming, characterized by rising average temperatures and an increasing frequency of extreme heatwaves, has detrimental effects on animals, resulting in decreased fitness, increased mortality rates, and shortened potential lifespans. These effects significantly contribute to the decline in animal biodiversity. Heat stress-induced damage to animals is a major contributor to these severe consequences, involving increased oxidative stress, immune suppression, and accelerated aging process. Although sporadic studies have established a link between shortened telomeres (an aging biomarker) under climate warming and the survival and lifespan of animals, it is still unknown whether and how climate warming accelerates the aging of animals at different layers.[1]

Extensive research in biomedical sciences has explored the processes and mechanisms of aging in multiple model animals. Animal aging is a multifaceted process that occurs at various levels, encompassing reduced survival and increased mortality at the individual level, compromised immunity at the physiological level, mitochondrial dysfunction at the subcellular level, and shortened telomeres at the biomolecular level.[1,2] Cellular senescence is connected to many hallmarks of aging, which is characterized by irreversible cell cycle arrest alongside preserved metabolic activity and cellular viability. Senescent cells display several distinct phenotypic changes, such as increased cell size, cytoplasmic vacuolization, elevated protein and RNA content, aggregation of endoplasmic reticulum proteins, enlarged and dysfunctional mitochondria, and impaired lysosomal function.[3]

Previous studies on the cellular senescence of model animals have identified numerous biomarkers.[3] As a result, integrating these biomarkers of cellular senescence into research on climate warming ecology has emerged as an innovative approach to comprehending the impact of climate warming on animals. Drawing upon recent advancements in aging hallmarks and biomarkers, the following phenotypes or biomarkers can be considered to assess the effects of climate warming on animal aging: telomere shortening, epigenetic alterations, cell cycle arrest, mitochondrial dysfunction, and the senescence-associated secretory phenotype (SASP)[2,4,5](Figure 1):

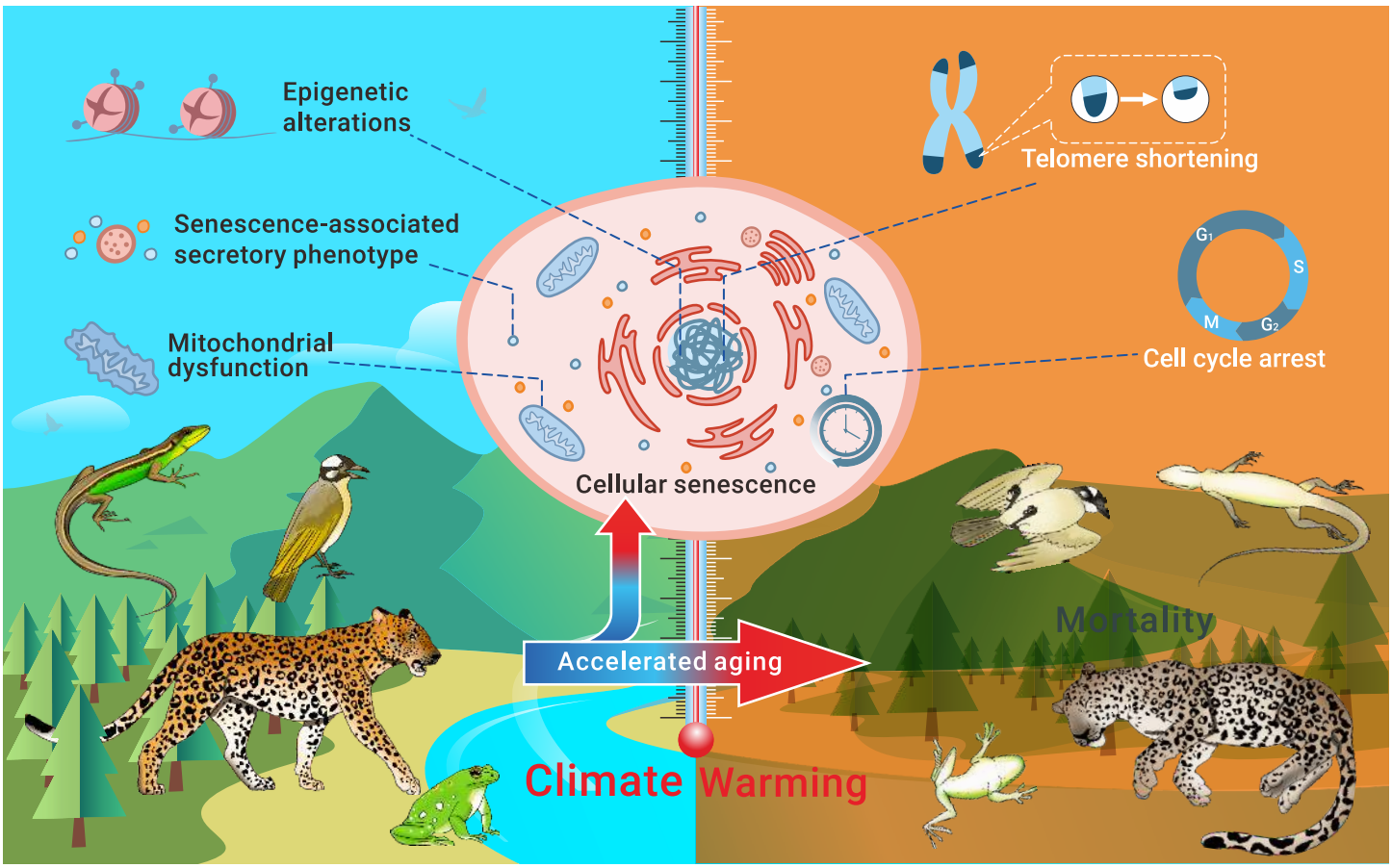

Figure 1. Potential phenotypes/biomarkers of cellular senescence that can be employed to detect the effects of climate warming on accelerated aging in animals.

1. Telomere length is one important biomarker of cellular aging,[2,4,5] and it has been utilized as an indicator to investigate the impacts of climate warming on animal aging.[1] Telomeres are intricate nucleoprotein structures found at the ends of linear chromosomes in eukaryotic cells, serving as protective caps for chromosome ends. Cellular senescence induced by telomere shortening can trigger mitochondrial dysfunction, leading to tissue and organ degeneration and functional decline. Correspondingly, the telomere length has been identified as a potentially important biomarker for assessing the impact of climate warming on the survival and life span of animals.[1]

2. Epigenetic alterations, including altered DNA methylation, abnormal histone modifications, loss of heterochromatin, and deregulated RNA modifications, have been established as crucial biomarkers of cellular senescence.[2,4,5] These changes profoundly influence gene expression and thus cellular function. Age-related epigenetic alterations have been observed across various tissues and species, indicating their conserved nature in the aging process and potential utilization for evaluating the influence of climate warming on animals.

3. Cell cycle arrest is considered to be one of the most well-defined hallmarks of cellular senescence. Pathways involving P53/$P21^{CIP1}$ and $P16^{INK4a}$/RB have been demonstrated to mediate cell cycle arrest. As such, the mediators of cell cycle arrest $P21^{CIP1}$ and $P16^{INK4a}$ have been widely used to monitor cellular senescence, both *in vivo* and *in vitro*. This has great potential in exploring the link between cellular senescence and climate warming.[4]

4. Mitochondrial dysfunction is not only a prominent hallmark of cellular aging but also a major driving factor for organ functional decline.[2,4] Rising temperatures can induce mitochondrial dysfunction, leading to various mitochondrial diseases as well as nuclear gene mutations involved in maintaining mitochondria and depressing survival. In addition, mitochondrial dysfunction such as impaired mitophagy, increased ROS generation, reduced unfolded protein response, and defects in the electron transport chain have been found to be associated with compromising normal mitochondrial functions and accelerating the aging process at both cellular and organismal levels.[2,4]

5. SASP, a highly sensitive and specific biomarker of aging, represents the phenotype of communication between senescent cells and neighboring cells. Senescent cells secrete a wide range of proinflammatory cytokines, chemokines, proteases, etc. SASP-associated proinflammatory cytokines regulate the cellular microenvironment, leading to chronic inflammation in aged tissues.[4,5] Prolonged SASP expression contributes to age-related inflammatory diseases, tissue damage, and accelerated aging. Through paracrine signaling, SASP can induce aging in neighboring cells, increasing the number of senescent cells in the organism. Cytokines like interleukin-6 (IL-6), IL1beta, TNFα and interleukin-8 (IL-8), which have been identified as components of SASP, can be used in the future for monitoring aging in animals under climate warming.[5]

The escalating consequences of global climate warming manifested through rising average temperatures and more frequent heatwaves, are posing significant threats to animal survival and lifespan, ultimately threatening the maintenance of biodiversity. Promisingly, recent progress in aging research brings us closer to identifying standardized and widely applicable aging biomarkers in the near future.[4] These advancements not only deepen our understanding of the intricate network of aging but also yield valuable insights into the impact of climate warming on animals. Furthermore, they have significant implications for the exploration of the link between climate warming and aging, the heterogeneity of climate-driven aging, and the evaluation of conservation strategies, thus facilitating the development of conservation applications. Some therapeutic interventions used in medical care to decelerate, stop, or reverse aging could also be applied in the future to slow the aging process in threatened animals under climate warming.

REFERENCES

1. Dupoué, A., Blaimont, P., Angelier, F., et al. (2022). Lizards from warm and declining populations are born with extremely short telomeres. Proc. Natl. Acad. Sci. USA ***119***, e2201371119.
2. Cai, Y., Song, W., and Li, J., (2022). The landscape of aging. Sci. China Life Sci. ***65***, 2354-2454.
3. Hernandez-Segura, A., Nehme, J., and Demaria, M., (2018). Hallmarks of cellular senescence. Trends Cell Biol. ***28***, 436-453.
4. Bao, H.N., Cao, J.N., Chen, M.T., et al. (2023). Biomarkers of aging. Sci. China Life Sci. ***66***, 893–1066.
5. López-Otín, C., Blasco, M.A., Partridge, L., et al. (2023). Hallmarks of aging: an expanding universe. Cell ***186***, 243–278.

ACKNOWLEDGMENTS

We would like to express our sincere gratitude to Weiguo Du and Jingyi Li for their invaluable consultations, guidance, and inspiration throughout the development of this work. We would also like to extend our appreciation to Zixuan Chen for the excellent drafting of the figure included in this manuscript. This work is supported by the National Key Research Development Program of China (#2022YFF0802300) and the National Natural Science Foundation of China (32271572). Baojun Sun is supported by the Youth Innovation Promotion Association of the Chinese Academy of Sciences (2019085).

DECLARATION OF INTERESTS

The authors declare no competing interests.