Integrating telomere biology into the ecology and evolution of natural populations: progress and prospects

Pat Monaghan[1], Mats Olsson[2], David Richardson[3], Simon Verhulst[4], and Sean Rogers[5]

[1]Glasgow University
[2]Goteborgs Universitet
[3]University of East Anglia
[4]University of Groningen
[5]University of Calgary

May 23, 2022

Integrating telomere biology into the ecology and evolution of natural populations: progress and prospects

Monaghan, Pat[1]; Olsson, Mats[2]; Richardson, David S.[3]; Verhulst, Simon[4]; and Rogers, Sean M.[5,6,*]

1. Institute of Biodiversity, Animal Health and Comparative Medicine, College of Medical, Veterinary and Life Sciences, University of Glasgow Glasgow, G12 8QQ, UK.

2. Department of BioEnv – Zoologen, University of Gothenburg, Sweden

3. School of Biological Sciences, University of East Anglia, Norwich Research Park, Norwich, Norfolk NR4 7TJ, UK

4. Groningen Institute for Evolutionary Life Sciences, University of Groningen, Groningen, The Netherlands.

5. Department of Biological Sciences, University of Calgary, Calgary, Canada

6. Bamfield Marine Sciences Centre, Bamfield, Canada

* corresponding author

Orcid Id:

Simon Verhulst: 0000-0002-1143-686

Pat Monaghan: 0000-0003-2430-0326

Mats Olssen; 0000-0002-4130-1323

Sean M Rogers; 0000-0003-0851-8050

David S Richardson: 0000-0001-7226-9074

Telomeres are fascinating stretches of protective DNA that cap the chromosome ends of eukaryotes. Without telomeres, during cell division and DNA replication, DNA repair proteins would misread the ends of chromosomes and attempt to repair or remove this region of the genome, leading to instability. Furthermore, the loss of DNA that inevitably occurs during cell replication due to the end replication problem and oxidative damage would erode the coding sequences of chromosomes, eventually causing genome malfunction. Telomeres protect the chromosome, but in the absence of restoration, some reduction in telomere length will occur with each cell division, eventually giving rise to cell replicative senescence often followed by cell death. Short and/or dysfunctional telomeres underly many disease states and are associated with ageing. Consequently, telomere biology is a vibrant area of biomedical research. However, until relatively recently, most of the research on telomeres has been focused on humans or animal models. That the basic pattern of progressive telomere loss and little restoration in most somatic tissues, as found in humans, might not apply to all eukaryotes had received relatively little attention. In fact, any variation in the expected pattern of decline in chromosomal telomere length with progressive rounds of cell replication, as observed in most human tissues, was initially attributed to methodological issues. Importantly, the science of studying telomeres has now expanded to encompass non-model organisms. Variation in the pattern of telomere loss and restoration across a range of species promises to reveal great insights into the drivers of life-history trade-offs and evolution, population ecology and consequences of exposure to environmental stress in natural populations.

The burgeoning interest in telomere dynamics in non-model organisms and increased communication between biomedical researchers and evolutionary ecologists is now enriching our understanding of the diversity of telomere dynamics. While the basics of telomere biology appear to be conserved across the eukaryotes, and the range of species studied is still phylogenetically restricted, differences in detail are increasingly being revealed (Monaghan et al. 2018). We now have information on how the pattern of telomere change can vary among species and include lengthening as well as shortening across the life course (Remot et al 202x, Brown et al. 2022). Our understanding of how these patterns relate to environmental factors, species, individual histories and population process is increasing. Furthermore, telomere biology has the potential to be used in conservation biology, providing information about individual and population health (e.g. Eastwood et al. 2022). The molecular ecology of telomeres in non-model organisms will have greater impact as discoveries will increase our understanding of the genomics, ecology and evolution underlying telomere diversity. This special issue brings together a collection of papers that illustrate the breadth of taxa now being investigated and ways in which emerging hypotheses, formed from the perspectives of ecology, evolution and conservation, are being tested. In this introduction, we highlight how this body of work, including new information and insights, points the way to many research questions that remain to be investigated in this emerging, cross-disciplinary area of biology.

Ecological and environmental stressors

Exposure to stressful environments can have long lasting effects on health and longevity, and some of these effects are linked to changes in telomere dynamics. In addition to furthering our understanding of the mechanism underlying these adverse effects, the study of telomere dynamics in relation to environmental conditions offers the potential to measure the scale and extent of their impact at individual and population levels (Kärkkäinen et al 202xa), evaluate environmental quality and examine the effect of conservation measures, such as habitat restoration. In this special issue, Brown et al. 2021 report apparent telomere lengthening in both sexes associated with increased survival in a small passerine bird, the Seychelles warbler *Acrocephalus sechellensis* . However, sex-specific effects of stressors influenced the patterns of telomere change. In females, stress induced by low food availability and malarial infection was associated with the expected telomere shortening, but there were no such effects in males. Moreover, less exposure to such stresses appeared to lead to telomere lengthening (Brown et al 2021). Reichard et al. (2021) also report intraspecific variation in the outcome of stress exposure using African killifish. This involves strains derived from wild populations of*Nothobranchius furzeri* and its sister species, *N. kadleci* , from sites along a strong gradient of aridity, which ultimately determines maximum natural lifespan in these species. Interestingly, they demonstrate that individual condition and environmentally-driven selection can modulate the relationship between telomere length and lifespan in opposite directions, validating the existence of inverse trends within a single taxon and again highlighting the importance of sex-specific effects. Altogether, the apparent association between telomere lengthening and stress exposure (see below for further examples) and among individual differences in telomere dynamics, for example in relation to age, sex or individual history, require further investigation. Such studies need to use accurate and repeatable within-individual measurements where possible and bear in mind the need to take measurement error into account (Steenstrup et al. 2013).

Intrinsic and extrinsic stress exposures in early life are known to have substantial and long-lasting effects on phenotypic development. Conditions experienced inside the cell or from the external environment during growth can influence telomere dynamics, as shown in this special issue. In European badgers *Meles meles* , van Lieshout et al. (2021) report that cubs born in warmer, wetter springs have longer telomere lengths, which is in turn linked to survival. In purple-crowned fairy wrens (*Malurus coronatus*) the rate of telomere shortening in the first year of life predicted lifespan (Sheldon et al 2021b). More broadly, it has been hypothesized that measuring the effects of adverse environmental conditions induced by anthropogenic stressors (such as chemical pollutants, noise and inappropriate light) on telomere dynamics could assist in the monitoring and conservation of wildlife. In this context telomere measurements have the potential advantage over many other biomarkers of representing a potential fitness proxy, allowing effects to be studied over a time scale that could be much shorter than required to measure actual fitness consequences. In line with this, Salmón and Burraco (2022) evaluated the use of changes in telomere dynamics as a way of assessing such anthropogenic impacts, providing an exhaustive literature review and meta-analysis. Oxidative stress induced by internal and external factors can be a major cause of DNA damage which could increase telomere attrition. Metcalfe and Olsson (2021) provide a compelling case that endogenous reactive oxygen species produced in the mitochondria create links between mitochondrial function, DNA integrity and telomere dynamics. They argue that telomere dynamics are best understood when considering the optimal solution to the trade-off between energetic efficiency and chromosomal protection that will differ among individuals and change over time, depending on resource availability, energetic demands and life history strategy. Such inferences may cumulatively help explain why the effects of stressors on telomere dynamics are evident (but apparently also stressor, taxon, and sometimes sex-specific). Clearly the research directions proposed in this special issue will contribute to a better understanding of these mechanisms that link environment, lifestyle and telomere dynamics.

At present, telomere research on non-model organisms has been primarily focused on the endothermic vertebrates - birds and mammals. Nucleated red blood cells are primarily used in bird studies while white blood cells are most often in mammals, particularly humans. Thus, tissue specificity in telomere dynamics associated with these cell types may itself underlie some of the differences reported. However, the majority of animals are ectotherms and often differ from many endotherms by having telomerase production in somatic tissues. Furthermore, many aspects of ectotherm development and performance are linked to environmental temperature, and are, therefore, potentially significantly affected by climate disruption. Friesen et al. (2021) suggest that developing thermal performance curves for the processes affecting telomere dynamics could assist in monitoring climate impacts, highlighting the pressing need for more experimental work in this area to isolate the causes of environmentally induced changes in telomere dynamics. Rouan et al. (2021) present such an experimental study on the coral, *Stylophora pistillata* , in which bleaching, the devastating loss of symbionts that can results from climate change, was induced by continuous darkness. This resulted in increased telomere loss. As well as telling us something about the damaging effects, these findings could inform methods for monitoring coral reef health. In a field experiment using young salmon *Salmo salar* , in freshwater streams, McLennan et al. (2021) found that both a lack of suitable substrate and living at high density were associated with reduced telomere length. However, in streams in which nutrient levels were experimentally restored, these adverse effects on telomere length were greatly reduced, demonstrating the potential utility of changes in telomere length in a conservation context. Further, the experiment presented by Bae et al. (2021) revealed that the effects of temperature can be influenced by interactions with pollutants. This appears to be especially prevalent in species with temperature-dependent sex determination, such as the American alligator*Alligator mississippiensis* . Here the effect of experimental exposure to an endocrine disrupting chemical depended on the environmental temperature; at temperatures promoting female development, the effect on telomere length was positive, while at the higher, male promoting temperature, the effect was negative. On the other hand, raising crickets at different temperatures, which strongly affected their growth, did not significantly affect their telomere dynamics Boonekamp et al. (2021). Much may depend on how severely the potential stressor is perceived by the organism in question.

In a somewhat different context, but still potentially linked to differences in stress exposure, a nonexperimental study by Wood et al. (2021) used extensive longitudinal assessments of within-individual rates of change in telomere length to investigate the impacts of dominance status on telomere dynamics in the co-operative breeder, the white-browed sparrow-weaver *Plocepasser mahali* . They found that social dominance and rainfall predicted telomere dynamics. Looking at mechanistic processes in more detail, Wolf et al. (2021) provided novel insight into the telomere dynamics of a natural system of tree swallows *Tachycineta bicolor* , reporting lower expression of the telomere regulatory gene POT1 in female breeders of higher quality. They also reported that experimentally induced stress exposure in chicks induced lower POT1 expression and telomere lengthening.

Collectively, these studies show that variation in stress exposure and individual resilience can contribute to intra-specific differences in telomere dynamics. They highlight the need to consider the biology of the species (including sex differences), the local conditions to which it has been exposed, what different levels of temperature change mean in terms of stress exposure for different species and populations, and the need to examine interacting environmental effects in natural populations. They also highlight that examining telomere dynamics in relation to differential expression of relevant genes in relation to ecological and environmental variables could potentially be of great interest.

Telomeres and life history trade-offs

Much of the interest in telomeres from ecologists relates to their potential in mediating life history trade-offs. For example, is increased telomere damage traded off against potential advantages of larger size or greater energy expenditure? The outcome of such trade-offs may be influenced by individual state. Such state-dependent relationships are difficult to measure but variation in telomere length, or loss, might provide a relative measure. Carrying elaborate sexual ornaments is thought to be costly thereby maintaining the honesty of the signal, but little work has yet been done to test the relative cost of ornamentation using telomeres. Kauzálová et al. (2022) found that barn swallows *Hirundo rustica* , with long tail streamers (a sexually selected ornament (Møller 1988), have shorter telomeres. This suggests a cost to elaborate ornamentation in this species. Ravindran et al. (2021) used bivariate analysis to decompose correlations between telomere length and reproduction into within- and among individual effects. They conclude that, in wild Soay sheep *Ovis aries* , females had shorter telomeres in August in years in which they gave birth in spring compared to years without the gestation effort, indicative of a trade-off involving reproduction. However, at the same time in years in which they gave birth, the mother's telomeres were longer when their lambs survived to August, compared with years when they lost their lambs earlier, suggesting complex state dependent effects. Sepp et al. (2021) conducted a cross-fostering experiment in common gulls (*Larus canus*), to tease apart pre- and post-natal parental age effects on offspring telomere length. Neither the age of the natal- nor the foster parents in this study predicted the length or rate of change of telomeres in chicks.

The above results are interesting, but also demonstrate that additional experimental work is needed, particularly in relation to evaluating parental state-induced telomere dynamics. A good example is provided by Atema et al. (2021) who manipulated individual state by equipping male great tits *Parus major* with a 'backpack' adding 5% to their body mass for a year. Surprisingly telomere dynamics were not affected by this extra burden, despite the duration of the experiment and large sample size. However, the absence of an effect was consistent with there being little evidence of a fitness costs of carrying this extra mass (Atema et al. 2016), information which is often lacking but critical for the interpretation of any result. In the dark-eyed junco *Junco hyemalis* , where experimentally elevated testosterone reduces male survival (Reed et al. 2006), elevated testosterone was also linked to accelerated telomere attrition Heidinger et al. (2021). This suggests that telomere dynamics may be part of the mechanism causing the testosterone effect on survival in this species, and that variation in state is an important issue.

Trade-offs involving telomeres may also occur very early in life, for example, when resources are allocated to growth at the expense of somatic maintenance, potentially being reflected in early life telomere dynamics (Monaghan and Ozanne 2018; Vedder et al. 2018). Growth is difficult to manipulate directly and is often done through dietary manipulations, which might have confounding systemic effects that can be difficult to fully take into account. Pepke et al. (2021) examined the effect of final body size on telomere length within an artificial selection experiment on body size (tarsus length) in free-living house sparrows *Passer domesticus* . They studied two island populations, with selection for large body size on one island, and selection for small body size on the other. The experiment was successful in creating a difference in tarsus length between the islands - of almost 10% in the final selection year. They found a significant decrease in telomere length on the island with selection for large body size, but no change on the island with selection for small body size. The approach of Pepke et al. (2021) will hopefully be followed by others, potentially using existing selection experiments on growth and body size. Though to fully understand the results it may be important to also know more about cell division rates and growth patterns in the individuals attaining different body sizes

While the general pattern from human studies is that telomeres shorten with age, findings in other species, including those in this special issue mentioned earlier in relation to stress exposure, suggest that this is not always the case (meta-analysed by Remot et al. 2021 in this issue). For example, there is evidence of telomere elongation in some hibernating mammals and snakes (Olsson 2018). This raises questions about the underlying mechanisms involved in telomere maintenance, with variation in telomerase activity as a likely candidate. Smith et al. (2021) review what is known about telomerase activity in ecological studies and discuss the challenges involved in measuring telomerase activity. They note that studies have not generally detected the expected link between telomere maintenance and telomerase activity, for which there can be different explanations. When telomeres are studied in blood, it is mainly the telomerase activity in the haemopoietic stem cells in the bone marrow that will affect the focal telomeres, but studying this within individuals is very difficult. Noguera et al. (2020) evaluated the effect of maternal glucocorticoids on telomerase activity in yellow-legged gulls *Larus michahellis* (e.g., corticosterone or cortisol) as their transmission to offspring is a potential cost associated with adverse or stressful conditions experienced by mothers. They found that egg corticosterone can stimulate telomerase activity and promote longer telomeres during embryo development, suggesting mechanistic links by which mothers may shape offspring life-history trajectories and phenotypes. In another study, Sheldon et al. (2021) tested levels of DNA methylation across early life in wild, nestling zebra finches, discovering that methylation was negatively correlated with telomere length changes, providing possible links between epigenetics and telomeres. Altogether, elucidating the ecology of gene expression and epigenetics in telomere maintenance across natural populations should therefore be considered an important task for the future.

Raven et al. (2022) discuss what is known about cancer and telomeres in the wild, a topic of considerable interest since telomeres have historically been studied in the context of cancer, with somatic down-regulation of telomerase postulated as a tumour protection mechanism in large bodies/long lived species. Telomerase activation has been identified as critical mutations that are associated with malignant cells. Raven et al. (2022) emphasize that telomere-cancer dynamics constitute a complex and a multifaceted process, in part because in humans both (too) long and (too) short telomeres can be associated with an increased cancer risk. Whether similar effects can be observed in natural populations of other species remains to be seen. Telomere length predicts survival *within* species (Wilbourn et al. 2018), raising the question as to whether long-lived species have relatively long telomeres. Among birds, this does not appear to be the case (Tricola et al. 2018), at least when using the available estimates of maximum lifespan. In contrast, Gomes et al. (2011) reported an inverse relationship between telomere length and maximum lifespan in mammals. Pepke and Eisenberg (2021) revised and extended the data set of Gomes et al. (2011) and confirmed this inverse relationship. A possible explanation for this pattern is that short telomeres protect against cancer, because cells with short telomeres have less scope for replication before critically short telomeres induce cell replicative senescence. In line with this explanation, Pepke & Eisenberg (2021) show a positive association between telomere length and the development of neoplasia, abnormal tissue growth that can develop into malignancy. They further show that domesticated species have substantially longer telomeres than wild species with similar mass. This may be because of artificial selection of certain phenotypes, or relaxation of selection pressures in domestic species; for example domesticated animals will often be culled before reaching the natural end of their lives, diminishing selection favouring protection against the development of cancer.

Heritability and Evolvability

One of the most remarkable aspects of telomere biology is the considerable range described for the heritability of telomere length (i.e., the parental genetic contribution additively affecting the telomere length variance in the offspring, i.e., its heritability,h^2 = VA/VP). Reviews on telomere biology report perhaps the widest range in heritability of any phenotypic trait ranging from near zero to more than one (likely due to sampling error, sinceh^2 cannot theoretically exceed one; Olsson et al. 2018). This makes telomere evolution difficult to reconcile with evolutionary expectations from existing quantitative genetics theory, the situation becoming more complex when the aim is to understand the potential of adaptive telomere evolution and the agents of selection. An alternative approach to using heritability for this procedure is to assess 'evolvability' as the expected proportional change under a unit strength of selection, yielding a mean-scaled additive variance (Houle 1992). These two measures, heritability and evolvability, have been shown to have near zero correlation, possibly due to positive correlations between the additive- and other components of the phenotypic variance (e.g., environmental-, epistatic- and dominance variance; Hansen 2011). In this special issue, aspects of quantitative genetics of telomeres and their dynamics are discussed. The main 'other' variance components for understanding telomere heritability, its limitations and usefulness for evolutionary inference, are epigenetic inheritance (Bauch et al. 2019), and the environmental variance (Dugdale and Richardson 2018). A straightforward expectation from theory is that when environmental variance is eliminated, heritability will be very high, which is what (Boonekamp et al. 2021; h^2[?] 1) found in their laboratory experiments on field crickets*Gryllus campestris* . Importantly, heritability estimates are environment-specific, so to what degree these estimates predict responses to ongoing telomere selection in the wild remains to be tested. An attempt to do this in a cross-fostering experiment on jackdaws *Corvus monedula* , showed that heritability for telomere length was high (0.74) whereas for telomere shortening rate it was considerably lower (0.09; Bauch et al. 2021). This agrees with evolutionary theory in that telomere shortening in this taxon is more strongly correlated with components of fitness than is telomere length*per se* (Bauch et al. 2021 and references therein). Interestingly, Bauch et al.'s evolvability estimate for telomere length was only 0.48% and uncorrelated with heritability, in agreement with Hansen et al.'s evolvability review (2011). In contrast, in a study with considerably greater sample size and thus power than most QG studies on telomeres in wild animals Sparks et al. (2021) found low heritability and evolvability for telomere length in Seychelles warblers, suggesting differences may exist among species.

Future Directions

The collection of wonderful studies in this special issue demonstrates the increasing interest in studying telomeres from an evolutionary and ecological perspective, and their potential value in areas such as conservation biology. The work reported here highlights several advances that collectively demonstrate the effect of environment on telomere dynamics and the corresponding impact on life history trade-offs and quantitative genetic consequences. In addition, the work also highlights taxonomic and conceptual areas where additional studies would benefit the field. For example, recent studies on plants have discovered that telomerase RNA homologs across the plant kingdom are structurally similar to ciliates and multicellular eukaryotes, supporting the hypothesis of a common ancestor for telomerase (Song et al. 2019) . They also provide growing evidence for the adaptive significance of plant telomeres for ecologically important traits such as flowering time (Choi et al. 2021)). However, databases on telomere traits in taxonomically diverse organisms, with variation in life histories, body sizes, growth patterns and regenerative capabilities remain limited. More work is needed on species with complex life cycles, high regenerative capacity and variable lifespans. Additional studies will hopefully enable testing of hypotheses of telomere evolutionary history, adaptive life-history strategies, and chromosomal integrity.

To date, studies of telomere dynamics have benefited from long-term studies of several animal systems. There is much to be gained from the within-individual data collected from such studies and variation in population trajectories. In quantitative genetics (QG), controlling for individuals having a shared environment between generations (which inflates the heritability measure) could be achieved by cross-fostering in many various species and/or and by releasing offspring at random locations in species without parental care (Olsson et al. 2011), or by controlling for environmental 'type' in longitudinal studies or experimental plant and animal systems. The large samples necessary for telomere QG work can be facilitated by choice of appropriate model systems and by applying emerging techniques in molecular ecology. qPCR continues to be particularly attractive for high-throughput processing, especially in species with limited interstitial telomeres (Boonekamp et al. 2021) (Rovatsos et al. 2015; Matsubara et al. 2015). However, the potential importance of how interstitial telomere repeats influence the biology of different taxa has hardly been investigated at all (see Nussey et al. (Methods in Ecol & Evolution) for discussion of methodology). It is important that telomeres measuring methodologies are as accurate and precise as possible, while allowing for large enough sample through-put to capture variation. Avoiding problems created by selective disappearance of phenotypes is also important. Some of these issues are discussed in this special issue in reviews revealing major methodological effects on estimates of individual repeatability (Karkkainen et al. 202xb) and heritability (Bauch et al. 2021).

A recently developed method, the single telomere absolute-length rapid (STAR) assay offers a high-throughput, digital real-time PCR approach for rapidly measuring the absolute lengths and quantities of individual telomere molecules (Luo et al. 2020) (Dwech-Maitre et al 021), although its precision remains to be evaluated. In the future the use of digital qPCR may yield higher throughput than traditional Telomere Restriction Fragment analysis (TRF) (Nussey et al 2014) and more precision than current qPCR methods. Pepke et al. (2021) examined heritability and genetic architecture using a combination of qPCR and next generation sequencing, supporting that new bioinformatic approaches using computerized telomere estimation may facilitate higher throughput and examination of non-terminal telomeres and their position effects on fitness (Nersisyan and Arakelyan 2015; Edwards 2021).

Finally, many exciting questions pertaining to telomere biology in relation to ecology evolution and conservation remain to be answered. For evolutionary biologists and ecologists, variation is the 'stuff of life' and understanding the causes and consequences of such variation, and the role of telomeres within that is an important and exciting challenge! We still know relatively little about how flexible telomere biology is under different selection pressures and to what extent it constrains the suite of potential life histories, for example in relation to growth, body size, reproduction and lifespan. In terms of fitness, we may ask what matters most, telomere loss or telomere length? Both length and loss rate have been found to be predictive of longevity within species and much may depend on the life stage at which each is measured; it seems unlikely that limited telomere length would curtail lifespan until relatively old age, when stem cell pools are depleted and stem cells themselves show age-related deterioration. That said, telomere loss might give us a better handle on understanding stress exposure and stress resilience. In humans and birds, there is evidence that telomere length variation stabilises at the end of growth and that telomere length at this time period is the best predictor of subsequent lifespan (Benetos et al. 2013, Daniali et al. 2013, Heidinger et al 2012). Will similar patterns be revealed in species with indeterminate growth? Currently, we simply do not have the data to answer this question so much more work is needed in this area. In a conservation context, can telomere biology help us identify populations at risk from rapid environmental disruption due to anthropogenic effects, and identify species that are likely to be resilient to climate change and stress exposure? Given that the genetic basis of adaptive traits are now used to project the distribution of species in response to climate change (Wuitchik et al. 2022), it is possible that the inclusion of telomere biology may further inform and refine such projections in species distribution models.

Altogether, this comprehensive collection of studies demonstrates the enormous potential for the integration of ecological and genomic approaches to continue to transform our understanding of the consequences of intrinsic and extrinsic environmental stressors and change on the ecology and evolution of natural populations. This special issue highlights how a deeper appreciation of the role of telomeres and associated properties of the genome will continue to benefit the field of Molecular Ecology.

Literature Cited

A.P, Moller. 1988. "Female Choice Selects for Male Sexual Tail Ornaments in the Monogamous Swallow." Nature 332: 640–42.

Atema, Els, Arie J. van Noordwijk, and Simon Verhulst. 2021. "Telomere Dynamics in Relation to

Experimentally Increased Locomotion Costs and Fitness in Great Tits." Molecular Ecology, September. https://doi.org/10.1111/mec.16162.

Bae, Junsoo, Emily M. Bertucci, Samantha L. Bock, Matthew D. Hale, Jameel Moore, Phil M. Wilkinson, Thomas R. Rainwater, et al. 2021. "Intrinsic and Extrinsic Factors Interact during Development to Influence Telomere Length in a Long-lived Reptile." Molecular Ecology, June. https://doi.org/10.1111/mec.16017.

Bauch, Christina, Jelle J. Boonekamp, Peter Korsten, Ellis Mulder, and Simon Verhulst. 2021. "High Heritability of Telomere Length and Low Heritability of Telomere Shortening in Wild Birds." Molecular Ecology, October. https://doi.org/10.1111/mec.16183.

Benetos, A., Kark, J. D., Susser, E., Kimura, M., Sinnreich, R., Chen, W., Steenstrup, T., Christensen, K., Herbig, U., von Bornemann Hjelmborg, J., Srinivasan, S. R., Berenson, G. S., Labat, C., & Aviv, A. 2013. Tracking and fixed ranking of leukocyte telomere length across the adult life course. *Aging cell* , *12* (4), 615–621. https://doi.org/10.1111/acel.12086

Boonekamp, Jelle, Rolando Rodriguez-Munoz, Paul Hopwood, Erica Zuidersma, Ellis Mulder, Alastair Wilson, Simon Verhulst, and Tom Tregenza. 2021. "Telomere Length Is Highly Heritable and Independent of Growth Rate Manipulated by Temperature in Field Crickets." Molecular Ecology, March. https://doi.org/10.1111/mec.15888.

Brown, Thomas J., Lewis G. Spurgin, Hannah L. Dugdale, Jan Komdeur, Terry Burke, and David S. Richardson. 2021. "Causes and Consequences of Telomere Lengthening in a Wild Vertebrate Population." Molecular Ecology, July. https://doi.org/10.1111/mec.16059.

Choi, Jae Young, Liliia R. Abdulkina, Jun Yin, Inna B. Chastukhina, John T. Lovell, Inna A. Agabekian, Pierce G. Young, et al. 2021. "Natural Variation in Plant Telomere Length Is Associated with Flowering Time." The Plant Cell 33 (4): 1118–34. https://doi.org/10.1093/plcell/koab022.

Daniali L, Benetos A, Susser E, Kark JD, Labat C, Kimura M, Desai K, Granick M, Aviv A. Telomeres shorten at equivalent rates in somatic tissues of adults. Nat Commun. 2013;4:1597. doi: 10.1038/ncomms2602. PMID: 23511462; PMCID: PMC3615479.

Dugdale, Hannah L., and David S. Richardson. 2018. "Heritability of Telomere Variation: It Is All about the Environment!" Philosophical Transactions of the Royal Society B: Biological Sciences 373 (1741): 20160450. https://doi.org/10.1098/rstb.2016.0450.

Eastwood JR, Connallon T, Delhey K, Hall ML, Teunissen N, Kingma SA, Verhulst S & Peters A, 2022. Higher temperatures are associated with shorter early-life telomeres: fitness implications under climate change. PNAS

Edwards, S. 2021. "First Glimpses of Pangenomes from Birds." In PGEC Workshop in Pangenomes.

Friesen, Christopher R., Erik Wapstra, and Mats Olsson. 2021. "Of Telomeres and Temperature: Measuring Thermal Effects on Telomeres in Ectothermic Animals." Molecular Ecology, September. https://doi.org/10.1111/mec.16154.

Gardner, Michael, David Bann, Laura Wiley, Rachel Cooper, Rebecca Hardy, Dorothea Nitsch, Carmen Martin-Ruiz, et al. 2014. "Gender and Telomere Length: Systematic Review and Meta-Analysis." Experimental Gerontology 51 (March): 15–27. https://doi.org/10.1016/j.exger.2013.12.004.

Gomes, Nuno M. V., Oliver A. Ryder, Marlys L. Houck, Suellen J. Charter, William Walker, Nicholas R. Forsyth, Steven N. Austad, et al. 2011. "Comparative Biology of Mammalian Telomeres: Hypotheses on Ancestral States and the Roles of Telomeres in Longevity Determination." Aging Cell 10 (5): 761–68. https://doi.org/10.1111/j.1474-9726.2011.00718.x.

Hansen, S. Christine. 2011. "Restoring Endangered Northern Abalone (Haliotis Kamtschatkana) Populations in British Columbia, Canada, Using Hatchery-Raised Individuals." Thompson Rivers University.

Heidinger, B. J., Blount, J. D., Boner, W., Griffiths, K., Metcalfe, N. B., & Monaghan, P. 2012. Telomere length in early life predicts lifespan. Proceedings of the National Academy of Sciences of the United States of America, 109(5), 1743–1748. https://doi.org/10.1073/pnas.1113306109

Heidinger, Britt J., Samuel P. Slowinski, Aubrey E. Sirman, Jeffrey Kittilson, Nicole M. Gerlach, and Ellen D. Ketterson. 2021. "Experimentally Elevated Testosterone Shortens Telomeres across Years in a Free-living Songbird." Molecular Ecology, February. https://doi.org/10.1111/mec.15819.

Houle, D. 1992. "Comparing Evolvability and Variability of Quantitative Traits." Genetics 130 (1): 195–204. https://doi.org/10.1093/genetics/130.1.195.

Karkkainen, Tiia, Michael Briga, Toni Laaksonen, and Antoine Stier. 2021. "Within-individual Repeatability in Telomere Length: A Meta-analysis in Nonmammalian Vertebrates." Molecular Ecology, September. https://doi.org/10.1111/mec.16155.

Tiia Karkkainen, Toni Laaksonen, Malcolm Burgess, Alejandro Cantarero, Jesus Martinez-Padilla, Jaime Potti, Juan Moreno, Robert L. Thomson, Vallo Tilgar, Antoine Stier. Population differences in the length and early-life dynamics of telomeres among European pied flycatchers. Molecular Ecology

Kauzalova, Tereza, Oldřich Tomášek, Ellis Mulder, Simon Verhulst, and Tomáš Albrecht. 2022. "Telomere Length Is Highly Repeatable and Shorter in Individuals with More Elaborate Sexual Ornamentation in a Short-lived Passerine." Molecular Ecology, February. https://doi.org/10.1111/mec.16397.

Ketterson, E. D., and V. Nolan. 1992. "Hormones and Life Histories: An Integrative Approach." The American Naturalist 140: S33-62.

van Lieshout, Sil H. J., Elisa P. Badás, Julius G. Bright Ross, Amanda Bretman, Chris Newman, Christina D. Buesching, Terry Burke, David W. Macdonald, and Hannah L. Dugdale. 2021. "Early-life Seasonal, Weather and Social Effects on Telomere Length in a Wild Mammal." Molecular Ecology, June. https://doi.org/10.1111/mec.16014.

Luo, Yongqiang, Ramya Viswanathan, Manoor Prakash Hande, Amos Hong Pheng Loh, and Lih Feng Cheow. 2020. "Massively Parallel Single-Molecule Telomere Length Measurement with Digital Real-Time PCR." Science Advances 6 (34). https://doi.org/10.1126/sciadv.abb7944.

Matsubara, Kazumi, Yoshinobu Uno, Kornsorn Srikulnath, Yoichi Matsuda, Emily Miller, and Mats Olsson. 2015. "No Interstitial Telomeres on Autosomes but Remarkable Amplification of Telomeric Repeats on the W Sex Chromosome in the Sand Lizard (Lacerta Agilis)." Journal of Heredity 106 (6): 753–57. https://doi.org/10.1093/jhered/esv083.

McLennan, Darryl, Sonya K. Auer, Simon McKelvey, Lynn McKelvey, Graeme Anderson, Winnie Boner, Jessica S. Duprez, and Neil B. Metcalfe. 2021. "Habitat Restoration Weakens Negative Environmental Effects on Telomere Dynamics." Molecular Ecology, July. https://doi.org/10.1111/mec.15980.

Metcalfe, Neil B., and Mats Olsson. 2021. "How Telomere Dynamics Are Influenced by the Balance between Mitochondrial Efficiency, Reactive Oxygen Species Production and DNA Damage." Molecular Ecology, September. https://doi.org/10.1111/mec.16150.

Monaghan, Pat, and Susan E. Ozanne. 2018. "Somatic Growth and Telomere Dynamics in Vertebrates: Relationships, Mechanisms and Consequences." Philosophical Transactions of the Royal Society B: Biological Sciences 373 (1741): 20160446.

https://doi.org/10.1098/rstb.2016.0446.

Monaghan Pat, Eisenberg Dan T. A., Harrington Lea and Dan Nussey. 2018. Understanding diversity in telomere dynamics. Philisophical Transactions of the Royal Society B:373, 20160435. http://doi.org/10.1098/rstb.2016.0435

Nersisyan, Lilit, and Arsen Arakelyan. 2015. "Computel: Computation of Mean Telomere Length from Whole-Genome Next-Generation Sequencing Data." PLOS ONE 10 (4): e0125201. https://doi.org/10.1371/journal.pone.0125201.

Noguera, Jose Carlos, Alberto Silva, and Alberto Velando. 2020. "Egg Corticosterone Can Stimulate Telomerase Activity and Promote Longer Telomeres during Embryo Development." Molecular Ecology, November. https://doi.org/10.1111/mec.15694.

Olsson, Mats, Pauliny, A., Wapstra, E., Uller, T., Schwartz, T., Miller, E. and Blomqvist, D. 2011. Sexual Differences in Telomere Selection in the Wild. Molecular Ecology 20 (10): 2085–99. https://doi.org/10.1111/j.1365-294X.2011.05085.x.

Olsson, Mats, Erik Wapstra, and Christopher Friesen. 2018. "Ectothermic Telomeres: It's Time They Came in from the Cold." Philosophical Transactions of the Royal Society B: Biological Sciences 373 (1741): 20160449. https://doi.org/10.1098/rstb.2016.0449.

Pepke, Michael Le, and Dan T. A. Eisenberg. 2021. "On the Comparative Biology of Mammalian Telomeres: Telomere Length Co-evolves with Body Mass, Lifespan and Cancer Risk." Molecular Ecology, March. https://doi.org/10.1111/mec.15870.

Pepke, Michael Le, Thomas Kvalnes, Sarah Lundregan, Winnie Boner, Pat Monaghan, Bernt-Erik Saether, Henrik Jensen, and Thor Harald Ringsby. 2021. "Genetic Architecture and Heritability of Early-life Telomere Length in a Wild Passerine." Molecular Ecology, December. https://doi.org/10.1111/mec.16288.

Raven, Nynke, Marcel Klaassen, Thomas Madsen, Frederic Thomas, Rodrigo K. Hamede, and Beata Ujvari. 2022. "Transmissible Cancer Influences Immune Gene Expression in an Endangered Marsupial, the Tasmanian Devil (Sarcophilus Harrisii)." Molecular Ecology 31 (8): 2293–2311. https://doi.org/10.1111/mec.16408.

Ravindran, Sanjana, Hannah Froy, Sarah L. Underwood, Jennifer Dorrens, Luise A. Seeker, Kathryn Watt, Rachael V. Wilbourn, et al. 2021. "The Association between Female Reproductive Performance and Leukocyte Telomere Length in Wild Soay Sheep." Molecular Ecology, October. https://doi.org/10.1111/mec.16175.

Reed, W. L., M. E. Clark, P. G. Parker, S. A. Raouf, N. Arguedas, D. S. Monk, E. Snajdr, V. Nolan Jr, and E. D. Ketterson. 2006. "Physiological Effects on Demography: A Long-Term Experimental Study of Testosterone's Effects on Fitness." The American Naturalist 167 (5): 667–83. https://doi.org/10.1086/503054.

Reichard, Martin, Kety Giannetti, Tania Ferreira, Ahmed Maouche, Milan Vrtilek, Matej Polačik, Radim Blažek, and Miguel Godinho Ferreira. 2021. "Lifespan and Telomere Length Variation across Populations of Wild-derived African Killifish." Molecular Ecology, December. https://doi.org/10.1111/mec.16287.

Remot, Florentin, Victor Ronget, Hannah Froy, Benjamin Rey, Jean-Michel Gaillard, Daniel H. Nussey, and Jean-François Lemaitre. 2021. "Decline in Telomere Length with Increasing Age across Nonhuman Vertebrates: A Meta-analysis." Molecular Ecology, September. https://doi.org/10.1111/mec.16145.

Rouan, Alice, Melanie Pousse, Eric Tambutte, Nadir Djerbi, William Zozaya, Laura Capasso, Didier Zoccola, Sylvie Tambutte, and Eric Gilson. 2021. "Telomere Dysfunction Is Associated with Dark-induced Bleaching in the Reef Coral Stylophora Pistillata." Molecular Ecology, October. https://doi.org/10.1111/mec.16199.

Rovatsos, Michail, Lukaš Kratochvíl, Marie Altmanová, and Martina Johnson Pokorná. 2015. "Interstitial Telomeric Motifs in Squamate Reptiles: When the Exceptions Outnumber the Rule." PLOS ONE 10 (8): e0134985. https://doi.org/10.1371/journal.pone.0134985.

Salmón, Pablo, and Pablo Burraco. 2022. "Telomeres and Anthropogenic Disturbances in Wildlife: A Systematic Review and Meta-analysis." Molecular Ecology, February. https://doi.org/10.1111/mec.16370.

Sepp, Tuul, Richard Meitern, Britt Heidinger, Kristina Noreikiene, Kalev Rattiste, Peeter Horak, Lauri Saks, Jeffrey Kittilson, Janek Urvik, and Mathieu Giraudeau. 2021. "Parental Age Does Not Influence Offspring Telomeres during Early Life in Common Gulls (Larus Canus)." Molecular Ecology, April. https://doi.org/10.1111/mec.15905.

Sheldon AL, Eastwood JR, Teunissen N, Roast MJ, Hidalgo Aranzamendi N, Fan M, Hall ML, Anne Kingma S, Verhulst S, & Peters A. 2021. Telomere dynamics in the first year of life, but not later in life, predict lifespan in a wild bird. Molecular Ecology, online

Sheldon, Elizabeth L., Riccardo Ton, Winnie Boner, Pat Monaghan, Shirley Raveh, Aaron W. Schrey, and Simon C. Griffith. 2021. "Associations between DNA Methylation and Telomere Length during Early Life: Insight from Wild Zebra Finches (Taeniopygia Guttata)." Molecular Ecology, October. https://doi.org/10.1111/mec.16187.

Smith, Steve, Franz Hoelzl, Sandrine Zahn, and Francois Criscuolo. 2021. "Telomerase Activity in Ecological Studies: What Are Its Consequences for Individual Physiology and Is There Evidence for Effects and Trade-offs in Wild Populations." Molecular Ecology, October. https://doi.org/10.1111/mec.16233.

Song, Jiarui, Dhenugen Logeswaran, Claudia Castillo-Gonzalez, Yang Li, Sreyashree Bose, Behailu Birhanu Aklilu, Zeyang Ma, Alexander Polkhovskiy, Julian J.-L. Chen, and Dorothy E. Shippen. 2019. "The Conserved Structure of Plant Telomerase RNA Provides the Missing Link for an Evolutionary Pathway from Ciliates to Humans." Proceedings of the National Academy of Sciences 116 (49): 24542–50. https://doi.org/10.1073/pnas.1915312116.

Sparks, Alexandra M., Lewis G. Spurgin, Marco Velde, Eleanor A. Fairfield, Jan Komdeur, Terry Burke, David S. Richardson, and Hannah L. Dugdale. 2021. "Telomere Heritability and Parental Age at Conception Effects in a Wild Avian Population." Molecular Ecology, February. https://doi.org/10.1111/mec.15804.

Steenstrup, T., Hjelmborg, J.V.B, Kark, J.D., Christensen, K. and A. Aviv 2013. The telomere lengthening conundrum–artifact or biology?, Nucleic acids research, 41: e131.

Tricola, Gianna M., Mirre J. P. Simons, Els Atema, Raoul K. Boughton, J. L. Brown, Donald C. Dearborn, G. Divoky, et al. 2018. "The Rate of Telomere Loss Is Related to Maximum Lifespan in Birds." Philosophical Transactions of the Royal Society B: Biological Sciences 373 (1741): 20160445. https://doi.org/10.1098/rstb.2016.0445.

Vedder, Oscar, Simon Verhulst, Erica Zuidersma, and Sandra Bouwhuis. 2018. "Embryonic Growth Rate Affects Telomere Attrition: An Experiment in a Wild Bird." Journal of Experimental Biology 221: jeb181586. https://doi.org/10.1242/jeb.181586.

Wilbourn, Rachael V., Joshua P. Moatt, Hannah Froy, Craig A. Walling, Daniel H. Nussey, and Jelle J. Boonekamp. 2018. "The Relationship between Telomere Length and Mortality Risk in Non-Model Vertebrate Systems: A Meta-Analysis." Philosophical Transactions of the Royal Society B: Biological Sciences 373 (1741): 20160447. https://doi.org/10.1098/rstb.2016.0447.

Wolf, Sarah E., Tiana L. Sanders, Sol E. Beltran, and Kimberly A. Rosvall. 2021. "The Telomere Regulatory Gene POT1 Responds to Stress and Predicts Performance in Nature: Implications for Telomeres and Life History Evolution." Molecular Ecology, November. https://doi.org/10.1111/mec.16237.

Wood, Emma M., Pablo Capilla-Lasheras, Dominic L. Cram, Lindsay A. Walker, Jenny E. York, Anke Lange, Patrick B. Hamilton, Charles R. Tyler, and Andrew J. Young. 2021. "Social Dominance and Rainfall Predict Telomere Dynamics in a Cooperative Arid-zone Bird." Molecular Ecology, May. https://doi.org/10.1111/mec.15868.

Sara J. S. Wuitchik, S. J. S. Wuitchik, Stephanie Mogensen, S. Mogensen, Tegan N. Barry, T. N. Barry, Antoine Paccard, A. Paccard, Heather A. Jamniczky, H. A. Jamniczky, Rowan D. H. Barrett, R. D. H.

Barrett, & Sean M. Rogers, S. M. Rogers. (2022). Evolution of thermal physiology alters the projected range of threespine stickleback under climate change. Molecular Ecology 31: 2312-2326. doi: 10.1111/mec.16396