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Do Telomeres Influence Pace-of-Life-Strategies in Response to Environmental Conditions Over a Lifetime and Between Generations?

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The complexity of the physiological phenotype currently prevents us from identifying an integrative measure to assess how the internal state and environmental conditions modify life-history strategies. In this article, it is proposed that shorter telomeres should lead to a faster pace-of-life where investment in self-maintenance is decreased as a means of saving energy for reproduction, but at the cost of somatic durability. Inversely, longer telomeres would favor an increased investment in soma maintenance and thus a longer reproductive lifespan (i.e., slower pace-of-life). Under this hypothesis, telomere dynamics could be such an integrative mediator, which will assemble the information about oxidative stress levels, inflammation status and stress reactivity, and relate this information to the potential lifespan of the organism and its pace-of-life strategy. The signaling function of telomere dynamics can also reach over generations, a phenomenon in which the telomere lengths of gametes would provide a channel through which offspring would receive information about their environment early in their development, hence increasing the possibilities for developmental plasticity.

1. Ecological Conditions Favor Particular Life-History Strategies

The pace-of-life syndrome hypothesis suggests that a given set of ecological conditions favors a particular life-history strategy that could in turn affect a whole series of coevolved reproductive, behavioral, and physiological traits in animals.[1–3] Organisms on the slow end of the pace-of-life axis classically exhibit slower growth and development, lower breeding rate, and longer lifespans, whereas those on the fast end tend to show opposite patterns.[4] This fast-to-slow continuum relies on the idea that organisms have to allocate limited resources toward competing life-history traits (i.e., life-history trade-offs).[5,6]

The pace-of-life therefore appears to be at least partly flexible, able to respond to current environmental challenges, maximizing individual fitness under specific environmental conditions.[1,2,7,8] There is now substantial evidence regarding the existence of such modulation of pace-of-life at the individual,[9,10] population,[11,12] and species levels[13] and even within an individual lifetime, depending, for example, on factors such as age or health status (i.e., terminal investment).[14–16] For example, both predation risk and parasite pressure can lead to a faster pace-of-life,[17,18] while abundant food supply coupled with reduced predator pressure can lead to a slower pace-of-life.[19] However, we are still lacking detailed knowledge about the modulators that integrate information about the internal and external environment, leading to individually variable life-histories.[20,21]

2. Several Mediators of Pace-of-Life Have Been Proposed

A few decades ago, metabolism has been suggested as the main driver of an animal's pace-of-life (reviewed in ref. [20]), mainly because metabolism is closely linked to several crucial life-history stages (reproduction, growth, molt, etc.) and is also involved in aging processes (metabolic activities are known to create reactive oxygen species and oxidative damage that can jeopardize longevity). There is now evidence that the link between metabolism and the pace of life is, however, more complex than previously thought, especially because other central physiological systems are involved in life-history decisions and may even modulate the impact of metabolism on life-history traits (e.g., ref. [22]). More recently, other organismal systems have therefore been suggested to be possible modulators of an organism's pace of life, widening our understanding of the possible links between environment

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and drivers of pace-of-life. For example, several endocrine mechanisms (e.g., hormones like testosterone and glucocorticoids) are known to mediate the relationship between environmental conditions, internal state, and life-history decisions.[23–26] These mechanisms are thought to mediate several life-history trade-offs,[27,28] such as the balance between reproductive investment and future survival (the cost of reproduction) and they are certainly involved in the adjustment of the pace-of-life to specific environmental conditions. The pace-of-life has also been linked with other physiological and behavioral systems, such as immunity,[7,29] personality,[2] or oxidative status.[30] However, here again, the link between these systems and life-history strategies is not always straightforward and there is now a general agreement that the direction of these relationships may depend on the environmental context (e.g., ref. [31]).

Importantly, all these systems seem to be functionally interconnected; for example, stress-coping endocrine mechanisms are known to be linked with metabolism,[32] immunity,[33] oxidative stress,[34] and personality.[35] Altogether, these multiple physiological and behavioral systems interact to determine a complex physiological phenotype, which probably governs allocation processes and pace-of-life ("the physiology/life-history nexus" *sensu*[23]). Unfortunately, the complexity of this physiological phenotype currently prevents us from identifying an integrative measure to assess how the internal state and environmental conditions may modify the pace of life. To contribute to understanding this problem, we need to identify a biological marker that: 1) is affected by life-history events (e.g., the cost of reproduction) and environmental conditions (e.g., infection); 2) is functionally connected to all the behavioral and physiological systems governing life-history decisions; 3) reliably predicts remaining lifespan. Here, we propose that telomere length and telomere dynamics could be such an alternative and integrative mediator of environmental cues, leading to long-term changes in pace-of-life. Under this hypothesis, telomeres would assemble the information about oxidative stress levels, inflammation status, personality, and stress axis reactivity, and relate this information directly to the potential lifespan of the organism and its pace-of-life.

3. A New Hypothesis: The Telomere Messenger Hypothesis

Telomeres are regions of non-coding, but highly structured DNA at the end of eukaryotic chromosomes, consisting of tandem repeated highly conserved DNA sequence.[36] Telomeres shorten at each cell division, resulting in shorter telomeres in older organisms, and telomere shortening with aging in most animals[37] (it should be noted however that telomere does not shorten in every species[38]). Notably, telomere shortening is slower in longer-lived animals than in shorter-lived animals.[39] Telomeres also shorten when cells are exposed to environmental stressors (pollution, inflammation[36]). Vulnerability to environmental stressors and direct link to cellular processes related to aging make telomeres and their shortening rate a likely, yet understudied candidate for a mediator of pace-of-life. Under the telomere messenger hypothesis, telomeres would gather information about the environmental factors that cause oxidative damage, inflammation, and physiological stress responses within the organism, and relate this information directly to the potential lifespan of the organism and its pace-of-life strategy (**Figure 1**). Shorter telomeres should lead to a "thrifty phenotype" (i.e., a faster pace-of-life) where investment in self-maintenance is decreased as a means of saving energy. A lowered maintenance effort would then free up resources for growth and reproduction, but at the cost of long-term function and/or somatic durability.[40] Inversely, longer telomeres would favor an increased investment in soma maintenance and thus a longer reproductive lifespan (i.e., a slower pace-of-life).

While the role of telomeres as environmental messengers has not been suggested before, the idea that telomere length and attrition rate may be internal regulators of life-history trajectory was recently proposed by Young,[41] under the life-history regulation hypothesis. According to Young, the telomere-attrition-mediated link between current and future reproduction is probably not maintained by mechanistic constraints. Since, at the mechanistic level, telomere attrition can be effectively avoided by the action of the telomerase enzyme that can extend telomeres via the addition of terminal telomeric repeats,[42] telomere shortening is probably not a proximate cause of life-history trade-offs. Instead, it might be an adaptive strategy that allows individuals to adjust their life-history strategies. While the cancer surveillance hypothesis (telomere-shortening-induced apoptosis in cells that constitute a cancer risk[43,44]) is currently the predominant adaptive explanation for telomere attrition, life-history regulation hypothesis offers an alternative, non-exclusive explanation. According to the life-history regulation hypothesis, telomere attrition and/or the accumulation of telomeric DNA damage, and their consequence for cell fates, allow adaptive regulation of organismal-level physiology, behavior, and life history in response to age-related declines in somatic integrity.[41]

Telomere Dynamics Might Be an Integrative Mediator Linking Environmental Conditions to Pace-of-Life Strategies

Current evidence of how environmental conditions that are known to affect pace-of-life strategies are associated with changes in telomere length and attrition are limited. One of the environmental factors that determines optimal pace-of-life is predation rate.[5,6,45] Numerous studies have now shown that predation influences growth rate,[46] start of reproduction and number of offspring,[47] and fecundity[48] of prey species. The effect of predator pressure on telomere dynamics have been studied in several model systems. For example, spadefoot toad (*Pelobates cultripes*) tadpoles had shorter telomeres in the presence of predators, but metamorphosed to larger body size and had larger fat bodies, which increased their short-term survival odds, and can be described as an indicator of faster pace-of-life.[49] Similarly, perceived predation risk (degree of nest crypsis) affected telomere length in hatching common eiders (*Somateria mollissima*), in which chicks hatching from uncovered nests have shorter telomeres.[50] The telomere-messenger hypothesis provides an adaptive explanation for these results. Hence, under high predation pressures, shorter telomeres would favor a fast pace-of life strategy and an increased

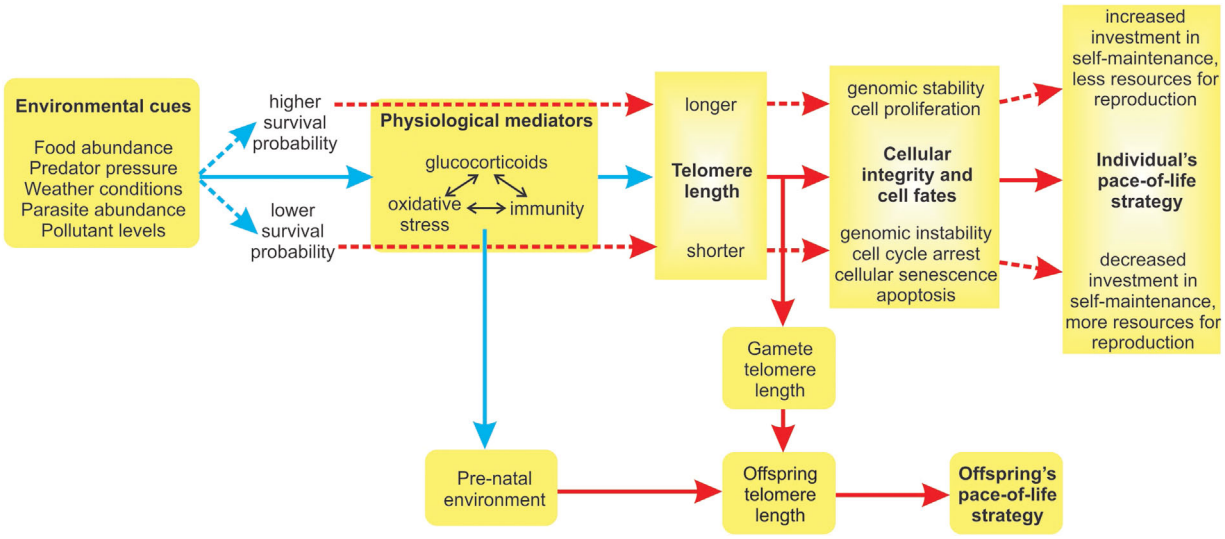

Figure 1. Conceptual model illustrating the relationships between environmental cues, telomere attrition, and pace of life strategies. Blue arrows indicate known relationships and red ones indicate relationships proposed under the telomere-messenger hypothesis.

investment in reproduction. In addition to predators, parasites are known to affect the pace-of-life of individuals. It is predicted that parasitism should always favor increased allocation to host reproduction,[51] leading to, for example, decreased size at maturation[52] or increased rate of growth and offspring production.[53] As parasite infections are known to affect telomere length,[54,55] we hypothesize that telomeres could be a link between changes in pace-of-life and population-level parasite pressure. Recent studies have also indicated a link between habitat pollution and faster telomere shortening in wild animals.[56,57] Studies in humans have suggested that this link between environmental pollution and telomere shortening might be mediated by a reduced telomerase activity.[58,59] Under the telomere-messenger hypothesis, this increased telomere attrition in polluted environments would favor a fast pace-of-life to maximize individual fitness in an environment where survival prospects are limited due to increased genomic mutation and oxidative stress levels. Supporting this idea, a recent study showed that insecticide pollution in aquatic environment reduced the life-span and increased the number of generations per year in macroinvertebrates.[60] However, the direct link between environmental pollution, telomere length, and pace-of-life remains to be studied.

Telomere attrition rates are often faster during the growth phase than later in life, and faster growth is associated with reduced lifespan (reviewed by ref. [61]). For example, a study on Atlantic salmon (*Salmo salar*) indicated that faster-growing fish had shorter telomeres and telomeres shortened faster if the growth occurred in a harsher environment.[62] While telomere loss has been suggested to be a cost of faster growth, and a physiological link between growth rate and lifespan, the causal role of telomeres in determining the lifespan of an organism is still under question (reviewed by ref. [41]). The signaling role of telomeres could provide an adaptive explanation for greater sensitivity of telomere length to environmental factors and physiological state early in life. Under the environmental matching hypothesis, early developmental conditions optimize phenotypes through developmental phenotypic plasticity, while there are often costs and constraints to changing phenotypes (including life-history strategies) later in life.[63] According to the telomere-messenger hypothesis, developmental conditions would provide cues for appropriate pace-of-life, since an environment that favors fast growth might also favor earlier maturation and faster reproduction. In this sense, faster telomere attrition rate during fast growth can be considered not a cost, but an internal switch toward faster pace-of-life. While, to our best knowledge, telomere attrition during development has never been discussed in the framework of environmental matching, the telomere-messenger hypothesis provides a link between early developmental conditions and pace-of-life of the individual.

The role of telomeres as messenger of life-history decisions might be strongly impacted by the telomere length, the rate of telomere erosion and the telomerase biology of any given species. However, in support of our hypothesis, lifespan seems generally associated with telomere length at the intraspecific level[55,64] and with telomere erosion at the inter-specific levels in species as different as birds and mammals[37] (even if some species seem to not show any telomere shortening[38]). Given that telomere length strongly differs between species, it is thus possible that the rate of telomere shortening more than the actual telomere length might be the variable influencing life-history decisions. In addition, it is also possible that the threshold telomere value – which is associated with mortality – may vary between species (depending on other physiological systems).

4. Telomere Length in Gametes Might Act as Messenger of Pace-of-Life Strategies

Under our hypothesis, the external-to-internal-environment signaling function of telomere dynamics could also reach over generations. Parental environment is predictive of the

environment likely to be faced by their offspring, and trans-generational cues would provide an effective channel through which offspring could receive adequate information very early in their development.[65,66] While non-genetic parental effects (influence of parental investment level on offspring telomere dynamics) have been considered to play a role in phenotypic plasticity as an environmental matching strategy, the telomere length of gametes could provide an even earlier information about parental environment, thereby increasing the possibilities for developmental plasticity.[67] We thus propose that, while telomere length is restored to some extent during gametogenesis and in the embryo after fertilization,[68] this level of reset depends on environmental conditions and parental phenotypes. For example, fathers' age has a strong impact on sperm telomere length, and telomere length in embryos and offspring.[69,70] In addition, a recent study in a long-lived bird, the black-browed albatross (*Thalassarche melanophrys*) showed that younger parents produced offspring with shorter telomeres,[71] which could indicate that breeding at an early age (a fast pace-of-life trait) is linked to shorter telomere length. These parental effects are proposed to be an adaptive signal of the expected age of reproduction in the environment offspring are born into.[40]

5. Is the Telomere-Messenger Hypothesis Currently Supported, and How Can It Be Further Tested?

5.1. Shorter Telomeres Seem to Favor a "spendthrift" Phenotype

Several approaches might now be used to study the telomere-messenger hypothesis and test if and how telomere length and attrition might act as mediators of pace-of-life strategies. The first step is observational and would consist in measuring if within-population variations in telomere length and attrition are related to differences in life history strategies (investment in self maintenance vs. reproduction). Ideally, these studies would use wild populations of known age individuals to account for the effect of chronological age on breeding performance or physiological performance (i.e. immune capacity[72]). To the best of our knowledge, only a handful of studies have used this approach so far to measure the potential association between parental telomere length at the time of breeding and reproductive investment. Recently, Bauer et al.[73] have shown, in a population of dark-eyed juncos (*Junco hyenalis*) where chronological age and telomere length are not significantly related, that individuals with shorter telomeres laid their first clutch earlier in the season. Given that breeding earlier in the season is generally associated with a better reproductive success[74,75] but also with costs (i.e. reduced survival prospect[76,77]), we propose that this study supports our idea that shorter telomeres should favor a "spendthrift" phenotype characterized by an increased investment in reproduction. Similarly, known-age common terns (*Sterna hirundo*) with shorter telomeres arrived and reproduced earlier in the season and had more chicks in the nest,[78] female tree swallows (*Tachycineta bicolor*) with longer telomeres fledged a smaller proportion of chicks[79] and both males and females with longer telomeres had lighter nestlings.[80] However, Le Vaillant et al.[81] found that king penguins (*Aptenodytes patagonicus*) with longer telomeres arrived earlier in the colony to breed and tended to have higher breeding success. In addition, telomere length was not a significant predictor of the investment in sexual signal coloration in male common yellowthroats (*Geothlypis trichas*)[82] and in male Australian painted dragons (*Ctenophorus pictus*).[83] However, in both of these cases, telomere length was measured several months after the start of the breeding season[83] or after the molt period[82] and a better examination of the telomere-messenger hypothesis would consist in measuring how telomere length measured before the development of sexual signals predicts investment in coloration.

When looking at the association between telomere length and self-maintenance, we found three studies supporting our hypothesis showing that individuals with longer telomeres developed stronger antioxidant defenses. Wild-derived house mice (*Mus musculus*) with longer telomeres had higher superoxide dismutase-activity and more glutathione than mice with shorter telomeres,[84] barn swallows (*Hirundo rustica*) with longer telomeres had a better antioxidant capacity (TAC, Total Antioxidant Capacity)[85] and breeding female pied flycatcher (*Ficedula hypoleuca*) had better antioxidant defenses (TAS, Total Antioxidant Status).[86] A fourth study where these two traits have been measured during development in great tits (*Parus major*) however found no significant relationships between antioxidants defenses and telomere length.[87]

At the moment, most of the studies looking for relationships between disease exposure and telomere dynamics have compared telomere length and attrition in sick vs healthy individuals[55,88] and, to the best of our knowledge, only one study has assessed how telomere length predicts investment in the immune response and the ability to cope with disease. Wild-derived house mice (*Mus musculus musculus*) experimentally infected with Salmonella enterica strains that cleared the infection by the termination of the experiment had significantly longer telomeres at the beginning of the experiment than those that were still infected. In addition, individuals with relatively long telomeres at the beginning of the experiment had lower bacterial loads at termination,[54] suggesting that higher proliferation capacity of leukocytes increases the efficiency of fighting infection.[89] All together, these results from observational studies seem to support the idea that long telomeres favor a thrifty strategy with a reduced investment in reproduction but an increased allocation of resources toward self-maintenance processes.

5.2. We Now Need Experimental Studies to Test the Telomere Messenger Hypothesis

Given the cross-sectional nature of the studies discussed above and the potential for a third variable (i.e. oxidative stress) to influence both telomere length and pace-of-life strategies without any direct and causal relationships between these two, it is also essential to use an experimental approach to test our hypothesis. To this end, a variety of molecules available to manipulate telomere length through an activation of the telomerase activity (see ref. [90] for an exhaustive list of these molecules) might represent exciting tools to explore the potential

role of telomeres length as mediators of life-history strategies. For example, TA-65 (a chemical compound extracted from the dried root of *Astragalus Membranaceus* that activates telomerase) has been successfully used in mice and zebra finches (*Taeniopygia guttata*) to experimentally increase the average telomere length in adults[91,92] and reduce telomere attrition in developing chicks of house sparrows (*Passer domesticus*) (BJ Heidinger 2017, unpublished data). In all these studies, the TA-65 was orally administered daily and an important step to use this compound in field studies would be the development and validation of slow release implants as is often done in physiological ecology.[90] In addition, future studies should validate the generality of the TA-65 action given that the positive effect of this compound on telomere length has only been measured in blood so far and that blood telomere length does not seem to be correlated with telomere length in other tissues.[93] Nonetheless, experiments where pace-of-life strategies (i.e. breeding investment, self-maintenance [antioxidant defenses, immune capacity]) are measured in response to an experimental manipulation of telomere length in adults and/or during development would represent the ultimate test of our hypothesis. In addition, manipulations of gamete telomere length in artificial insemination experiments would allow us to test if the potential signaling function of telomere dynamics could also reach over generations. We predict that offspring from gametes with longer telomeres would show a reduced/delayed investment in reproduction but better antioxidant defenses and responses against pathogens.

6. Conclusion

While it is known that environmental cues can lead to changes in pace-of-life strategies within species and even populations, the knowledge about the modulators that integrate information about the environment and lead to individually variable life-histories is still lacking. We propose that telomere length and/or attrition could be such an integrative mediator, combining the information not only of internal physiological processes, but also of environmental cues, leading to long-term changes in life-history strategies. Our telomere-messenger hypothesis provides an adaptive explanation to the shortening of telomeres under harsh environmental conditions (i.e. high predation pressure, high parasite prevalence, polluted environment), leading to a switch toward a faster pace-of-life, with reduced investment in self-maintenance and increased investment in current reproduction. In this context, it is noteworthy that telomeres seem to be especially sensitive to environmental conditions during the development, which is also the life-stage with the greatest phenotypic plasticity in terms of life-history strategies. While several correlative studies seem to support our hypothesis, experimental evidence testing this hypothesis still needs to be gathered. We suggest that studies manipulating telomere length at the early developmental stages and following up with a study of longitudinal effects on life-history traits, but also studies reaching over generations, could be a promising way to test this hypothesis. In addition, studies manipulating environmental conditions simultaneously with telomere length could provide valuable information about the adaptive role of telomeres as mediators of life-history strategies. While the intriguing idea that telomere attrition could be an adaptive strategy as opposed to a cost of cellular activity is still relatively new and untested, we suggest that as a trait vulnerable to environmental conditions and linked to the lifespan of the organisms, telomere attrition should not be overlooked as a possible mediator of pace-of-life.

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Conflict of Interest

The authors declare no conflict of interest.

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[1] L. B. Martin, D. Hasselquist, M. Wikelski, *Oecologia* **2006**, *147*, 565.
[2] D. Reale, D. Garant, M. M. Humphries, P. Bergeron, V. Careau, P. O. Montiglio, *Phil. Trans. R. Soc. B* **2010**, *365*, 4051.
[3] M. Wikelski, L. Spinney, W. Schelsky, A. Scheuerlein, E. Gwinner, *Proc. Royal Soc. London. Series B: Biol. Sci*. **2003**, *270*, 2383.
[4] W. D. Robinson, M. Hau, K. C. Klasing, M. Wikelski, J. D. Brawn, S. H. Austin, C. Tarwater, R. E. Ricklefs, *Auk* **2010**, *127*, 253.
[5] S. C. Stearns, Oxford University Press, Oxford **1992**.
[6] D. Roff, Chapman & Hall, New York **1992**, p. 548.
[7] L. B. Martin, Z. M. Weil, R. J. Nelson, *Ecology* **2007**, *88*, 2516.
[8] P. T. Niemelä, A. Vainikka, J. T. Forsman, O. J. Loukola, R. Kortet, *Ecol. Evol*. **2013**, *3*, 457.
[9] K. Hooper, F. Spagopoulou, Z. Wylde, A. A. Maklakov, R. Bonduriansky, *Evolution* **2017**, *71*, 671.
[10] M. Barbosa, A. E. Deacon, M. J. Janeiro, I. Ramnarine, M. B. Morrissey, A. E. Magurran, *Proc. R. Soc. B* **2018**, *285*, 20171499.
[11] Charmantier, V. Demeyrier, M. Lambrechts, S. Perret, A. Grégoire, *Front. Ecolo. Evol*. **2017**, *5*, 53.
[12] T. Sepp, K. J. McGraw, A. Kaasik, M. Giraudeau, *Global Change Biol*. **2018**, *24*, 1452.
[13] P. Wiersma, A. Munoz-Garcia, A. Walker, J. B. Williams, *Proc. Nat. Acad. Sci*. **2007**, *104*, 9340.
[14] T. H. Clutton-Brock, *Am. Naturalist* **1984**, *123*, 212.
[15] Bonneaud, J. Mazuc, O. Chastel, H. Westerdahl, G. Sorci, *Evolution* **2004**, *58*, 2823.
[16] A. Velando, H. Drummond, R. Torres, *Proc. Royal Soc. London B: Biol. Sci*. **2006**, *273*, 1443.
[17] J. F. Stephenson, C. van Oosterhout, J. Cable, *Biol. Lett*. **2015**, *11*, 20150806.
[18] J. A. LaManna, T. E. Martin, *Ecol. Lett*. **2016**, *19*, 403.
[19] R. E. Ricklefs, C. D. Cadena, *Ecol. Lett*. **2007**, *10*, 867.
[20] J. B. Williams, R. A. Miller, J. M. Harper, P. Wiersma, *Integrat. Comparative Biol*. **2010**, *50*, 855.
[21] P. O. Montiglio, M. Dammhahn, G. D. Messier, D. Réale, *Behav. Ecol. Sociobiol*. **2018**, *72*, 116.
[22] J. R. Speakman, D. A. Talbot, C. Selman, S. Snart, J. S. McLaren, P. Redman, E. Krol, D. M. Jackson, M. S. Johnson, M. D. Brand, *Aging Cell* **2004**, *3*, 87.

[23] R. E. Ricklefs, M. Wikelski, *Trends Ecol. Evol*. **2002**, *17*, 462.
[24] J. C. Wingfield, R. M. Sapolsky, *J. Neuroendocrinol*. **2003**, *15*, 711.
[25] V. Bokony, A. Z. Lendvai, A. Liker, F. Angelier, J. C. Wingfield, O. Chastel, *Am. Naturalist* **2009**, *173*, 589.
[26] M. Hau, R. E. Ricklefs, M. Wikelski, K. A. Lee, J. D. Brawn, *Proc. Royal Soc. Lond. B: Biol. Sci*. **2010**, *277*, 3203.
[27] F. Angelier, J. C. Wingfield, *General Comparative Endocrinol*. **2013**, *190*, 118.
[28] C. Taff, M. N. Vitousek, *Trends Ecol. Evol*. **2016**, *31*, 476.
[29] B. I. Tieleman, *Behav. Ecol. Sociobiol*. **2018**, *72*, 55.
[30] C. Selman, J. D. Blount, D. H. Nussey, J. R. Speakman, *Trends Ecol. Evol*. **2012**, *27*, 570.
[31] L. A. Schoenle, C. Zimmer, M. N. Vitousek, *Integrative Comparative Biol*. **2018**, *58*, 777.
[32] M. M. Landys, M. Ramenofsky, J. C. Wingfield, *General Comparative Endocrinol*. **2006**, *148*, 132.
[33] L. B. Martin, *General Comparative Endocrinol*. **2009**, *163*, 70.
[34] Costantini, V. Marasco, A. P. Møller, *J. Comparative Physiol. B* **2011**, *181*, 447.
[35] M. Hau, W. Goymann, *Front. Zoo*. **2015**, *12*, S7.
[36] M. F. Haussmann, N. M. Marchetto, *Curr. Zoology* **2010**, *56*, 714.
[37] M. F Haussmann, D. W Winkler, K. M O'Reilly, C. E Huntington, I. C. T Nisbet, C. M Vleck, *Proc. Royal Soc. Lond. B: Biol. Sci*. **2003**, *270*, 1387.
[38] Kipling, H. J. Cooke. *Nature* **1990**, *347*, 400.
[39] Dantzer, Q. E. Fletcher, *Exp. Gerontol*. **2015**, *71*, 38.
[40] D. T. Eisenberg, *Am. J. Hum. Biol*. **2011**, *23*, 149.
[41] J. Young, *Phil. Trans. R. Soc. B* **2018**, *373*, 20160452.
[42] Y. S. Cong, W. E. Wright, J. W. Shay, *Microbiol. Mol. Biol. Rev*. **2002**, *66*, 407.
[43] de Lange, T. Jacks, *Cell* **1999**, *98*, 273.
[44] J. W. Shay, *Cancer Discov*. **2016**, *6*, 584.
[45] D. N. Reznick, H. Bryga, J. A. Endler, *Nature* **1990**, *346*, 357.
[46] O. Bjærke, T. Andersen, J. Titelman, *Marine Ecol. Prog. Series* **2014**, *510*, 15.
[47] H. Stibor, *Oecologia* **1992**, *92*, 162.
[48] M. Jennions, S. Telford, *Oecologia* **2002**, *132*, 44.
[49] P. Burraco, C. Díaz-Paniagua, I. Gomez-Mestre, *Scientific Rep*. **2017**, *7*, 7494.
[50] K. Noreikiene, M. Öst, M. W. Seltmann, W. Boner, P. Monaghan, K. Jaatinen, *Canadian J. Zool*. **2017**, *95*, 695.
[51] S. Gandon, P. Agnew, Y. Michalakis, *Am. Naturalist* **2002**, *160*, 374.
[52] J. Ohlberger, Ø. Langangen, E. Edeline, E. M. Olsen, I. J. Winfield, J. M. Fletcher, J. B. James, N. C. Stenseth, L. A. Vøllestad, *Proc. R. Soc. B* **2011**, *278*, 35.
[53] J. A. Thornhill, J. T. Jones, J. R. Kusel, *J. R. Parasitol*. **1996**, *93*, 443.
[54] P. Ilmonen, A. Kotrschal, D. J. Penn, *PLoS ONE* **2008**, *3*, e2143.
[55] M. Asghar, D. Hasselquist, B. Hansson, P. Zehtindjiev, H. Westerdahl, S. Bensch, *Science* **2015**, *347*, 436.
[56] P. Blévin, F. Angelier, S. Tartu, S Ruault, P Bustamante, D. Herzke, B Moe, C Bech, G. W. Gabrielsen, J. O. Bustnes, O. Chastel, *Sci. Total Env*. **2016**, *563*, 125.
[57] P. Salmón, J. F. Nilsson, A. Nord, S. Bensch, C. Isaksson, *Biol. Lett*. **2016**, *12*, 20160155.
[58] L. Dioni, M. Hoxha, F. Nordio, M. Bonzini, L Tarantini, B Albetti, A Savarese, J Schwartz, P. A. Bertazzi, P. Apostoli, L. Hou, L. Hou, *Env. Health Perspect*. **2011**, *119*, 622.
[59] P. K. Senthilkumar, A. J. Klingelhutz, J. A. Jacobus, H. Lehmler, L. W. Robertson, G. Ludewig, *Toxicol. Lett*. **2011**, *204*, 64.
[60] C. P. Mondy, I. Muñoz, S. Dolédec, *Sci. Total Env*. **2016**, *572*, 196.
[61] P. Monaghan, S. E. Ozanne, *Phil. Trans. R. Soc. B* **2018**, *373*, 20160446.
[62] D. McLennan, J. D. Armstrong, D. C. Stewart, S. Mckelvey, W. Boner, P. Monaghan, N. B. Metcalfe, *Mol. Ecol*. **2016**, *25*, 5425.
[63] E. T. Krause, O. Krüger, H. Schielzeth, *Anim. Behav*. **2017**, *128*, 103.
[64] B. J. Heidinger, J. D. Blount, W. Boner, K. Griffiths, N. B. Metcalfe, P. Monaghan, *Proc. Nat. Acad. Sci*. **2012**, *109*, 1743.
[65] P. Monaghan, *Philos. Trans. R. Soc. B* **2008**, *363*, 1635.
[66] L. Engqvist, K. Reinhold, *Methods Ecol. Evol*. **2016**, *7*, 1482.
[67] D. T. Eisenberg, C. W. Kuzawa, *Phil. Trans. R. Soc. B* **2018**, *373*, 20160442.
[68] S. Turner, G. M. Hartshorne, *MHR: Basic Sci. Reproductive Med*. **2013**, *19*, 510.
[69] M. Kimura, L. F. Cherkas, B. S. Kato, S. Demissie, J. B. Hjelmborg, M. Brimacombe, A. Cupples, J. L. Hunkin, J. P. Gardner, X. B. Lu, X. J. Cao, M. Sastrasinh, M. A. Province, S. C. Hunt, K. Christensen, D. Levy, T. D. Spector, A. Aviv, *PLoS Genet*. **2008**, *4*, e37.
[70] J. C. Noguera, N. B. Metcalfe, P. Monaghan, *Proc. Biol. Sci*. **2018**, *285*, 1874.
[71] S. M. Dupont, C. Barbraud, O. Chastel, K. Delord, S. Ruault, H. Weimerskirch, F. Angelier, *PLoS ONE* **2018**, *13*, e0193526.
[72] M. G. Palacios, D. W. Winkler, K. C. Klasing, D. Hasselquist, C. M. Vleck, *Ecology* **2011**, *92*, 952.
[73] C. M. Bauer, J. L. Graham, M. Abolins-Abols, B. J. Heidinger, E. D. Ketterson, T. J. Greives, *Am. Natural*. **2018**, *191*, 777.
[74] T. Price, M. Kirkpatrick, S. J. Arnold. *Science* **1988**, *240*, 798.
[75] T. D. Williams, Princeton University Press, Princeton, NJ **2012**.
[76] C. R. Brown, M. B. Brown, *Condor* **1999**, *101*, 230.
[77] B. C. Sheldon, L. E. B. Kruuk, J. Merila, *Evolution* **2003**, *57*, 406.
[78] C. Bauch, P. H. Becker, S. Verhulst, *Proc. R. Soc. B* **2013**, *280*, 20122540.
[79] Belmaker, The role of telomere length in Tree Swallow behavior and life history. **2016**, PhD thesis, Cornell University.
[80] J. Q. Ouyang, A. Z. Lendvai, I. T. Moore, F. Bonier, M. F. Haussmann, *Integrative Comparative Biol*. **2016**, *56*, 138.
[81] M. Le Vaillant, V. A. Viblanc, C. Saraux, C. Le Bohec, Y. Le Maho, A. Kato, F. Criscuolo, Y. Ropert-Coudert, *Polar Biol*. **2015**, *38*, 2059.
[82] C. Taff, C. R. Freeman-Gallant, *Ecol. Evol*. **2017**, *7*, 3436.
[83] M. Giraudeau, C. R. Friesen, J. Sudyka, N. Rollings, C. M. Whittington, M. R. Wilson, M. Olsson, *Biol. Lett*. **2016**, *12*, 20160077.
[84] J. Stauffer, B. Panda, P. Ilmonen, *P. Mechanisms Ageing Dev*. **2018**, *169*, 45.
[85] L. Khoriauli, A. Romano, M. Caprioli, M. Santagostino, S. G. Nergadze, A. Costanzo, D. Rubolini, E. Giulotto, N. Saino, M. Parolini, *Behav. Ecol. Sociobiol*. **2017**, *71*, 124.
[86] J. López-Arrabé, P. Monaghan, A. Cantarero, W. Boner, L. Pérez-Rodríguez, J. Moreno, *Physiol. Biochem. Zoology* **2018**, *91*, 868.
[87] J. Stauffer, B. Panda, T. Eeva, M. Rainio, P. Ilmonen, *Sci. Total Env*. **2017**, *575*, 841.
[88] M. Sebastiano, M. Eens, F. Angelier, K. Pineau, O. Chastel, D. Costantini, *Conserv. Physiol*. **2017**, *5*, 1.
[89] N. P. Weng, B. L. Levine, C. H. June, R. J. Hodes, *Proc. Nat. Acad. Sci*. **1995**, *92*, 11091.
[90] F. Criscuolo, S. Smith, S. Zahn, B. J. Heidinger, M. F. Haussmann, *Phil. Trans. R. Soc. B* **2018**, *373*, 20160440.
[91] B de Jesus, K. Schneeberger, E. Vera, A. Tejera, C. B. Harley, M. A. Blasco, *Aging Cell* **2011**, *10*, 604.
[92] S. Reichert, P. Bize, M. Arrive, S. Zahn, S. Massemin, F. Criscuolo, *Exp. Gerontol*. **2014**, *52*, 36.
[93] M. Asghar, V. Palinauskas, N. Zaghdoudi-Allan, G. Valkiūnas, A. Mukhin, E. Platonova, A. Farnet, S. Bensch, D. Hasselquist, *Proc. R. Soc. B* **2016**, *283*, 20161184.