

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

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1	Do telomeres influence pace-of-life-strategies in response to environmental conditions over
2	a lifetime and between generations?
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ABSTRACT

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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 lifehistory strategies. We propose 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 our hypothesis, telomere dynamics could be such an integrative mediator, which would 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 could also reach over generations, a phenomenon in which the telomere lengths of gametes would provide a channel through which offspring would receive about information their environment early development, in their 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 (Martin *et al.*, 2006; Réale *et al.*, 2010; Wikelski *et al.*, 2003). 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 (Robinson *et al.*, 2010). This fast-to-slow continuum relies on the idea that organisms have to allocate limited resources towards competing life-history traits (i.e., life-history trade-offs, Stearns, 1992; Roff, 1992).

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 (Martin *et al.*, 2007; Martin *et al.*, 2006; Niemelä *et al.*, 2013; Réale *et al.*, 2010). There is now substantial evidence regarding the existence of such modulation of pace-of-life at the individual (Hooper *et al.*, 2017; Barbosa *et al.*, 2018), population (Charmantier *et al.*, 2017, Sepp *et al.*, 2017) and species levels (Wiersma *et al.* 2007) and even within an individual lifetime, depending, for example, on factors such as age or health status (i.e. terminal investment, Clutton-Brock, 1984, Bonneaud *et al.* 2004; Velando *et al.* 2006). For example, both predation risk and parasite pressure can lead to a faster pace-of-life (Stephenson *et al.*, 2015; LaManna & Martin, 2016), while abundant food supply coupled with reduced predator pressure can lead to a slower pace-of-life (Ricklefs & Cadena, 2007). 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 (Williams *et al.* 2010; Montiglio *et al.*, 2018).

2 Several mediators of pace-of-life have been proposed

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A few decades ago, metabolism has been suggested as the main driver of an animal's pace-of-life (reviewed in Williams et al., 2010), mainly because metabolism is closely linked to several crucial life-history stages (reproduction, growth, molt, etc.) and is also involved in ageing 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. Speakman et al., 2004). 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 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 (Ricklefs & Wikleski 2002; Wingfield & Sapolsky, 2003, Bokony et al., 2009; Hau et al., 2010). These mechanisms are thought to mediate several life-history trade-offs (Angelier & Wingfield 2013; Taff & Vitousek 2016), 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 behavioural systems, such as immunity (Martin et al. 2007; Tieleman 2018), personality (Reale et al. 2010), or oxidative status (Selman et al., 2012). 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. Schoenle *et al.*, 2018).

Importantly, all these systems seem to be functionally interconnected; for example, stress-coping endocrine mechanisms are known to be linked with metabolism (Landys et al., 2006), immunity (Martin 2009), oxidative stress (Costantini et al., 2011), and personality (Hau & Goymann 2015). Altogether, these multiple physiological and behavioural systems interact to determine a complex physiological phenotype, which probably governs allocation processes and pace-of-life ('the physiology/life-history nexus' sensu Ricklefs & Wikelski 2002). 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 behavioural 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.

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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 (Haussmann & Marchetto 2010). Telomeres shorten at each cell division, resulting in shorter telomeres in older organisms, and telomere shortening with aging in most animals (Haussmann *et al.* 2003, it

should be noted however that telomere does not shorten in every species, Kipling and Cooke 1990). Notably, telomere shortening is slower in longer-lived animals than in shorter-lived animals (Dantzer & Fletcher, 2015). Telomeres also shorten when cells are exposed to environmental stressors (pollution, inflammation, Haussmann & Marchetto 2010). 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 (Eisenberg 2011). 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 (2018), under the life-history regulation hypothesis. According to Young (2018), 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 (Cong et al., 2002), telomere shortening

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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, de Lange and Jacks, 1999, Shay 2016) 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, behaviour and life history in response to age-related declines in somatic integrity (Young 2018).

4 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 (Reznick *et al.*, 1990, Roff, 1992, Stearns, 1992). Numerous studies have now shown that predation influences growth rate (Bjaerke *et al.* 2014), start of reproduction and number of offspring (Stibor, 1992), and fecundity (Jennions and Telford, 2002) 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 (Burraco *et al.* 2017). 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 (Noreikiene et al., 2017). 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 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 (Gandon et al., 2002), leading to, for example, decreased size at maturation (Ohlberg et al., 2011) or increased rate of growth and offspring production (Thornhill et al., 1996). As parasite infections are known to affect telomere length (i.e. Ilmonen et al., 2008, Asghar et al., 2015), 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 (i.e. Blevin et al., 2016, Salmon et al., 2016). Studies in humans have suggested that this link between environmental pollution and telomere shortening might be mediated by a reduced telomerase activity (Dioni et al., 2011, Senthilkumar et al., 2011). 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 (Mondy et al., 2016). However, the direct link between environmental pollution, telomere length, and pace-oflife 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 Monaghan & Ozanne, 2018). For

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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 (McLennan et al., 2016). 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 Young et al., 2018). 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 (Krause et al., 2017). 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 towards 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 (Heidinger et al. 2012, Asghar et al. 2015) and with telomere erosion at the inter-specific levels in species as different as birds and mammals (Haussman et al. 2003, even if some species seem to not show any telomere shortening (Kipling and Cooke 1990)). Given that telomere length strongly differs between species, it is thus possible that the rate of

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telomere shortening more than the actual telomere length might be the variable influencing lifehistory 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).

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5 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 (Monaghan 2008, Engquist & Reinhold, 2016). 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 (Eisenberg et al. 2018). We thus propose that, while telomere length is restored to some extent during gametogenesis and in the embryo after fertilization (Turner and Hartshorne 2013), 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 (Kimura et al. 2008, Noguera et al. 2018). 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 (Dupont et al., 2018), which could indicate that breeding at an early age (a fast paceof-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 (Eisenberg et al. 2011).

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6 Is the telomere-messenger hypothesis currently supported, and how can it be further tested?

6.1 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, Palacios et al. 2011). 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. (2018) 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 (Price et al. 1988, Williams 2012) but also with costs (i.e. reduced survival prospect, Brown and Brown 1999, Sheldon et al. 2003), 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 (Bauch et al. 2013), female tree swallows (*Tachycineta bicolor*) with longer telomeres fledged a smaller proportion of chicks (Belmaker 2016) and both males and females with longer telomeres had lighter nestlings (Ouyang et al. 2016). However, Le Vaillant et al. (2015) 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*, Taff and Freeman-Gallant 2017) and in male Australian painted dragons (*Ctenophorus pictus*, Giraudeau et al. 2016). However, in both of these cases, telomere length was measured several months after the start of the breeding season (Giraudeau et al. 2016) or after the molt period (Taff and Freeman-Gallant 2017) 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 (Stauffer *et al.* 2018), barn swallows (*Hirundo rustica*) with longer telomeres had a better antioxidant capacity (TAC, Total Antioxidant Capacity, Khoriauli *et al.* 2017) and breeding female pied flycatcher (*Ficedula hypoleuca*) had better antioxidant defenses (TAS, Total Antioxidant Status, Lopez-Arrabe *et al.* 2018). 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 (Stauffer et al. 2017).

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 (Asghar *et al.* 2015, Sebastiano *et al.* 2017) 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 (Ilmonen *et al.* 2008), suggesting that higher proliferation capacity of leukocytes increases the efficiency of fighting infection (Weng *et al.* 1995). 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.

6.2 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 Criscuolo *et al.* 2018 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 (Bernardes de Jesus et al. 2011, Reichert et al. 2014) 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 (Criscuolo et al. 2018). 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 (Asghar et al. 2016). Nonetheless, experiments where pace-oflife 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.

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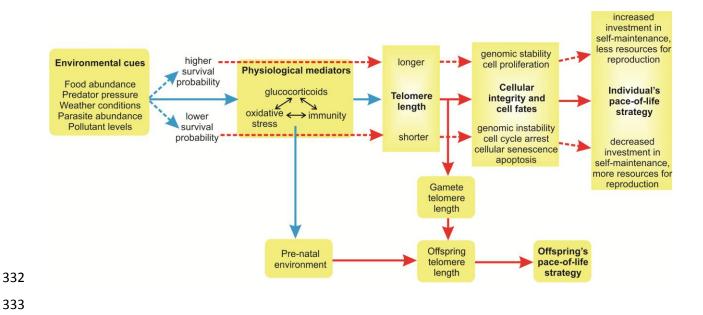
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Figure 1: Conceptual model illustrating the relationships between environmental cues, telomere attrition and pace of life strategies. Blue arrows indicate known relationships and red ones indicate relationships proposed under the telomere-messenger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



336 **8 References**

1. L. B. Martin, D. Hasselquist, M. Wikelski, *Oecologia*, **2006**, *147*, 565.

338

D. Reale, D., Garant, M. M. Humphries, P. Bergeron, V. Careau, P. O. Montiglio, *Phil. Trans. R. Soc. B* **2010**, *365*, 4051.

341

M. Wikelski, L. Spinney, W. Schelsky, A. Scheuerlein, E. Gwinner, *Proceedings of the Royal Society of London. Series B: Biological Sciences*, 2003, 270, 2383.

344

W. D. Robinson, M. Hau, K. C. Klasing, M. Wikelski, J. D. Brawn, S. H. Austin, C.
 Tarwater, R. E. Ricklefs, *The Auk*, **2010**, *127*, 253.

347

5. S. C. Stearns, **1992**, Oxford: Oxford University Press.

349

6. D. Roff, **1992**, New York: Chapman & Hall. 548 p.

351

352 7. L. B. Martin, Z. M. Weil, R. J. Nelson, *Ecology* **2007**, 88, 2516.

353

8. P. T. Niemelä, A. Vainikka, J. T. Forsman, O. J. Loukola, R. Kortet. *Ecology and Evolution* **2013**, *3*, 457.

356

K. Hooper, F. Spagopoulou, Z. Wylde, A. A. Maklakov, R. Bonduriansky,
 Evolution, 2017, 71, 671.

359

10. M. Barbosa, A. E. Deacon, M. J. Janeiro, I. Ramnarine, M. B. Morrissey, A. E.
 Magurran, *Proc. R. Soc. B*, **2018**, 285, 20171499.

362

11. Charmantier, V. Demeyrier, M. Lambrechts, S. Perret, A. Grégoire, Frontiers in Ecology
 and Evolution, 2017, 5, 53.

365

12. T. Sepp, K. J. McGraw, A. Kaasik, M. Giraudeau, *Global change biology*, **2018**, *24*,
 1452.

368

13. P. Wiersma, A. Munoz-Garcia, A. Walker, J. B. Williams, *Proceedings of the National Academy of Sciences*, 2007, 104, 9340.

371

372 14. T. H. Clutton-Brock, *The American Naturalist*, **1984**, *123*, 212.

373

15. Bonneaud, J. Mazuc, O. Chastel, H. Westerdahl, G. Sorci, *Evolution*, **2004**, *58*, 2823.

375

16. A. Velando, H. Drummond, R. Torres, *Proceedings of the Royal Society of London B: Biological Sciences*, **2006**, 273, 1443.

378

17. J. F. Stephenson, C. van Oosterhout, J. Cable, *Biology Letters*, **2015**, *11*, 20150806.

381 18. J. A. LaManna, T. E. Martin, *Ecology Letters*, **2016**, *19*, 403.

382

383 19. R. E. Ricklefs, C. D. Cadena, *Ecology Letters*, **2007**, *10*, 867.

384

- 385 20. J. B. Williams, R. A. Miller, J. M. Harper, P. Wiersma, *Integrative and comparative biology* 2010, *50*, 855.
- 21. P. O. Montiglio, M. Dammhahn, G. D. Messier, D. Réale, *Behavioral Ecology and Sociobiology*, **2018**, *72*, 116.

389

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.

392

23. R. E. Ricklefs, M. Wikelski, Trends in Ecology & Evolution 2002, 17, 462.

393 394

395 24. J. C. Wingfield, R. M. Sapolsky, *Journal of neuroendocrinology* **2003,** *15*, 711.

396

397 25. V. Bokony, A. Z. Lendvai, A. Liker, F. Angelier, J. C. Wingfield, O. Chastel, *The American Naturalist*, **2009**, *173*, 589-598.

399

400 26. M. Hau, R. E. Ricklefs, M. Wikelski, K. A. Lee, J. D. Brawn, *Proceedings of the Royal Society of London B: Biological Sciences*, **2010**, 277, 3203.

402 403

27. F. Angelier, J. C. Wingfield, General and Comparative Endocrinology 2013, 190, 118.

404

405 28. C. Taff, M. N. Vitousek, *Trends in ecology & evolution*, **2016**, *31*, 476.

406 407

407 29. B. I. Tieleman, *Behavioral ecology and sociobiology*, **2018**, 72, 55.

408

409 30. C. Selman, J. D. Blount, D. H. Nussey, J. R. Speakman, *Trends in ecology & evolution* **2012**, 27, 570.

411

31. L. A. Schoenle, C. Zimmer, M. N. Vitousek, *Integrative and comparative biology* **2018**,

413

414 32. M. M. Landys, M. Ramenofsky, J. C. Wingfield, *General and comparative endocrinology*, **2006**, *148*, 132.

416

33. L. B. Martin, General and comparative endocrinology, **2009**, 163, 70.

418

34. Costantini, V. Marasco, A. P. Møller, *Journal of Comparative Physiology B* **2011**, *181*,
447.

421

35. M. Hau, W. Goymann, Frontiers in zoology 2015, 12, S7.

422 423

36. M. F. Haussmann, N. M. Marchetto, *Current 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, *Proceedings of the Royal Society of London B: Biological Sciences*, 2003,
 270, 1387.

429

430 38. Kipling, H. J. Cooke. *Nature* **1990**, 347, 400 – 402.

431

39. Dantzer, Q. E. Fletcher, *Experimental Gerontology*, **2015**, *71*, 38-47.

433

434 40. D. T. Eisenberg, American Journal of Human Biology **2011**, 23, 149.

435

436 41. J. Young, *Phil. Trans. R. Soc. B* **2018**, *373*, 20160452

437

42. Y. S. Cong, W. E. Wright, J. W. Shay, Microbiol. *Mol. Biol. Rev.* **2002**, *66*, 407.

439

440 43. de Lange, T. Jacks, Cell, **1999**, 98, 273.

441

44. J. W. Shay, Cancer Discov. 2016, 6, 584

443

444 45. D. N. Reznick, H. Bryga, J. A. Endler, *Nature* **1990**, *346*, 357.

445

46. O. Bjærke, T. Andersen, J. Titelman, Marine Ecology Progress Series 2014, 510, 15-24.

447

448 47. H. Stibor, *Oecologia* **1992**, 92, 162.

449

48. M. Jennions, S. Telford, *Oecologia* **2002**, 132, 44.

451

49. P. Burraco, C. Díaz-Paniagua, I. Gomez-Mestre, *Scientific reports*, **2017**, *7*, 7494.

453

50. K. Noreikiene, M. Öst, M. W. Seltmann, W. Boner, P. Monaghan, K. Jaatinen, *Canadian Journal of Zoology* **2017**, 95, 695.

456

51. S. Gandon, P. Agnew, Y. Michalakis, The American Naturalist **2002**, 160, 374.

458

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.

461

53. J. A. Thornhill, J. T. Jones, J. R. Kusel, J.R. *Parasitology* **1996,** *93*, 443.

463

54. P. Ilmonen, A. Kotrschal, D. J. Penn, *PloS one*, **2008**, 3, e2143.

464 465

55. M. Asghar, D. Hasselquist, B. Hansson, P. Zehtindjiev, H. Westerdahl, S. Bensch, *Science*, **2015**, *347*, 436.

468

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, *The Science of the total environment* 2016.
 563, 125.

- 472
- 57. P. Salmón, J. F. Nilsson, A. Nord, S. Bensch, C. Isaksson, *Biology Letters* **2016**, *12*, 20160155.
- 475
- 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, Environmental health perspectives, **2011**, 119, 622.
- 479
- 59. P. K. Senthilkumar, A. J. Klingelhutz, J. A. Jacobus, H. Lehmler, L. W. Robertson, G. Ludewig, *Toxicology letters* **2011**, *204*, 64.

482

483 60. C. P. Mondy, I. Muñoz, S. Dolédec. Science of The Total Environment 2016, 572, 196.

484

485 61. P. Monaghan, S. E. Ozanne. *Phil. Trans. R. Soc. B* **2018**, *373*, 20160446.

486

62. D. McLennan, J.D. Armstrong, D. C. Stewart, S. Mckelvey, W. Boner, P. Monaghan, N.
 B. Metcalfe, *Mol. Ecol.* **2016**, *25*, 5425.

489

63. E. T. Krause, O. Krüger, H. Schielzeth, Animal Behaviour 2017, 128, 103.

490 491

- 64. B. J. Heidinger, J. D. Blount, W. Boner, K. Griffiths, N. B. Metcalfe, P. Monaghan.
 Proceedings of the National Academy of Sciences, 2012, 109, 1743-1748.
 - 65. P. Monaghan, *Philos. Trans. R. Soc. B*, **2008**, *363*, 1635.

494 495

496 66. L. Engqvist, K. Reinhold, *Methods in Ecology and Evolution* **2016,** 7, 1482.

497

498 67. D. T. Eisenberg, C. W. Kuzawa, *Phil. Trans. R. Soc. B*, **2018**, *373*, 20160442.

499

500 68. S. Turner, G. M. Hartshorne. *MHR: Basic science of reproductive medicine*, **2013**, *19*, 510-518.

501 502

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 Genetics* 2008, 4.

506

507 70. J. C. Noguera, N. B. Metcalfe, P. Monaghan, *Proc Biol Sci.* **2018**, 285, 1874.

508

71. S. M. Dupont, C. Barbraud, O. Chastel, K. Delord, S. Ruault, H. Weimerskirch, F.
 Angelier, *PLoS ONE*, **2018**, *13*, e0193526.

511

72. M. G. Palacios, D. W. Winkler, K. C. Klasing, D. Hasselquist, C. M.
 Vleck, *Ecology*, **2011**, *92*, 952.

514

73. C. M. Bauer, J. L. Graham, M. Abolins-Abols, B. J. Heidinger, E. D. Ketterson, T. J. Greives *The American Naturalist*, **2018**, *191*, 777.

518 74. T. Price, M. Kirkpatrick, S. J. Arnold. *Science* **1988**, 240, 798.

519

75. T. D. Williams, **2012**, Princeton University Press, Princeton, NJ.

521

522 76. C. R. Brown, M. B. Brown. *Condor*, **1999**, *101*, 230.

523

524 77. B. C. Sheldon, L. E. B. Kruuk, J. Merila, *Evolution* **2003**, *57*, 406.

525

526 78. C. Bauch, P. H. Becker, S. Verhulst, *Proc. R. Soc. B*, **2013**, 280, 20122540.

527

79. Belmaker, The role of telomere length in Tree Swallow behavior and life history. **2016**, PhD thesis, Cornell University.

530

531 80. J. Q. Ouyang, A. Z. Lendvai, I. T. Moore, F. Bonier, M. F. Haussmann, *Integrative and comparative biology*, **2016**, *56*, 138.

533

81. M. Le Vaillant, V. A. Viblanc, C. Saraux, C. Le Bohec, Y. Le Maho, A. Kato, F. Criscuolo, Y. Ropert-Coudert, *Polar Biology*, **2015**, *38*, 2059-2067.

536

82. C. Taff, C. R. Freeman- Gallant, *Ecology and evolution*, **2017**, 7, 3436.

538

83. M. Giraudeau, C. R. Friesen, J. Sudyka, N. Rollings, C. M. Whittington, M. R. Wilson,
M. Olsson, *Biology letters*, 2016, 12, 20160077.

541

542 84. J. Stauffer, B. Panda, P. Ilmonen, P. Mechanisms of ageing and development **2018**, 169, 45.

544

85. L. Khoriauli, A. Romano, M. Caprioli, M. Santagostino, S. G. Nergadze, A. Costanzo, D.
 Rubolini, E. Giulotto, N. Saino, M. Parolini, *Behavioral Ecology and Sociobiology*, 2017,
 71, 124.

548

86. J. López-Arrabé, P. Monaghan, A. Cantarero, W. Boner, L. Pérez-Rodríguez, J. Moreno,
 Physiological and Biochemical Zoology 2018, 91, 868.

551

552 87. J. Stauffer, B. Panda, T. Eeva, M. Rainio, P. Ilmonen, *Science of the Total Environment*, **2017**, *575*, 841.

554

555 88. M. Sebastiano, M. Eens, F. Angelier, K. Pineau, O. Chastel, D. Costantini, *Conservation physiology* **2017**, 5, 1.

557

89. N. P. Weng, B. L. Levine, C. H. June, R. J. Hodes, *Proceedings of The National Academy Of Sciences*, **1995**, *92*, 11091.

560

90. F. Criscuolo, S. Smith, S. Zahn, B. J. Heidinger, M. F. Haussmann, *Phil. Trans. R. Soc.* B, **2018**, *373*, 20160440.

- 91. Bernardes de Jesus, K. Schneeberger E. Vera, A. Tejera, C. B. Harley, M. A. Blasco,
 Aging Cell, 2011, 10, 604–621.
- 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.