



HAL
open science

Does IGF-1 shape life-history trade-offs? Opposite associations of IGF-1 with telomere length and body size in a free-living bird

Bibiana Montoya, Zsófia Tóth, Ádám Lendvai, Antoine Stier, Francois Criscuolo, Sandrine Zahn, Pierre Bize

► To cite this version:

Bibiana Montoya, Zsófia Tóth, Ádám Lendvai, Antoine Stier, Francois Criscuolo, et al.. Does IGF-1 shape life-history trade-offs? Opposite associations of IGF-1 with telomere length and body size in a free-living bird. *Frontiers in Ecology and Evolution*, 2022, 10, pp.853674. 10.3389/fevo.2022.853674 . hal-03599220

HAL Id: hal-03599220

<https://hal.science/hal-03599220>

Submitted on 7 Mar 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1 **Does IGF-1 shape life-history trade-offs? Opposite associations of IGF-1 with telomere length and**
2 **body size in a free-living bird**

3 **Bibiana Montoya^{1*}, Zsófia Tóth^{2,3}, Ádám Z. Lendvai², Antoine Stier^{4,5}, Francois Criscuolo^{6*},**
4 **Sandrine Zahn⁶ and Pierre Bize^{7*}**

5

6 ¹Estación Científica La Malinche, Centro Tlaxcala de Biología de la Conducta (CTBC), Universidad
7 Autónoma de Tlaxcala, Tlaxcala, México

8 ²Department of Evolutionary Zoology, University of Debrecen, Debrecen, Hungary

9 ³Juhász-Nagy Pál Doctoral School of Biology and Environmental Sciences, University of Debrecen,
10 Hungary

11 ⁴Department of Biology, University of Turku, Turku, Finland

12 ⁵Univ Lyon, Université Claude Bernard Lyon 1, CNRS, ENTPE, UMR 5023 LEHNA, F-69622,
13 Villeurbanne, France

14 ⁶Institut Pluridisciplinaire Hubert Curien, UMR 7178, Université de Strasbourg, CNRS, Strasbourg,
15 France

16 ⁷School of Biological Sciences, University of Aberdeen, Aberdeen, United Kingdom

17

18 ***Correspondence:**

19 Corresponding authors

20 Pierre Bize, pierre.bize@abdn.ac.uk; Bibiana Montoya, bibianac.montoyal@uatx.mx

21

22 **Key words:** Ageing, IGF-1, Life-history, Lifespan, Pace-of-Life syndrome, Telomeres, Trade-off.

23

24 **Running head:** IGF-1 and life-history trade-offs

25

26

27 **Abstract**

28 Hormonal pathways have been proposed to be key at modulating how fast individuals grow and reproduce
29 and how long they live (*i.e.* life history trajectory). Research in model species living under controlled
30 environment is suggesting that insulin-like growth factor 1 (IGF-1), which is an evolutionarily conserved
31 polypeptide hormone, has an important role in modulating animal life histories. Much remains however to
32 be done to test the role played by IGF-1 in shaping the phenotype and life history of animals in the wild.
33 Using a wild long-lived bird, the Alpine swift (*Tachymarptis melba*), we show that adults with higher
34 levels of IGF-1 had longer wings and shorter telomeres. Hence, telomeres being a proxy of lifespan in this
35 species, our results support a potential role of IGF-1 at shaping the life-history of wild birds and suggest
36 that IGF-1 may influence the growth-lifespan trade-off.

37

38

In review

39 1 Introduction

40 How fast an individual grows and reproduces and how long it lives are referred to as its life history
41 trajectory (Flatt and Heyland 2011). Although life history traits exhibit a wide range of variation among
42 species, consistent patterns of covariation between traits are widespread (Gaillard et al. 1989). Such
43 patterns of covariation are thought to be regulated by competitive allocation of limited resources (Stearns
44 1992), although other proximate mechanisms have also been suggested (Harshman and Zera 2007).
45 Accordingly, hormonal pathways have been proposed to play a key role in regulating life-history trade-
46 offs (Ricklefs and Wikelski 2002). One candidate hormone is insulin-like growth factor 1 (IGF-1), which
47 is an evolutionarily conserved polypeptide known to have effects on three key life-history traits: growth,
48 reproduction, and survival (Swanson and Dantzer 2014, Lodjak and Verhulst 2020). Moreover, IGF-1 is
49 suspected to be involved in the regulation of the trade-offs among these three life-history traits, but this
50 hypothesis has only been scarcely tested in free-living animals (Swanson and Dantzer 2014, Lodjak and
51 Verhulst 2020).

52 In laboratory models (*i.e.* worms, flies, and mice), IGF-1 signalling and circulating levels are linked
53 to the growth of somatic (Musarò et al. 2001, Yakar et al. 2002) and reproductive structures (Kaaks et al.
54 2000), gonadal function regulation (Bartke et al. 2013), and reproductive performance (Li et al. 2011).
55 Moreover, the inhibition of IGF-1 signalling is associated with increased lifespan (Holzenberger et al
56 2003), but the proximate mechanisms underlying this association are less well understood. Although IGF-
57 1 levels are highly repeatable within individuals, 0.41 – 0.85 (Roberts et al. 1990, Yuan et al. 2009), they
58 respond to environmental fluctuations on nutritional resource availability and temperature (Gabillard et al.
59 2003, Sparkman et al. 2009, Reagan et al 2020). Therefore, studies on the role played by IGF-1 on growth,
60 reproduction, and survival, in natural settings may be particularly relevant. In free-living animals,
61 ecological conditions have been shown to influence the direction of the links between IGF-1 and life-
62 history traits. For example, in free-ranging garter snakes (*Thamnophis elegans*) the presence of a positive
63 association between IGF-1 levels and adult body size is dependent on the habitat type (Sparkman 2009).
64 So far, general conclusions reached in laboratory models, on the positive association between IGF-1 with
65 growth have been (at least partially) confirmed in several non-model species (inter-specific comparison,
66 Lodjak et al. 2018). Moreover, although the number of studies evaluating the link between IGF-1 and
67 lifespan in non-model species has been very limited, they mostly confirmed the negative association
68 between IGF-1 and lifespan reported in model organisms, both at the interspecific (Swanson and Dantzer
69 2014; Lodjak et al. 2018) and at the intraspecific level (Lewin et al. 2017, but see Chaulet et al. 2012,
70 Lendvai et al 2020). Still, the nature of the proximate mechanisms implicated remains elusive, and one of

71 the putative candidates is oxidative stress (Holzenberger et al. 2003), which is known to accelerate the
72 shortening of telomeres (Reichert and Stier 2017), one of the hallmarks of ageing (López-Otín et al. 2013).

73 Although understanding variation in lifespan is a major focus of evolutionary ecology, accurately
74 measuring lifespan in the wild can be logistically challenging (Nussey et al. 2008). Remarkably, telomere
75 length has been shown to be linked to life expectancy in non-model species (Wilbourn 2018). Telomeres
76 are non-coding sequences of repetitive DNA located at the end of linear chromosomes that shorten with
77 each cellular replication (Backburn and Epel 2012), in response to cellular stressors including oxidative
78 stress (Reichert and Stier 2017), and under increased metabolic demand (Casagrande and Hau 2019).
79 Both, IGF-1 and telomere length, have been shown to diminish with age (Moverare-Skrtic et al. 2009) and
80 are linked to longevity (Deelen et al. 2013). The association between IGF-1 and telomeres has mainly
81 been explored in laboratory animals and human patients exhibiting pathological disorder of their
82 somatotrophic axis as well as cancer cell lines (Aulinas et al. 2013, Matsumoto et al. 2015). While cross-
83 sectional and correlative studies in humans and laboratory animals showed that IGF-1 and telomere length
84 are positively related (Barbieri et al. 2009, Moverare-Skrtic et al. 2009, Yeap et al. 2019), studies
85 conducted in cell lines found a negative association between these variables (Matsumoto et al. 2015,
86 Matsumoto and Takahashi 2016). Hence, the direction and strength of association between IGF-1 and
87 telomeres is still equivocal, and much remains to be done to understand whether telomere dynamics is part
88 of the mechanisms underlying the covariation observed between IGF-1 and lifespan.

89 The Alpine swift (*Tachymarptis melba*) is an insectivorous migratory bird that live up to 26 years of
90 age and has a slow pace of life (*i.e.* late age at sexual maturity, only one reproductive attempt *per* year,
91 and small clutch size *per* breeding attempt) (Bize et al 2009). The fact that adult Alpine swifts with longer
92 telomeres have higher survival rate (Bize et al. 2009) makes them a good model for exploring the links
93 between IGF-1 and telomere length. We propose that, if IGF-1 is a proximate mechanism underlying
94 trade-offs between growth and lifespan, then IGF-1 should show a positive association with body size and
95 a negative relationship with telomere length. As effects of IGF-1 on size can be tissue specific (Sharma et
96 al. 2012), and thus may affect the growth of different body parts in dissimilar ways, we measured both
97 wing length, sternum length and body mass as proxies of body size.

98

99 **2 Methods**

100 Fieldwork was carried out in 2018 in two Alpine swift colonies located in Bienne and Solothurn,
101 Switzerland, where nestlings have been ringed each year since at least 1968 and adults have been
102 subjected to an individual based study since 2000 (Bize et al. 2009). Forty-three adult Alpine swifts were

103 captured on their nests or roosting during the breeding season. After capture, each adult was weighed with
104 a digital scale to the nearest 0.1g, the same person (PB) measured their wing with a ruler to the nearest
105 mm and their sternum with a calliper to the nearest 0.1 mm. **Wing length was measured as the distance on**
106 **the closed wing from the foremost extremity of the carpus to the tip of the longest primary feathers; the**
107 **wing being flattened and straightened to give maximal wing length. Sternum was measured from one end**
108 **to the other of the keel.** We collected a 200 μ L blood sample from the foot vein using heparinized
109 microvette tubes (Sarstedt, Germany) to quantify telomere length and IGF-1 levels. Blood samples were
110 kept on ice in the field before being centrifuged at 10 000 g \times 10 min to separate plasma from red blood
111 cells, and then stored at -80°C until laboratory analyses. The Alpine swift is a monomorphic bird species,
112 and thus adults were genetically sexed (Bize et al. 2005). The exact chronological age was known for 38
113 birds that had been ringed as nestlings (range: 2 – 17 years).

114

115 **2.1 Telomere length**

116 Multiplex quantitative PCR was used to quantify relative telomere length (RTL). Full protocols for genomic
117 DNA extraction using nucleated red blood cells and of multiplex qPCR description adapted for swifts are
118 available in (Criscuolo et al. 2017). The concentration and purity (presence of residuals proteins or solvents)
119 of the extracted DNA were checked with a Nano-Drop ND-1000 spectrophotometer (Thermo Fisher
120 Scientific, Massachussets, USA). The quality and the integrity of DNA were confirmed by gel
121 electrophoresis on 1% agarose gels stained with ethidium bromide (checking for the absence of DNA smears
122 corresponding to degraded DNA). Our 43 adults' RTL were measured within a batch of chick and adult
123 samples (total 109 samples) measured in duplicates over one 384 wells plate. Amplification efficiencies of
124 control and telomere sequences were of 99.6% (identical for both sequences) and r^2 of dilution curves of
125 0.97 and 0.98, respectively. Based on duplicates within plates, intra-class correlation coefficient for final
126 RTL values was 0.689.

127

128 **2.2 Insulin Like Growth Factor-1**

129 IGF-1 concentrations were measured from 10 μ l of plasma using an enzyme-linked immunosorbent assay
130 (for further details see Mahr et al. 2020). We used chicken plasma in quadruplicates to determine intra-
131 (5.3%) and inter-assay coefficient of variations (10.4%). We validated the assay for the Alpine swifts by
132 showing that serially diluted plasma samples were parallel with the standard curve.

133

134 **2.3 Statistical analyses**

135 Statistical analyses were performed in R version 4.0.0, using the R package lmerTest (Kuznetsova et al.
136 2017, R Core Tea 2021). A preliminary analysis exploring the effect of sampling date, hour, and breeding
137 site on IGF-1 levels showed that only sampling date accounted for variation in IGF-1 levels; sampling
138 date was therefore retained as a covariate when analysing variation in IGF-1. Firstly, we tested for an
139 association between IGF-1 and wing length, sternum length and/or body mass by fitting a general linear
140 model with IGF-1 as response variable and all three biometric traits, plus sampling date, as explanatory
141 variables (model 1). Variance inflation factors in this first model were below 1.24 indicating no
142 collinearity issues between biometric traits. Secondly, we investigated how IGF-1 (response variable) was
143 related to telomere length by including as explanatory variables telomere length while controlling for
144 possible confounding effect of chronological age and traits identified as significant in our model 1.
145 **Sample sizes vary across analyses due to missing values in some of the traits.**

146

147 **3 Results**

148 Plasma levels of IGF-1 in adult Alpine swifts were positively associated with wing length (Fig 1a, Table
149 1a) but not related to body mass and sternum, those results being obtained after controlling for the date of
150 sampling (Table 1a). Adults sampled later in the season had lower IGF-1 levels (Table 1). Hence, wing
151 length and sampling date were included as covariates in the follow-up analysis. Adult birds with higher
152 IGF-1 levels had shorter telomeres (Fig. 1b, Table 1b), after controlling for the date of sampling, wing
153 length, and chronological age (Table 1b).

154

155 **4 Discussion**

156 Overall, as predicted, we found that circulating levels of IGF-1 were positively associated with wing
157 length and negatively to telomere length, in adult Alpine swifts. Those opposite associations of IGF-1 with
158 body size and telomere length support the idea that IGF-1 may regulate, at least partially, the life-history
159 of this long-lived bird species.

160 Our results show that adult birds with higher levels of IGF-1 had longer wings, which matches
161 recent findings in adult bearded reedlings (*Panurus biarmicus*) showing a positive association of between
162 IGF-1 levels and tail feather length (Mahr et al. 2020) and in nestling pied flycatchers (*Ficedula*
163 *hypoleuca*) showing a positive association between IGF-1 and growth and size at fledging (Lodjak et al.
164 2016). The positive association between IGF-1 and wing length in adult swifts may be caused either by
165 the effects of IGF-1 on wing bone growth early in life and/or primary feather growth. An experimental

166 elevation of IGF-1 in adult bearded reedlings had no effects on feather growth, but increased moult
167 intensity (Lendvai et al. 2021), whereas an experimental administration of IGF-1 to nestling pied
168 flycatchers positively affected the growth of their tarsi but not of their wings [44]. Hence, the present
169 finding in adult Alpine swifts of a link between IGF-1 and wing length is likely to be dependent on wing
170 bones length rather than primary feathers length. A positive effect of IGF-1 on bone growth has been
171 reported on numerous occasions [e.g. Yakar et al. 2002, Lodjak et al. 2016, Lendvai et al. 2021]. The
172 effect of IGF-1 on bone growth appears however to be stronger on short than long bones, at least in
173 laboratory models (Wang et al. 2006). It may explain why we only observed an association between IGF-1
174 with wing bones length (carpals and metacarpals) but not with sternum length, with the carpals and
175 metacarpals being short boned whereas the sternum is one of the longest bones in swifts. The contrasting
176 finding between IGF-1 and wing length in experimentally manipulated nestling pied flycatchers and adult
177 swifts may come from differences between species in the influence of IGF-1 on wing bone growth,
178 considering that Alpine swifts spend most of their lifetime aloft (Liechti et al. 2013). Hence, one
179 hypothesis is that the positive association between IGF-1 and wing length in adult swifts comes from
180 early-life allocation of resources into wing bone growth. This hypothesis also assumes that IGF-1 should
181 be repeatable through the individual's life, from the nestling to adult stage, which has been previously
182 reported (Roberts et al. 1990, Yuan et al. 2009). In this study, IGF-1 was found to vary with sampling
183 date, and thus IGF-1 may potentially change during the breeding season. Yet, variation in IGF-1 levels
184 among individuals can still being higher than those within individuals, making the trait flexible but
185 repeatable. Many examples of this can be found in the literature regarding different physiological traits
186 such as glucose levels (Montoya et al. 2018; 2020), antioxidant defenses (Recapet et al. 2019) or
187 mitochondrial function (Stier et al. 2019). Further studies are now needed in swifts and other bird species
188 to examine the repeatability through individual's life in IGF-1 and test for effects early in life of IGF-1 on
189 the growth of short (e.g. carpals and metacarpals) and long (tarsi, sternum) bones.

190 Our results also show that IGF-1 and telomere length were negatively related in adult swifts.
191 Studies in laboratory models and humans indicate that IGF-1 has a positive effect on telomerase activity
192 (Bayne and Liu 2005), suggesting that IGF-1 and telomere length could be positively correlated (e.g.
193 Barbieri et al. 2009, Moverare-Skrtic et al. 2009, Yeap et al. 2019, but see Matsumoto et al. 2015,
194 Matsumoto and Takahashi 2016). However, the experimental disruption of IGF-1 signalling pathway in
195 laboratory animals has been found to extend lifespan (Holzenberger et al. 2003, Yuan et al. 2009), and the
196 few studies performed in free-living animals corroborate such an inverse correlation between IGF-1 and
197 lifespan (Lodjak and Mägi 2017, Lewin et al. 2017) or in our study with a proxy of lifespan such as
198 telomere length (Sirman 2019). So, if the link between IGF-1 and telomere length is not due to telomerase,
199 an alternative mechanism may be oxidative stress. Interestingly, reduced IGF-1 signalling has also been

200 associated with increased *in vivo* resistance to oxidative stress in laboratory models (Holzenberger et al.
201 2003). Furthermore, administration of IGF-1 in wild birds was found to lead to greater oxidative damage
202 (Lendvai et al. 2020, Vágási et al. 2020) and higher activity of glutathione peroxidase (Lodjak and Mägi
203 2017, Lendvai et al. 2020), the later possibly reflecting up-regulated antioxidant activity in response to
204 oxidative stress (Lodjak and Mägi 2017, Lendvai et al. 2020). Variation in oxidative stress and telomere
205 length have been linked to the ageing process, with individuals with enhanced resistance to oxidative
206 stress and/or longer telomeres having higher annual survival or better fitness (Bize et al. 2009), and
207 importantly exposure to oxidative stress is thought to accelerate telomere shortening (Reichert and Stier
208 2017, but see Pérez-Rodríguez et al. 2019). Therefore, a negative association between IGF-1 and telomere
209 length as reported here in adult swifts and other previous studies (Barbieri et al. 2009, Moverare-Skrtic et
210 al. 2009, Yeap et al. 2019) may come from cascading effects of IGF-1 on oxidative stress, affecting in turn
211 telomere dynamics through direct or indirect pathways (Casagrande and Hau 2019), an idea that requires
212 now further empirical examination.

213 **In conclusion, negative associations of IGF-1 with wing and telomere length found here suggest**
214 **that IGF-1 may play a role in regulating life-histories, and welcome future studies exploring the**
215 **association of IGF-1 with direct measurements of growth and lifespan in wild organisms.**

216

217 **5 Competing interests.** The authors declare that the research was conducted in the absence of any
218 commercial or financial relationships that could be construed as a potential conflict of interest.

219

220 **6 Ethics Statement.** Birds were caught, handled, blood sampled, and ringed under the legal
221 authorization of the Swiss Agency for the Environment

222

223 **7 Authors' contributions.** BM, PB, and ÁZL designed the study. BM, PB and AS carried out the
224 fieldwork. SZ and FC carried the laboratory analysis and interpretation of TL measures. ZT and ÁZL
225 carried the laboratory analysis and interpretation of IGF-1 measures. BM and PB carried out the data
226 analyses. BM wrote the first draft, and all the co-authors critically revised the manuscript.

227

228 **8 Funding.** PB, FC and AS were supported by a Carnegie Research Incentive Grant (RIG007773).
229 BM was supported by a Godfrey Hewitt Mobility Award from the European Society for Evolutionary
230 Biology. ÁZL was supported by a grant from the National Research and Development Office (K139021).

231

232 **9 References**

233 Aulinas A, Ramírez MJ, Barahona MJ, Mato E, Bell O, Surrallés J, Webb SM. 2013. Telomeres and
234 endocrine dysfunction of the adrenal and GH/IGF-1 axes. *Clin. Endocrinol.* **79**, 751-759.
235 (doi.org/10.1111/cen.12310)

236 Blackburn EH, Epel ES. 2012 Telomeres and adversity: too toxic to ignore. *Nature* **490**,169–171.
237 (doi:10.1038/490169a)

238 Barbieri M, Paolisso G, Kimura M, Gardner JP, Boccardi V, Papa M, Hjelmborg JV, Christensen K,
239 Brimacombe M, Nawrot TS, Staessen JA, Pollal MN, Aviv A. 2009. Higher circulating levels of
240 IGF-1 are associated with longer leukocyte telomere length in healthy subjects. *Mech. Ageing Dev.*
241 **130**, 771-776. (doi.org/10.1016/j.mad.2009.10.002)

242 Bartke A, Sun LY, Longo V. 2013 Somatotropic signaling: trade-offs between growth, reproductive
243 development, and longevity. *Physiol. Rev.* **93**, 571–598. (doi.org/10.1152/physrev.00006.2012)

244 Bayne S, Liu JP. 2005. Hormones and growth factors regulate telomerase activity in ageing and cancer.
245 *Mol. Cell. Endocrinol.* **240**, 11–22. (doi:10.1016/j.mce.2005.05.009)

246 Bize P, Roulin A, Tella JL, Richner H. 2005. Female-biased mortality in experimentally parasitized
247 Alpine Swift *Apus melba* nestlings. *Func Ecol* **19**, 405-413. (doi: 10.1111/j.1365-
248 2435.2005.00995.x)

249 Bize P, Criscuolo F, Metcalfe NB, Nasir L, Monaghan P. 2009. Telomere dynamics rather than age
250 predict life expectancy in the wild. *Proc. R. Soc. B.* **276**, 1679-1683.
251 (doi.org/10.1098/rspb.2008.1817)

252 Casagrande S, Hau M. 2019. Telomere attrition: metabolic regulation and signalling function?. *Biol Lett*
253 **15**, 20180885. (doi.org/10.1098/rsbl.2018.0885)

254 Chaulet A, Medesani DA, Freitas J, Cervino A, Cervino N, Rodríguez EM. 2012. Induction of somatic
255 growth in juvenile crayfish *Cherax quadricarinatus* (Decapoda, Parastacidae), by ecdysone and
256 insulin growth factor. *Aquaculture* **370**, 1-6. (doi.org/10.1016/j.aquaculture.2012.09.026)

257 Criscuolo F, Zahn S, Bize P. 2017. Offspring telomere length in the long lived Alpine swift is negatively
258 related to the age of their biological father and foster mother. *Biol Lett* **13**, 20170188.
259 (doi:10.1098/rsbl.2017.0188)

260 Deelen J, Uh HW, Monajemi R, van Heemst D, Thijssen PE, Böhringer S, van der Akker EB, de Craen
261 AJ, Rivadeneira F, Uitterlinden AG, Westendorp R, Goeman JJ, Slagboom PE, Houwing-
262 Duistermaat JJ, Beekman M. 2013. Gene set analysis of GWAS data for human longevity highlights
263 the relevance of the insulin/IGF-1 signaling and telomere maintenance pathways. *Age* **35**, 235-249.
264 (doi.org/10.1007/s11357-011-9340-3)

265 Flatt T, Heyland A. (Eds.). 2011. *Mechanisms of life history evolution: the genetics and physiology of life*
266 *history traits and trade-offs*. New York, NY: Oxford University press.

267 Gabillard JC, Weil C, Rescan PY, Navarro I, Gutiérrez J, Le Bail PY. 2003. Effects of environmental
268 temperature on IGF1, IGF2, and IGF type I receptor expression in rainbow trout (*Oncorhynchus*
269 *mykiss*). *Gen. Comp. Endocr.* **133**, 233–242. (doi.org/10.1016/S0016-6480(03)00167-9)

270 Gaillard JM, Pontier D, Allaine D, Lebreton JD, Trouvilliez J, Clobert J. 1989. An analysis of
271 demographic tactics in birds and mammals. *Oikos* **56**, 59-76. (doi.org/10.2307/3566088)

272 Harshman LG, Zera AJ. 2007. The cost of reproduction: the devil in the details. *Trends Ecol. Evol.* **22**, 80-
273 86. (doi.org/10.1016/j.tree.2006.10.008)

274 Holzenberger M, Dupont J, Ducos B, Leneuve P, Géloën A, Even PC, Cervera P, Le Bouc Y. 2003. IGF-1
275 receptor regulates lifespan and resistance to oxidative stress in mice. *Nature* **421**, 182-187.
276 (doi.org/10.1038/nature01298)

277 Kaaks R, Lukanova A, Sommersberg B. 2000. Plasma androgens, IGF-1, body size, and prostate cancer
278 risk: a synthetic review. *Prostate Cancer Prostatic Dis.* **3**, 157-172.
279 (doi.org/10.1038/sj.pcan.4500421)

280 Kuznetsova A, Brockhoff PB, Christensen RH. 2017. lmerTest package: tests in linear mixed effects
281 models. *J. Stat. Softw.* **82**, 1-26. (doi.org/10.18637/jss.v082.i13)

282 Lendvai ÁZ, Tóth Z, Mahr K, Osváth G, Vogel-Kindgen S, Gander A. 2021. Effects of experimental
283 increase in insulin-like growth factor 1 on feather growth rate, moult intensity and feather quality in
284 a passerine bird. *J. Exp. Biol.* **224**, jeb242481. (doi:10.1242/jeb.242481)

285 Lendvai AZ, Tóth Z, Péntzes J, Vogel-Kindgen S, Gander BA, Vágási CI. 2020. Insulin-like growth factor
286 1 induces oxidative damage, but does not affect survival in a songbird. *BioRxiv*.

287 Lewin N, Swanson EM, Williams BL, Holekamp KE. 2017. Juvenile concentrations of IGF-1 predict life-
288 history trade-offs in a wild mammal. *Funct. Ecol.* **31**, 894-902. (doi.org/10.1111/1365-2435.12808)

289 Li L, Fu YC, Xu JJ, Chen XC, Lin XH, Luo LL. 2011. Caloric restriction promotes the reproductive
290 capacity of female rats via modulating the level of insulin-like growth factor-1 (IGF-1). *Gen. Comp.*
291 *Endocrinol.* **174**, 232-237. (doi.org/10.1016/j.ygcen.2011.09.005)

292 Liechti F, Witvliet W, Weber R, Bächler E. 2013. First evidence of a 200-day non-stop flight in a bird.
293 *Nat. Commun.* **4**, 1-7. (doi.org/10.1038/ncomms3554)

294 Lodjak J, Mägi M. 2017. Crosstalk between growth and somatic maintenance in young animals. *J. Avian*
295 *Biol.* **48**, 1360-1363. (doi.org/10.1111/jav.01519)

296 Lodjak J, Mänd R, Mägi M. 2018. Insulin-like growth factor 1 and life-history evolution of passerine
297 birds. *Funct. Ecol.* **32**, 313-323. (doi.org/10.1111/1365-2435.12993)

298 Lodjak J, Tilgar V, Mägi M. 2016. Does the interaction between glucocorticoids and insulin-like growth
299 factor 1 predict nestling fitness in a wild passerine?. *Gen. Comp. Endocrinol.* **225**, 149-154.
300 (doi.org/10.1016/j.ygcen.2015.10.016)

301 Lodjak J, Verhulst S. 2020. Insulin-like growth factor 1 of wild vertebrates in a life-history context. *Mol.*
302 *Cell. Endocrinol.* **518**, 110978. (doi.org/10.1016/j.mce.2020.110978)

303 López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. 2013. The hallmarks of aging. *Cell* **153**,
304 1194-1217. (doi.org/10.1016/j.cell.2013.05.039)

305 Mahr K, Vincze O, Tóth Z, Hoi H, Lendvai ÁZ. 2020. Insulin-like growth factor 1 is related to the
306 expression of plumage traits in a passerine species. *Behav. Ecol. Sociobiol.* 74, 39.
307 (doi.org/10.1007/s00265-020-2821-6)

308 Matsumoto R, Fukuoka H, Iguchi G, Odake Y, Yoshida K, Bando H, Suda K, Nishizawa H, Takahashi M,
309 Ogawa W, Takahashi Y. 2015. Accelerated telomere shortening in acromegaly; IGF-I induces
310 telomere shortening and cellular senescence. *PloS one* **10**, e0140189.
311 (doi.org/10.1371/journal.pone.0140189)

312 Matsumoto R, Takahashi Y. 2016. Telomeres and Cellular Senescence in Metabolic and Endocrine
313 Diseases. In *Telomere: A Complex End of a Chromosome*, pp. 143. Croatia: Tech Publisher Rijeka.

314 Montoya B, Briga M, Jimeno B, Verhulst S. 2020. Glucose regulation is a repeatable trait affected by
315 successive handling in zebra finches. *J Comp Physiol B*, **190**, 455-464. (doi.org/10.1007/s00360-
316 020-01283-4)

317 Montoya B, Briga M, Jimeno B, Moonen S, Verhulst S. 2018. Baseline glucose level is an individual trait
318 that is negatively associated with lifespan and increases due to adverse environmental conditions
319 during development and adulthood. *J Comp Physiol B*, **188**, 517-526. (doi.org/10.1007/s00360-017-
320 1143-0)

321 Moverare-Skrtic S, Svensson J, Karlsson M, Orwoll E, Ljunggren Ö, Mellström D, Ohlsson C. 2009.
322 Serum Insulin-Like Growth Factor-1 concentration is associated with leukocyte telomere length in a
323 population-based cohort of elderly men. *J. Clin. Endocrinol. Metab.* **94**, 5078–5084.
324 (doi.org/10.1210/jc.2009-1450)

325 Musarò A, McCullagh K, Paul A, Houghton L, Dobrowolny G, Molinaro M, Barton ER, Sweeney HL,
326 Rosenthal N. 2001. Localized Igf-1 transgene expression sustains hypertrophy and regeneration in
327 senescent skeletal muscle. *Nat. Genet.* **27**, 195-200. (doi.org/10.1038/84839)

328 Nussey DH, Coulson T, Festa-Bianchet M, Gaillard JM. 2008. Measuring senescence in wild animal
329 populations: towards a longitudinal approach. *Funct. Ecol.* **22**, 393-406. (doi.org/10.1111/j.1365-
330 2435.2008.01408.x)

331 Pérez-Rodríguez L, Redondo T, Ruiz-Mata R, Camacho C, Moreno-Rueda G, Potti J. 2019. Vitamin E
332 supplementation—but not induced oxidative stress—influences telomere dynamics during early
333 development in wild passerines. *Front. Ecol. Evol.* **7**, 173. (doi.org/10.3389/fevo.2019.00173)

334 R Core Team. 2021. R: A language and environment for statistical computing. R Foundation for Statistical
335 Computing, Vienna, Austria. URL <https://www.R-project.org/>.

336 Récapet C, Arrivé M, Doligez B, Bize P. 2019. Antioxidant capacity is repeatable across years but does
337 not consistently correlate with a marker of peroxidation in a free-living passerine bird. *J Comp*
338 *Physiol B*, **189**, 283-298. (doi: 10.1007/s00360-019-01211-1)

339 Regan JC, Froy H, Walling CA, Moatt JP, Nussey DH. 2020. Dietary restriction and insulin-like
340 signalling pathways as adaptive plasticity: A synthesis and re-evaluation. *Funct Ecol*, **34**, 107-128.
341 (doi.org/10.1111/1365-2435.13418)

342 Reichert, S., & Stier, A. 2017. Does oxidative stress shorten telomeres in vivo? A review. *Biol. Lett.* **13**,
343 20170463. (doi.org/10.1098/rsbl.2017.0463)

344 Ricklefs RE, Wikelski M. 2002. The physiology/life-history nexus. *Trends Ecol. Evol.* **17**, 462-468.
345 (doi.org/10.1016/S0169-5347(02)02578-8)

346 Roberts CA, McCutcheon SN, Blair HT, Gluckman PD, Breier BH. 1990. Developmental patterns of
347 plasma insulin-like growth factor-1 concentrations in sheep. *Domest. Anim. Endocrinol.* **7**, 457-463.
348 (doi.org/10.1016/0739-7240(90)90003-1)

349 Sharma N, Castorena, CM, Cartee GD. 2012. Tissue-specific responses of IGF-1/insulin and mTOR
350 signaling in calorie restricted rats. *PLoS one* **7**, e38835. (doi.org/10.1371/journal.pone.0038835)

351 Sirman A. 2019. Biological mechanisms underpinning growth and ageing in wild birds. PhD thesis. North
352 Dakota State University. Fargo, North Dakota, USA.

353 Sparkman AM, Vleck CM, Bronikowski AM. 2009. Evolutionary ecology of endocrine-mediated life-
354 history variation in the garter snake *Thamnophis elegans*. *Ecology* **90**, 720-728.
355 (doi.org/10.1890/08-0850.1)

356 Stearns SC. 1992. *The evolution of life histories*. New York, NY: Chapman & Hall.

357 Stier A, Bize P, Hsu B-Y, Ruuskanen S. 2019. Plastic but repeatable: rapid adjustments of mitochondrial
358 function and density during reproduction in a wild bird species. *Biol Lett* **15**, 20190536.
359 (doi.org/10.1098/rsbl.2019.0536)

360 Swanson EM, Dantzer B. 2014. Insulin-like growth factor-1 is associated with life-history variation across
361 Mammalia. *Proc. R. Soc. B.* **281**, 20132458. (doi.org/10.1098/rspb.2013.2458)

362 Swanson EM, Dantzer B. 2014. Insulin-like growth factor-1 is associated with life-history variation across
363 Mammalia. *Proc. R. Soc. B.* **281**, 20132458. (doi.org/10.1098/rspb.2013.2458)

- 364 Vágási CI, Tóth Z, Péntes J, Pa, PL, Ouyang JQ, Lendvai ÁZ. 2020. The Relationship between
365 Hormones, Glucose, and Oxidative Damage Is Condition and Stress Dependent in a Free-Living
366 Passerine Bird. *Physiol. Biochem. Zool.* **93**, 466-476. (doi.org/10.1086/711957)
- 367 Wang Y, Nishida S, Sakata T, Elalieh HZ, Chang W, Halloran BP, Doty SD, Bikle, D. D. 2006. Insulin-
368 like growth factor-I is essential for embryonic bone development. *Endocrinology* **147**, 4753-4761.
369 (doi.org/10.1210/en.2006-0196)
- 370 Wilbourn RV, Moatt JP, Froy H, Walling CA, Nussey DH, Boonekamp JJ. 2018. The relationship
371 between telomere length and mortality risk in non-model vertebrate systems: a meta-analysis.
372 *Philos. Trans. R. Soc. B.* **373**, 20160447. (doi.org/10.1098/rstb.2016.0447)
- 373 Yakar S, Rosen CJ, Beamer WG, Ackert-Bicknell CL, Wu Y, Liu JL, Ooi GT, Setser J, Frystyk J,
374 Boisclair YR, LeRoith D. 2002. Circulating levels of IGF-1 directly regulate bone growth and
375 density. *J. Clin. Investig.* **110**, 771-781. (doi.org/10.1172/JCI15463)
- 376 Yeap BB, Hui J, Knuiiman M, Chubb SA, Ho KK, Flicker L, Divitini ML, Arscott GM, Twigg SM,
377 Almeida OP, Hankey GJ, Golledge J, Beilby JP. 2019. Associations of plasma IGF1, IGFBP3 and
378 estradiol with leucocyte telomere length, a marker of biological age, in men. *Eur. J. Endocrinol.*
379 **182**, 23-33. (doi.org/10.1530)
- 380 Yuan R, Tsaih SW, Petkova SB, De Evsikova CM, Xing S, Marion MA, Bogue MA, Mills KD, Peters
381 LL, Bult CJ, Rosen CJ, Sundberg JP, Harrison DE, Churchill GA, Paigen B. 2009. Aging in inbred
382 strains of mice: study design and interim report on median lifespans and circulating IGF1 levels.
383 *Aging Cell* 8, 277-287. (doi.org/10.1111/j.1474-9726.2009.00478.x)

384

385 **Figure Legends**

386 **Figure 1.** Panel (a) shows the relationship between wing length and plasma levels of insulin-like growth
387 factor 1, in adult Alpine swifts. Panel (b) presents the association of plasma levels of relative telomere
388 length and plasma levels of insulin-like growth factor 1, in adult Alpine swifts.

In review

389 **Tables**

390 **Table 1.** Linear models showing positive association between plasma levels of insulin-like growth factor 1
 391 and wing length (model 1), and negative relation between plasma levels of insulin-like growth factor 1 and
 392 relative telomere length (model 2), in adult Alpine swifts. Table shows results from the initial model, no
 393 stepwise deletion was performed.

(a) Model 1: Linking IGF-1 to body size			
<i>Variable</i>	<i>Estimate ± SE</i>	<i>F</i>	<i>P</i>
Wing	1.46 ± 0.71	4.21	0.049
Sternum	2.34 ± 2.45	0.92	0.34
Body mass	-1.06 ± 0.59	3.20	0.08
Sampling date	-1.14 ± 0.51	4.91	0.03
Residual DF		30	
(b) Model 2: Linking IGF 1 to telomere length			
<i>Variable</i>	<i>Estimate ± SE</i>	<i>F</i>	<i>P</i>
Telomere length	-16.62 ± 5.56	8.92	0.006
Wing	0.83 ± 0.63	1.75	0.20
Chronological age	-0.54 ± 0.70	0.59	0.45
Sampling date	-0.68 ± 0.49	1.93	0.18
Residual DF		29	

394

Figure 1.JPEG

