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Evolution of Longevity in Tetrapods: Safety Is More Important than Metabolism Level

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Abstract—Various environmental morphological and behavioral factors can determine the longevity of representatives of various taxa. Long-lived species develop systems aimed at increasing organism stability, defense, and, ultimately, lifespan. Long-lived species to a different extent manifest the factors favoring longevity (gerontological success), such as body size, slow metabolism, activity of body's repair and antioxidant defense systems, resistance to toxic substances and tumorigenesis, and presence of neotenic features. In continuation of our studies of mammals, we investigated the characteristics that distinguish long-lived ectotherms (crocodiles and turtles) and compared them with those of other ectotherms (squamates and amphibians) and endotherms (birds and mammals). We also discussed mathematical indicators used to assess the predisposition to longevity in different species, including standard indicators (mortality rate, maximum lifespan, coefficient of variation of lifespan) and their derivatives. Evolutionary patterns of aging are further explained by the protective phenotypes and life history strategies. We assessed the relationship between the lifespan and various studied factors, such as body size and temperature, encephalization, protection of occupied ecological niches, presence of protective structures (for example, shells and osteoderms), and environmental temperature, and the influence of these factors on the variation of the lifespan as a statistical parameter. Our studies did not confirm the hypothesis on the metabolism level and temperature as the most decisive factors of longevity. It was found that animals protected by shells (e.g., turtles with their exceptional longevity) live longer than species that have poison or lack such protective adaptations. The improvement of defense against external threats in long-lived ectotherms is consistent with the characteristics of long-lived endotherms (for example, naked mole-rats that live in underground tunnels, or bats and birds, whose ability to fly is one of the best defense mechanisms).

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INTRODUCTION

Aging manifests both biologically, as body deterioration and impairment of motor, physiological, and cognitive characteristics, and demographically (mathematically), as an increase in mortality with age [1-3].

Patterns of aging have been described by numerous evolutionary theories, e.g., the theories of age-related attenuation of selection pressure [4] and antagonistic pleiotropy [5]. Disposable soma theory [6] complements these concepts by stating that deleterious somatic mutations may accumulate if the selection pressure on these mutations is less than to mutations harmful to the germline.

The probability of death, however, is not always determined only by the degree of organism deterioration,

Abbreviations: CV, coefficient of variation; LS, life span; ROS, reactive oxygen species.

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which increases with age and includes accumulation of damage and errors [7]. In some cases, such deterioration happens very quickly, for example, after reproduction (in semelparous animals) or to prevent the spread of infection in a population. Academician V. P. Skulachev has pointed out this fact, when he suggested the concept of acute and chronic phenoptosis [8].

The lifespan (LS) and severity of aging processes highly vary in different species.

In most animal groups, evolution has been accompanied by the increase in the complexity of organization and appearance of new types of cells and tissues, as well as new behavioral responses. This implies that each evolutionary round along the path of increasing complexity will lead to the emergence of new types of degenerative disorders and impairments that would determine both the maximum LS and the structure of mortality in general.

The number of cells in organisms also increases with the increase in the organism complexity (and size).

Traits contributing to longevity (gerontological success) in Metazoa. Multicellular animals (Kingdom Metazoa) lack a single common LS trend, but rather demonstrates various local trends in this parameter.

First, a large number of primitive Metazoa are characterized by the lack of aging, or negligible senescence [9].

Jones et al. [10] classified the red Gorgonian coral *Paramuricea clavata* as a non-aging species, as the probability of death for this coral does not increase with age, with its LS reaching hundreds of years [10]. The jellyfish *Turritopsis dohrnii* is potentially immortal due to the ability to return from the medusa stage back to a polyp, thereby looping its life cycle [11]. The freshwater *Hydra magnipapillata* is considered as potentially immortal species as its death in laboratory settings is close to zero and does not increase with age [12], although according to Comfort [1], in nature, this organism lives for no more than three years. At the same time, LS_{95} (age at which 95% of individuals die at a given level of mortality) of *H. magnipapillata* in a laboratory is more than 1400 years [10].

All the above long-lived species inhabit aquatic habitats; however, the list of traits promoting longevity has significantly expanded after the water-to-land transition [13-15]. The more primitive a species, the easier to maintain the longevity traits of the taxa preceding this species on the evolutionary tree. It was suggested [10] that aging is slowed down by asexual reproduction [16], modularity, absence of germ–soma differentiation [14, 16], absence of predation pressure, shelter security [17], ability for regeneration, and presence of a small number of cell types [12].

At the same time, the difference in the size of cells of the same type in different species is much less than the difference in the size of organisms. This implies that the number of cells in large organisms is higher and, since a tumor can theoretically develop from a single transformed cell, resistance to oncogenesis is an important aspect in the predisposition to longevity in large animals (Peto's paradox) [18, 19]. It is believed that retention of ability for growth and regeneration, as well as slow metabolism and low body temperature (which contribute to slower generation of oxidizing radicals), are among the basic mechanisms ensuring slow aging in animals. These features are typical for the all-time LS champions, such as the small bivalve mollusk *Arctica islandica* (507 years) and large and very slow Greenland shark *Somniosus microcephalus* (392 years).

Previously, we published an article on the evolution of longevity in mammals [15]. In this work, we studied the mechanism of LS formation as a species-specific trait and evolution of longevity in cold-blooded (ectothermic) Tetrapoda, as well as gerontological success as a special type of biological success. Here, we have focused on reptiles and amphibians *vs*. mammals. We analyzed the traits contributing to longevity (gerontological success) and compared the efficiency of using these traits (gerontological success efficiency) in different clades of amphibians and reptiles (the latter include many long-lived species, first of all, turtles). The article also discusses mathematical indicators used to assess the propensity for longevity in different species. These include standard and basal mortality rates and their dispersion (coefficient of variation, CV), as well as their derivatives. We chose to analyze the species from the ectothermic taxa (with low metabolic rate but great variation in size), in particular, the mechanisms providing safety of these species and features of ecological niches occupied by these animals. The LS values of vertebrate species used in this work were taken from the largest Anage database [20] unless stated otherwise. The tree for the LS distribution was constructed using the classification of vertebrates from the Ensembl database [21] and the LS data from the Anage database. In this work, the LS value was defined as the maximum age known for a discussed species.

THE TRAITS OF GERONTOLOGICAL SUCCESS AND LONGEVITY IN DIFFERENT TAXA OF TETRAPODA

From the evolutionary point of view, the main goal of living organisms is to maximize their fitness as the extent of organism's genetic contribution to subsequent generations. Therefore, all other things being equal, a long life is preferable to a short life. However, in reality, fitness is affected by multiple factors.

Beside the LS, fitness is influenced by fecundity, extent of offspring protection, sociality, reproductive effort at various ages, parental contribution, etc.

Hence, in terms of evolution, LS values optimal in different situations can be different (either low or high). Therefore, there is no single global trend toward an increase in the LS in the evolution of living organisms, as well as there is no global trend toward, for example, an increase in fecundity or parental contribution (although other things being equal, both high fecundity and high parental contribution increase fitness).

The pattern of distribution of species with high and low LS values along the phylogenetic tree of animals is quite complex. Analysis of this distribution for vertebrates might help to identify and understand the main factors involved in the evolution of longevity.

As we have mentioned previously, high LS is uncommon in nature and, apparently, not the most important trait for adaptation. Or this trait is too "expensive" in terms of selection, if most of mutations increasing longevity are at the same time detrimental to other components of adaptation (e.g., fecundity or parental care).

The relationship between the aging rate and LS is far from unambiguous.

While life is short at high aging rates, it can be either long or short at low aging rates, as it depends on the basal mortality rate, including predation pressure. Generally recognized traits contributing to longevity in vertebrates (traits determining their gerontological success) are retention of ability for growth and regeneration in adulthood [22], slow metabolism (fish, amphibians, reptiles) [23], retention of juvenile features in adult animals (neoteny) (amphibians) [24-26], and tolerance to high metabolic rates (due to the acquired ability to fly) (birds) [27].

A high capacity for transitory reparative regeneration after a damage/loss of some organ parts is retained in echinoderms (close relatives of vertebrates) [28, 29]. Later in the evolution of vertebrates, such regenerative capacity has decreased along with the increase in the level of organization. For example, the *c-Answer* gene discovered at the Institute of Information Transmission Problems encodes a protein responsible for regeneration in amphibians. However, this gene has not been retained in mammals, which has promoted (due to a decrease in the Fgf8 activity) the development of the forebrain, a distinctive feature of higher vertebrates [30]. The metabolic rate and, accordingly, the rate of free radical generation by the mitochondria in ectothermic vertebrates, including fish, reptiles, and amphibians, are lower compared to those in endothermic vertebrates (birds and mammals).

This might has contributed to the evolution of high LS and delayed aging in some species, including emergence of extremely long-lived species (some sharks) [22] and species with negligible senescence (some members of the Cyprinidae family) [31]. Reinke et al. [32] found that 26 out of 30 known vertebrate species that can survive up to 100 years are ectotherms. These data suggest that the factor contributing most to the longevity in ectothermic vertebrates may be such gerontological success-related trait as slow metabolism.

The emergence of long-livers in favorable habitats results from the adaptive changes that include emergence of traits favorable for longevity at the molecular and cellular levels (maintenance of genetic stability, etc.) or at the entire organism level (e.g., neoteny) [33, 34].

HALLMARKS OF GERONTOLOGICAL SUCCESS IN REPTILES AND AMPHIBIANS

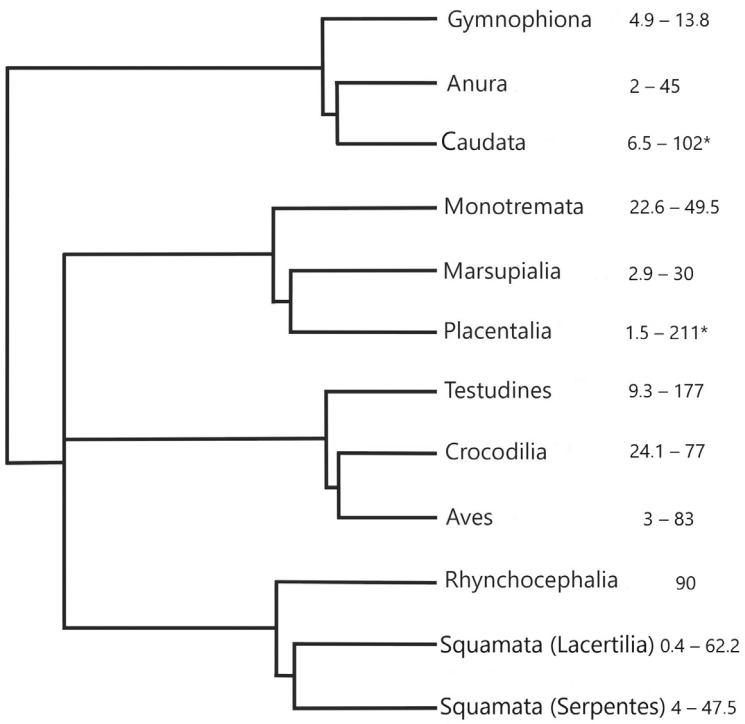
Amphibians and reptiles have their own gerontological success-related features. Negligible senescence was observed in at least one species in each group of the ectotherms (frogs, salamanders, lizards, crocodiles, and turtles) [1, 32].

Aging and longevity in reptiles and amphibians. Slowly aging wild turtles are the leaders among the studied Tetrapoda with respect to the degree of association between low metabolism and slow aging/long LS.

For example, the longest LS was found for the largest representatives of tortoises (Testudinidae), such as the Galapagos giant tortoise (reaching the length of 2 m and weighing up to 500 kg) and Aldabra giant tortoise (*Aldabrachelys gigantea*, or *Testudo gigantea*). The latter is a little smaller, although it holds the record for the LS among reptiles [32]. According to the Anage database, the LS of the largest (up to 7 m in length and weighing up to 2000 kg) representative of the Order Crocodilia, the saltwater crocodile *Crocodylus porosus*, is more than 100 years, although this information needs verification ("…might be true"). The factors favoring long LS in this crocodile include an extremely high resistance to infections (and, as a result, acute phenoptosis), which is due, inter alia, to the specific features of its microbiome [18], ability to rapidly switch metabolism and undergo hibernation, when necessary, well-developed osmoregulation, parental care (protection of eggs), and almost complete absence of natural enemies [35]. In amphibians, a relatively long LS is typical of tailed amphibians. The longevity champion among these animals is the olm (*Proteus anguinus*), whose (calculated) LS exceeds 100 years. Large salamanders have a longer LS compared to the small ones. The maximum LS in tailless amphibians does not exceed 30-45 years (figure).

The record holders include the common toad *Bufo bufo* (40 years) and very large (up to 1.4 kg with a body length of more than 24 cm) African bullfrog *Pyxicephalus adspersus* (45 years).

Below, we discuss the traits contributing to longevity (gerontological success) that are typical of long-lived ectotherms (crocodiles and tortoises) and com-



The life span (LS) values for different taxa of Tetrapoda. Numerical intervals indicate the LS range (in years) within a given taxon. In case the Anage database contains only one species of the indicated taxon, the LS for this species is shown; * calculated value.

pare them with the traits of other representatives of ectotherms (scaled reptiles) and endotherms (birds and mammals). Revealing the trends in the pace and shape of aging in animals requires a well-developed mathematical apparatus. Thus, the maximum LS values for mammals (211 years for the bowhead whale) and amphibians (over 100 years for the olm) have been calculated. In addition to the approaches used for studying physiological, morphological, and behavioral characteristics, various mathematical methods have been developed for analyzing the data on the LS (value characterizing the fast–slow continuum), pace of aging (relative rate of age-related increase in mortality), and association between the LS and various factors, such as body size and temperature, encephalization, protection of occupied ecological niches, presence of protective structures (e.g., carapace and osteoderms), habitat temperature, etc., as well as the effect of these factors on the distribution of LS as a statistical value.

Thermoregulation. Another important factor influencing longevity is temperature [36]. On one hand, active thermoregulation promotes adaptation by allowing colonization of colder habitats and increasing mobility [37], while many ectothermic animals (e.g., amphibians and reptiles) are active only at certain ambient temperatures. On the other hand, endothermic animals (birds and mammals) spend a large amount of energy to maintain a relatively constant body temperature at varying ambient temperatures. The evolution of endothermy is associated with changes in many parameters, such as metabolic rate, resilience, and aerobic capacity. High body temperature promotes an increase in the production of reactive oxygen species (ROS), which are important factors of aging [38-40].

Moreira et al. [36] have shown that the body temperature of endothermic animals is not significantly higher than that of ectotherms. At the same time, the rates of changes in the body temperature vary considerably in the evolution of terrestrial tetrapods. Moreira et al. [36] have calculated the body temperatures for the ancestors of major clades of tetrapods using a multiple variance Brownian motion model. The estimated body temperature for the ancestor of tetrapods was 28.0°C (95% confidence interval 23.7-32.4). The estimated body temperatures of the ancestors of crocodilians (θ = 30.1°C [27.3-32.9], lepidosaurs (Squamata and Rhynchocephalia) (θ = 28.5°C [24.0-32.9]), and turtles (θ = 27.5°C [23.6-31.3]) were similar to the body temperature of the inferred ancestor of tetrapods. The ancestors of mammals (θ = 32.3°C [28.8-35.6]) and birds (θ = 39.4°C [37.5-41.4]) had higher body temperatures, while the ancestors of amphibians (θ = 24.0°C [20.2-27.9]) had evolved lower body temperatures.

Within-group variance of body temperature is much lower in mammals and birds than in amphibians. Values for crocodiles, lepidosaurians, and turtles are intermediate and close to the average value for the entire tree.

The authors found that body temperatures show strong phylogenetic signal and conservatism, i.e., body temperature usually reflects the evolutionary history of a species. Closer species have more similar body temperatures, while some lineages have retained similar temperatures during surprisingly long periods of time (hundreds of millions of years). The body temperatures of tetrapods are often unrelated to the climate, but is significantly associated with the day-night activity patterns. Phylogenetic analysis of variance revealed no significant differences between the mean body temperatures of nocturnal and diurnal tetrapods in general, nor within turtles and amphibians; however, the differences between the body temperatures in the clades of birds and lepidosaurs were significant, and mammals approached significance. Importantly, the differences between nocturnal and diurnal species were significant across ectotherms and across endotherms. In ectothermic animals and, surprisingly, in endotherms, the body temperatures are usually higher in diurnal species than in nocturnal ones. Therefore, the body temperatures are largely related to the phylogeny and diurnal/nocturnal activity patterns within and among the groups of tetrapods, rather than to the climate and the endotherm–ectotherm divide [36].

Physiological aging. In contrast to mammals, turtles and crocodiles continue to grow throughout the lifetime and are characterized by extremely slow demographic senescence and physiological aging [41]. It is believed that some species, such as turtles and tortoises, can manifest negligible senescence, without a marked increase in the mortality rate [42] and worsening of body physiological state with age [43]; scaled reptiles take an intermediate position [44]. Some authors assign crocodiles to the group of species with negligible senescence that also includes tortoises [18, 41]. At the same time, scaled reptiles (Squamata) display both physiological aging (accumulation of age-related degenerative changes, such as increased collagen stiffness, increased content of defective enzyme molecules, slower metabolic rate, and impaired stress response), and reproductive senescence (age-related decline in reproductive capacity and fertility and increase in the reproductive productivity per gram of female body weight) [41, 45]. The data on the gradual senescence of lizards (oriental garden lizard *Calotes versicolor*) and snakes (grass snake *Natrix natrix*) confirm the concept on the commonality of aging events in scaled reptiles and vertebrates [41]. The aging events common for amphibians and mammals include an increase in the number of collagen crosslinks, accumulation of pigments lipofuscin and melanin (hallmarks of aging), decrease in the metabolic rate, and loss of immunocompetence. An advantage of scaled reptiles compared to mammals is a less pronounced age-related increase in mortality [10] and reproductive senescence [41]. In contrast to mammals, amphibians are characterized by polyphyodonty, as well as the maintenance of neurogenesis, myogenesis, and oogenesis throughout adulthood [46]. A similar assumption (based on the idea of positive relationship between the metabolic rate and accumulation of damage) states that cold-blooded animals living in a warm climate age faster than their relatives inhabiting colder areas. Reinke et al. [32] verified this hypothesis using the data on the average, maximum, and minimum temperatures in the habitats occupied by the studied populations. It was found that reptiles indeed demonstrate a weak positive relationship between the environmental temperature and aging rate. In amphibians, however, this relationship is the opposite: frogs and salamanders living in cool climates age on average faster than their counterparts inhabiting warmer regions. At high temperatures, aging is faster in reptiles and slower in amphibians. It was shown that the age of sexual maturity, median age, and LS of the Andrew's toad (*Bufo andrewsi*) increased with the decrease in the mean annual temperature, while the age of sexual maturity increased with the decrease in the temperature seasonality, implying that temperature is the most important factor of the habitat. At the same time, the body size increased with the increase in precipitation during the driest month and UV-B seasonality, but did not depend on temperature, which is against the Bergmann's rule [47].

Age-related changes in the mortality rate (actuarial aging rate). An extensive comparative study of turtles living in nature and at zoos and aquariums revealed that ~75% of 52 investigated species demonstrated slow or negligible aging. The body mass of turtles positively correlated with the adult LS. For approximately 80% turtle species, the aging rates were lower than in modern humans [43]. It should be noted that although turtles in particular and reptiles in general have been considered as "icons" of longevity and resistance to aging [23, 48], there are some studies refuting this idea [49, 50]. However, this controversy does not apply to large turtles with the unlimited growth, but rather to several small members of the Emydidae family (American freshwater turtles), such as the common box turtle *Terrapene carolina* (138 years), European pond turtle *Emys orbicularis* (120 years), Blanding's turtle (*Emydoidea blandingii*, 77 years), and painted turtle *Chrysemys picta* (61 years), which are considered to be non-aging despite their limited growth. Similar to the freshwater turtle *Chrysemys picta* (Emydidae) described by Warner et al. [49], a slow age-related increase in the mortality was demonstrated for small (shell size, 23-35 cm) terrestrial African tortoises, such as the forest hinge-back tortoise *Kinixys erosa* (LS 24.8 years), Home's hinge-back tortoise *Kinixys homeana*, and Bell's hinge-back tortoise *Kinixys belliana nogueyi* (LS 26.5 years) of the Testudinidae family, i.e.,

the family that includes the gopher tortoise, for which Jones et al. [10] have shown negative aging. The relationship between the mortality rate and age in nature was almost linear and reached 100% at 17 years [51]. In view of the above, it becomes even more important to assess the mortality persistence (the period during which mortality does not increase; a plateau in the survival curve) and the characteristics of LS distribution.

Jones et al. [10] analyzed the mortality of animals and plants in the period from puberty to the age corresponding to 95% death of the original sexually mature cohort using as a criterion the presence/absence of senescence (the ratio of mortality at the age corresponding to 95% death of the cohort to the average mortality for the entire period under study). Although the gopher tortoise (*Gopherus agassizii*) was declared the most non-aging animal, the freshwater crocodile *Crocodylus johnstoni* ended up in the middle of the list, while long-living humans (Japanese women) and animals demonstrating a near-zero mortality for a long period of time (Southern fulmar *Fulmarus glacialoides*) were classified as the most aging species. Due to the high background mortality at the early age, the LS_{95} for the extremely long-lived Scots pine *Pinus sylvestris* was 30 years. Regarding long-lived species with a less marked age-related increase in mortality (e.g., freshwater crocodile *C. johnstoni*, long-wristed hermit crab *Pagurus longicarpus*, Scots pine *Pinus sylvestris*), as well as animals with the average LS that reach the barrier of 5% survival before they demonstrate physiological senescence, the method suggested by Jones et al. allows to characterize only a small part of their life cycle, but not to assess manifestations of aging at its late stages. For example, the great tit *Parus major* was assigned to non-aging species, although it simply has no time to age because of a high external mortality caused by predation pressure (the impact of mortality due to internal causes will be low here). Its population comes to an end even before reaching 50% of the species-specific LS.

In terms of gerontological success, it should be noted that although the great tit is a biologically successful species, it has no traits contributing to longevity that would distinguish it among other birds. Its LS (15.4 years) is not something outstanding for birds either. At the same time, humans and Southern fulmars, despite being susceptible to senescence (their mortality rate increases starting at a certain age), have the traits contributing to the gerontological success (see the article by Skulachev et al. [33] for such traits in humans and naked mole-rats).

Similarly, Cayuela et al. [51] compared the age-dependent dynamics of mortality in three species of terrestrial tortoises of the Testudinidae family [forest hinge-back tortoise *K. erosa* (LS 24.8 years), Home's hinge-back tortoise *K. homeana*, and Bell's hinge-back tortoise *K. belliana noguey* (LS 26.5 years)] and three snake species [Gaboon viper *Bitis gabonica*, rhinoceros viper *Bitis nasicornis*, and spotted night adder *Causus maculatus* (LS 6.6 years)]. The relationship between the mortality rate and age in *Kinixys* tortoises was positive and linear, suggesting a gradual slow increase in mortality throughout the entire lifetime of these animals. On the contrary, in the *Bitis* and *Causus* snakes, the relationship between the mortality rate and age was dramatically negative, indicating a positive senescence in tortoises and negative senescence in snakes [51]. In other words, according to Gompertz, it would be much more difficult to predict the percentage of individuals with the average LS, the number of individuals with 25% and 75% of the maximum species-specific LS, as well as the number of long-livers (90%) and super-long-livers (95%) for amphibians and reptiles (not to mention long-lived cnidarians or, even so, woody plants) than for humans. We have arrived to a conclusion that the classification proposed by Jones et al. [10] allows to divide animals and plants only approximately based on the degree of age-related increase in the probability of death, while assessment of susceptibility to physiological senescence requires more complex models and indicators [34, 52, 53].

Coefficient of variation of LS (CV_{LS}). We have studied CV_{LS} (as a standard deviaton of values relative to the mean, %), as well as the asymmetry and excess coefficients, in various representatives of the Animalia [52, 53] using the data of the Max Planck Institute for Demographic Research [10]. In contrast to humans and laboratory animals, the values obtained for the overwhelming majority of studied species were heterogeneous due to a great influence of background mortality in nature, as well as the non-monotonous total mortality, especially at the earliest age. According to our analysis [52, 53] of the data obtained by Jones et al. [10], the CV_{LS} value for the entire cohort of the freshwater crocodile (C. *johnstoni*) was 195%, i.e., the sample was extremely heterogenous (table).

To smooth out the problem of abnormally high mortality (for example, infant and child mortality), a truncation of the age interval under consideration is used, for example, ages only up to the death of 95% of individuals, or only the age from reaching sexual maturity until the death of 95% of individuals (LS_{95}) can be considered [10, 32].

As mentioned above, this parameter is not ideal but yet more reliable for testing the models (verifying the association between the effects of various environmental factors and LS) than the maximum LS, which strongly depends on the sample size. If an animal can die with a 1-to-100 probability of at the age of 10 years and with the same probability at the age of 90 years, the senescence is negligible. When using truncated data sets, the parameters of LS distribution in human are calculated starting from the age of 10 years (when

Comparison of parameters of LS distribution for reptiles and humans

Species	Order	LS	Number of years since birth excluded from analysis	CV_{LS}, %	A_s	E_s
Reptiles						
Viviparous lizard (*Lacerta vivipara*)	Scaled reptiles (Squamata)	11	**0**	**69**	**2.41**	**5.3**
			1	56	0.84	–0.29
Desert tortoise (*G. agassizii*)	Turtles (Testudines)	64	**1**	**160**	**5.59**	**44.9**
			1	135	4.42	26.51
			11	117	1.89	3.3
Freshwater crocodile (*C. johnstoni*)	Crocodiles (Crocodilia)	55	**0**	**195**	**3.46**	**12.44**
			1	92	1.08	0.38
			2	60	0.79	–0.01
			11	34	0.86	0.38
Humans (*Homo sapiens*)						
Japanese women in 2009	Apes (Primates)	122	**0**	**16**	**–2.23**	**8.28**
			10	16	–1.73	4.63
Swedish women born in 1881			**0**	**58**	**–0.6**	**–1.12**
			1	47	–0.85	–0.51
			10	37	–0.91	–0.08
Ache people			**0**	**101**	**0.54**	**–1.25**
			2	61	–0.1	–1.29
			10	55	–0.17	–1.2

Note. Coefficients of asymmetry (A_s), excess (E_s), and variation (CV_{LS}) of LS in reptiles as compared to humans from different countries (Japanese and Swedish women, and Ache people living in the wild). The values for the entire cohort are shown in bold. The values within a species are grouped with respect to the number of years since birth excluded from analysis.

the increase in the age-related mortality starts) [54] or from the age of 12-15 years (age of sexual maturity) [10]. Thus, reducing the contribution of the age-independent component resulted in the CV_{LS} decrease from 60% to 15-20% (table). Similar CV_{LS} values were found in twins (i.e., when the difference in the effect of genetic component was close to zero) [55].

To illustrate to what extent 100% CV_{LS} indicates the scatter of LS values, let us consider the dispersion of LS values in a cohort for which the LS is determined by the coin toss: tails correspond to 0 years, heads – to 100 years. Therefore, in addition to the maximum LS, there will be one more region, in which the values will concentrate, and this region will be most distant from the longest LS (the situation that maximizes the CV_{LS}). The average LS in this case will be 50, the standard deviation will also be 50, and their ratio (CV_{LS}) will be 1 (or 100%). Accordingly, in the case of even greater variance, with a larger number of low LS values (predominance of external mortality, which prevents individuals from reaching their species LS of 100 years), the CV_{LS} value can increase even more.

The heterogeneity of a cohort with the excluded first year of life (CV_{LS} = 92%) decreases due to the removal of infant mortality. When the first two years of life are excluded from the analysis, CV_{LS} decreases to 60%. Exclusion of the first 11 years of life (i.e., before the age of sexual maturity according to Jones et al.) results in the CV_{LS} decrease to 34% (table), while the asymmetry and excess do not change significantly.

Therefore, exclusion of the first two years of life is enough to eliminate the effect of extremely high infant mortality, while truncation at the age of sexual maturity decreases CV_{LS} more than threefold. In all the cases, there is a significant right-side asymmetry, indicating a high mortality rate at the early age that decreases later in life.

The value of excess (kurtosis) for the entire cohort is unacceptably high; in other cases, the excess is close to zero. The CV_{LS} value for the entire cohort of the *Lacerta vivipara* lizard was 69% due to the high mortality rate in the first year of life. Exclusion of individuals that had died during the first year decreased CV_{LS} to 56%, indicating that the heterogeneity of the population was preserved. The sample of the desert tortoise *G. agassizii* was most heterogeneous, as CV_{LS} for the entire cohort was 160% (an extremely high value). It can be suggested that at such values, neither CV_{LS}, nor the mean characterize the course of aging of a studied population. Apparently, despite the long LS and resistance to aging, the effect of infant mortality was too high. When individuals that had died in the first year of life (infant mortality) were excluded, the CV_{LS} in this cohort was 98%. When the first 11 years of life were excluded, CV_{LS} became 56%. Although CV_{LS} decreased after exclusion of 11 years (due to the removal of infant mortality, as well as to the reduction in the number of individuals), it still remained very high. High mortality rate was observed at an early age only; it became low later in life and did not increase with age. Our calculations showed that in tortoises, it is necessary to exclude the first 25 years of life for a cohort to reach a partial homogeneity with respect to LS (CV_{LS} = 33%). Until that age, the LS of tortoises to a great extent depends on the background mortality. Probably, this can explain the debates on whether tortoises get old (whether the probability of their death increases with age) that have flared up in recent years.

Maintenance of ability for growth and reproduction. A unique physiology of reptiles, indeterminate growth, and fecundity increasing throughout the entire lifetime of adult females have motivated a number of the studies aimed to elucidate how physiology at the mechanistic level, life at the organismal level, and natural selection at the evolutionary time scale regulate LS in this diverse taxonomic group [56-60]. In terms of gerontological success, both rapid growth (with an increase in the metabolic rate) and its quick cessation upon reaching a species-specific size seem to be unfavorable. From the longevity point of view, the most efficient strategy would be retaining the ability to grow slowly throughout the lifetime [18]. The examples of such strategy can be found across the entire evolutionary tree, from hydras, corals, and sponges to baleen whales. Modern Archosauria have retained all of the above growth strategies [61]. In each taxon, there are idioadaptations ensuring biological success of its members and, accordingly, different LSs. For example, short LS of a large animal would make this animal uncompetitive; therefore, the larger the animal, the longer the LS (in a general case). On the other hand, large size makes an animal more sensitive to abrupt environmental changes (due to high requirements of such organism for resources and its sensitivity to the living conditions) [62, 63]. Giant species have become extinct in almost all orders of vertebrates, although their size made them virtually invulnerable (giant tortoises and crocodiles, giant sloths, deer, rhinos, etc.). Large amphibian *Rhinesuchus whaitsi* that looked like a crocodile because of its size and general appearance (“rasp crocodile”) had not survived the Permian–Triassic extinction 250 million years ago.

The rate of evolution in reptiles is usually low, but sometimes they develop quickly in response to environmental changes (e.g., their size increases with the climate warming) [64]. Ancestral forms of Archosauria were characterized by a more rapid growth and higher metabolic rate compared to their descendants [65, 66]. The transition to slow growth took place upon the emergence of early Crocodilomorpha in the Late Triassic. The Archosauria clade contained rapidly growing species of Pseudosuchia, which also had not survived the mass extinction in the Late Triassic [61]. Crocodiles, which have not changed their appearance or ecological niche (tropical wetlands), are a characteristic example of stabilizing selection [67]. Having found the optimal state, crocodiles maintain it until the environment forces them to adapt to new conditions [64].

Although many representatives of the order Crocodilia continue growing throughout the entire lifetime [41], it was reported that the growth of the American alligator (*Alligator mississippiensis*; Alligatoridae) stops sometime after maturation. Tortoises demonstrate two types of growth: there are non-aging species of land tortoises (Testudinidae) that grow unlimitedly throughout the lifetime [Aldabra giant tortoise *T. gigantea* (=*A. gigantea*), desert tortoise *G. agassizii*] and small tortoises, whose growth stops by the age of 30-40 years. The latter are primarily small representatives of the Emydidae family (American freshwater turtles), including the common box turtle *T. carolina* (LS, 138 years), European pond turtle *E. orbicularis* (120 years), the Blanding’s turtle *E. blandingii* (77 years), and pained turtle *C. picta* (61 years). However, some members of this group this group (*T. carolina* and *E. orbicularis*) demonstrate negligible senescence [1, 48, 68]. It was also suggested that sea turtles have a determinate growth [69]. However, even if the growth is determinate, its continuation after reaching sexual maturity is normal for reptiles and distinguishes them from mammals and birds [70]. For example, the ratio between the body length at the age of sexual maturity and maximum

body length of an adult individual is 0.95 for the Asian elephant (*Elephas maximus*), 0.9 for the fur seal (*Arctocephalus forsteri*) and 0.97 for the polar bear (*Ursus maritimus*) [71-73]. In snakes, tortoises, and lizards, this ratio is on average 0.68, 0.70, and 0.74, respectively [74, 75].

Safety provision. As we have already discussed [15], the evolution of longevity is promoted by the development and improvement of defense mechanisms and mechanisms for colonization of protected ecological niches. Amphibians have a number of adaptive limitations, such as living in wet habitats, inability to live in sea water because of the lack of pelvic kidneys, primitive defense systems (mainly, venoms), relatively small size (there are no amphibians weighing more than 100 kg), the absence of egg amniotic membrane, and the absence of well-developed active defense systems. In reptiles, such defense systems are shells in tortoises and impenetrable skin in crocodiles (adaptations that amphibians lack). Some examples of "more active" defense adaptations in tetrapods are venoms excreted by skin glands or special structures (e.g., fangs). Phylogenetic studies have shown that each order has its own model of evolution with respect to venomousness. In particular, the evolution of venom production is much less dynamic than the evolution of intake of toxins with food. Finally, in contrast to amphibians, reptiles demonstrate a positive association between a higher species diversity and evolution of production and use of venoms [76]. If an animal is protected against predators, e.g., by a strong carapace or inedibility/toxicity/venomousness, we can expect that, all other things being equal, it will grow old slower than its unprotected relatives. Reinke et al. [32] considered two types of protective adaptations – physical (tortoise shells, strong scales in crocodiles and some scaled reptiles) and chemical (various venoms) – and showed that the aging of species with protective adaptations is indeed on average slower compared to the unprotected species. The mean value of the coefficient β_1 in the Gompertz equation characterizing the rate of aging is 0.05 in physically protected species, 0.28 in chemically protected species, and 0.47 in unprotected species, demonstrating that protected species are tenfold more advantageous with respect to this parameter.

Encephalization (increase in the brain size relatively to the body size), which positively correlates with longevity in mammals, can negatively correlate with longevity in other vertebrates due to the extreme energy consumption by the brain that might exceed the benefit of cognitive advantages of a large, more developed brain. For example, in cartilaginous fishes (but not in bony fishes), encephalization correlates negatively with the species-specific LS [77]. Studying the trade-off between changes in the brain size and longevity in 265 species has shown a negative correlation between the brain size and LS in reptiles (similar to cartilaginous fishes [77]), but not in amphibians [78]. Analysis of this correlation in 40 frog species (taking into account the influence of their common phylogenetic origin and body size) has shown a positive correlation between the brain size, age of sexual maturation, and LS (despite the fact that tailless amphibians generally do not have a high LS compared to other amphibians) [79]. Moreover, frogs with longer LS have more developed ventral regions of the brain, including olfactory bulbs [79].

DISCUSSION

Combination of evolutionary success and longevity (evolutionary strategies). The evolutionary success of a taxonomic group is determined by its biological progress. The criteria of biological progress include an increase in the number of individuals, area expansion, and progressive differentiation, i.e., an increase in the number of systematic groups comprising this taxon. A long-term presence of a particular group in the history of life on Earth *vs*. rapid extinction is also regarded as an evolutionary success. A high number of individuals in a population can be maintained by a large number of offspring (born at one time or over N generations) and a short LS (strategy 1) or by a small number of offspring (born at one time or over N generations) and a long LS (strategy 2). A combination of high fecundity and long LS (strategy 3) is relatively rare and usually associated with a high early mortality (turtles, fish). Species with a short LS and small number of offspring (strategy 4) are typically unable to maintain a large population size and become extinct. In contrast to mammals, the longevity champions among amphibians and reptiles discussed in this article, namely, turtles and crocodiles, follow strategy 3 (a combination of high fecundity and long LS). In our opinion, such combination of elements of the r- and K-strategies can be explained by a high offspring mortality at the early growth stages. Thus, the number of offspring remaining at the beginning of cohort's life is already small (which is characteristic of the K-strategy organisms). The mechanisms and features of longevity assurance in the course of evolution were discussed in our previous article [15]. Briefly, they include (i) *direct selection for delayed aging*. All other things being equal, a long life is always better than a short one as it leaves more time for reproduction and, hence, higher fitness (genetic contribution to subsequent generations). This makes us wonder why such apparently harmful trait as aging is conserved in the evolution; (ii) *indirect selection for delayed aging*, which leads to the development of adaptations that increase the organism's defense against certain dangers. Such adaptations can,

as a side effect, result in the extension of life. For example, high regeneration capacity protecting against injuries can also occasionally slow down aging; (iii) *direct selection for accelerated aging* (phenoptosis hypothesis), when aging either accelerates the evolution of some useful traits or ensures inheritance of resources and kin selection, as it has been shown for *Caenorhabditis elegans* and some salmonids [15, 80, 81]. In reptiles, acute phenoptosis leading to rapid aging and death (similar to the death of marsupial mice after mating and salmonid fish after spawning) has been shown for the African skink *Mabuya buettneri* [41]; (iv) *indirect selection for accelerated aging* (antagonistic pleiotropy hypothesis [5]), which is based on the fact that many alleles increase adaptability at the early age (e.g., early fecundity) at the cost of more rapid decrease in the adaptability at the older age. Selection favors such alleles because the number of individuals that live to an older age is always less than the number of individuals who survive to an earlier age even in the absence of aging. Hence, the overall damage to the adaptability from the late-onset deleterious traits is always less than the damage from the early-onset ones (i.e., early-onset traits are more important to selection than the late-onset traits). As external nonselective mortality increases, the early-onset traits become more important for selection than the late-onset ones; in other words, the evolution of longevity favors safety; (v) "*drift threshold*," when the probability of surviving to a certain age decreases with age even in nonaging organisms, because there is no zero mortality [4]. Therefore, later manifestation of a harmful effect of an allele suggests weaker selection against it. Sooner or later, there comes an age when the selection eliminating mutations deleterious at that or later age can no longer resist the drift, leading to the free accumulation of such mutations. Medawar called it "selection shadow" (implying an existence of the age that cannot be reached by the "light" of purifying selection), while a more common name is the "drift limit." The higher the external nonselective mortality rate, the earlier the age of the drift threshold for deleterious mutations of a fixed level of harmfulness. Therefore, the safety of an organism contributes to the evolution of longevity.

Efficiency of gerontological success in reptiles and amphibians. Below, we summarized the factors of gerontological success, both critical and less significant for the longevity in reptiles and amphibians. The first of the tentative causes of longevity is cold-bloodedness; the second one is body size (generally, the larger the size, the longer the LS). However, in reptiles and amphibians, lower metabolic rate (compared to mammals) and ectothermy do not necessarily result in high LS (figure). Thus, there are long-livers among large crocodiles and tortoises (in contrast to mammals, long-livers are found among terrestrial species but not among sea turtles). We also noted a trend toward an increase in the LS for the largest species in mammalian taxa, which is due to the association between these parameters in the evolution. In mammals, this is true for the baleen and toothed whales, walruses and seals, primates, odd-toed ungulates, and some other groups. The exceptions are the taxa in which the size of animals has not increased but rather decreased during the evolution (bats) and animals that had diverged early from a given branch of the evolutionary tree (e.g., family Bathyergidae that diverged from other rodents). The tuatara (*Sphenodon punctatus*) is also characterized by a long LS (90 years), but, unfortunately, it is the only representative of Rhynchocephalia. Scaled reptiles (Squamata) do not typically include long-lived species [82]. Nevertheless, the studies of aging in snakes have confirmed the hypothesis that links longer LS to the mechanisms of free radical generation and DNA repair [56].

Phylogenetic analysis of variance (ANOVA) of body temperature at the clade level showed a significant difference between the ectothermic and endothermic animals. The difference became even more pronounced for the amniote clades solely, when amphibians were excluded from analysis. Endothermic animals have lower rates of evolutionary changes in body temperature than ectotherms. Amphibians show strong differences in this parameter between each other compared to other tetrapods. They have lower average body temperatures and higher rates of evolutionary changes in the body temperature. Therefore, the greatest differences in the evolution of body temperature in tetrapods can be seen between amphibians and amniotes. No correlation between the LS and body temperature was found in reptiles and amphibians. The dependence on external temperatures and a low metabolic rate do not guarantee longevity in cold-blooded animals [32].

Similar to ectotherms, lower metabolic rate in endotherms does not imply an increase in the species-specific LS. For example, birds usually age more slowly than mammals of a similar size, although their body temperature tends to be higher. Previously [15], we discussed the fact that mammals have almost entirely opted for a greater mobility and lesser dependence on low temperatures, while losing a potential longevity as a trade-off. Mammals live shorter lives than birds, reptiles, and amphibians of the same body weight. As for the all-time record holders, only baleen whales have an approximately 20% longer LS than giant tortoises, with a more than a 100-fold difference in weight. Nevertheless, LS is unevenly distributed across the evolutionary trees of mammals, amphibians, and reptiles. As has already been mentioned, such universal approach to the longevity assurance as slowing down metabolism is untypical for mammals

and observed in the groups that had separated early from the common evolutionary tree, e.g., in the Bathyergidae rodents (mole-rats). Representatives of the Bathyergidae family live longer lives (especially considering their body weight) [83] compared to other evolutionary successful but generally short-lived rodents [84]. Austad [2] has established that marsupials (which form a sister clade to placental mammals) are characterized by a low metabolic rate compared to placentals, but have no long-lived species, i.e., have not achieved longevity in return (figure). A placental animal with a comparable body weight will live longer than a marsupial. Moreover, marsupials have lost the evolutionary race on all continents except Australia and, in part, South America (while only one species lives in North America).

Since accumulation of molecular damage, including that resulting from oxidative stress, is an important component of aging, it can be assumed that due to a higher metabolic rate, accumulation of damage in endothermic animals is more rapid than in ectotherms. In this case, warm-blooded animals should age more rapidly than amphibians and reptiles. However, our analysis of data in the present work does not support this assumption. After introduction of necessary corrections for the body mass and evolutionary relationships, the rate of aging in cold-blooded animals proved to be not significantly different from that in warm-blooded animals. At the same time, the rate of aging strongly varies between the species [32, 36].

Slower aging has been shown for amphibians and reptiles protected by shells, osteoderms, or venom; at the same time, species with shells or osteoderms live longer than species with venom or without any protective adaptations [32]. The data on warm-blooded animals do not always confirm the "metabolic hypothesis" either. This hypothesis works well at the level of intraspecific variability (more rapid aging of individuals with a higher body temperature), but is not that obvious when comparing different species. For example, birds usually age slower than mammals of a similar size, although their body temperature is generally higher. There is no correlation between the LS and body temperature in reptiles and amphibians. Neither low metabolic rate, nor dependence on external temperature guarantee longevity in ectotherms [32].

Evolutionary theories of aging and longevity. The theory proposed by Medawar [4] is based on the classical evolutionary theory of aging, which states that the main cause of aging is an insufficiently strong effect of purifying selection on the late-onset harmful mutations. Even if an animal does not age, it is not immortal and, sooner or later, it will die from some external causes (be it unfavorable environmental temperature/humidity, lack of food, or predation pressure). If the probability of death is constant (does not increase with age), then the probability of surviving until the age X decreases exponentially as X increases. If a mutation reduces organism's viability at the age that few individuals survive to, then this mutation cannot be eliminated by selection. Therefore, harmful mutations with the late-onset effects would accumulate in the population over time, and that is what causes aging [32, 85]. Hence, the overall aging rate determined by the mutation accumulation/selection balance should depend on the level of external, age-independent mortality. For example, if predation pressure is so great that the prey has almost no chance to live for more than two or three years, selection will not efficiently eliminate mutations that reduce the viability beyond that age. As a result, the prey will evolve toward rapid aging (and early reproduction). Conversely, if external threats are minimal, selection will favor the evolution of slow aging. The role of protective adaptations is as follows: if there are any (e.g., hard shell or inedibility/venomousness, etc.), it should be expected that, all other things being equal, members of a given species will age more slowly than unprotected members of the related taxa. Reinke et al. [32] distinguished two types of protective adaptations: physical (tortoise shells, bony scutes in crocodiles and some scaled reptiles) and chemical (all kinds of venoms), and showed that protected species age on average slower than the unprotected ones. We should note that the slower aging of birds compared to mammals is also well accounted for by the "hypothesis of protective adaptations." After all, beside an enhanced resistance to oxidative stress at the cellular level, birds have one of the best protective adaptations invented by nature – the ability to fly. Moreover, birds are threatened only by predators belonging to the same taxon (birds), while terrestrial predatory species are more numerous and more diverse in their taxonomic composition. In addition, predatory species in the bird clade have appeared relatively late, so that the evolution had been occurring for a long time in the absence of predatory birds (not belonging to the Neoaves taxon) [86]. The same is true for bats (no predatory bat species have emerge at all), which live on average much longer than nonflying animals of the same size. In mammals, including naked mole-rats and humans, the role of protective adaptations contributing to the evolution of slow aging and long life might have been played by the developed sociality and existence of protected shelters [33, 34, 87].

In addition to the idea of age-associated weakening of selection pressure, the classic evolutionary theory of aging includes the concept of a balance between early adaptability (i.e., reproductive efficiency at the early age) and long-term maintenance of viability. Other things being equal, what happens at the early reproductive age is more important for selection than what happens later, because it is yet unknown whether

an individual will survive to a later age or not. Therefore, if there is a mutation increasing early adaptability at the cost of a comparable decrease in late adaptability, selection will most likely favor it, even if many individuals have a chance to live until manifestation of the negative effects of this mutation [5]. Apparently, mutations enhancing reproductive efficiency at a young age often do it at the cost of accelerated body deterioration or have other negative late-onset effects (antagonistic pleiotropy). Therefore, we can expect a negative correlation between the components of early adaptability (the rate of attaining sexual maturity, fecundity) and longevity (high LS, slow aging). Depending on the conditions (e.g., predation pressure), some species will choose faster life history strategies ("live fast, die young"), while other species will follow the maxim "make haste slowly". The data on reptiles and amphibians are in good agreement with this hypothesis. Reptiles that reach sexual maturity at a later age are characterized by slower aging and longer life than those with early maturation. Amphibians demonstrate a significant positive relationship between fecundity (the number of eggs hatched per year) and aging rate. Similar to reptiles, the rate of attaining sexual maturity in amphibians shows a negative correlation with the LS. These data can explain an exceptional longevity of tortoises, since they have both good defense mechanisms and a slow lifestyle (although advanced cognitive functions are not associated with longer LS). Therefore, the most important factors influencing the aging rate and LS in tetrapods are environmental temperature, protective adaptations, and age of the reproduction and fecundity onset. An amazing longevity of tortoises is apparently due to the fact that they have shells protecting them from predators. It should be also noted that the LS of large crocodiles seems to be greatly underestimated and, in fact, is more than 100 years for the largest species (see above). As regards to the brain development (encephalization), the cognitive advantages of a larger brain (e.g., better perception of sensory information, cognitive processing, and behavioral flexibility) provide more efficient resistance to the external mortality factors and, consequently, indirectly contribute to slower aging that extends the LS (cognitive buffer hypothesis) [77, 88]. However, according to the disposable soma theory [6], significant energy costs associated with the maintenance of nervous tissue would jeopardize the energy budget of organisms with larger brains, as well as their investment in the maintenance and repair of somatic cells, thereby accelerating aging and reducing the LS. Among ectothermic animals, the high metabolic costs of the nervous tissue formation seem to exceed the cognitive benefits of developing a larger brain. Therefore, natural selection favors optimization of energy expenditures rather than benefits provided by advanced cognitive functions. Other popular hypotheses suggesting that endotherms should age faster than ectotherms because of more active metabolism and that ectotherms living in warm climates should age faster than those living in cooler regions have not been confirmed either.

CONCLUSIONS

In vertebrates, long-lived species can appear among (i) representatives of evolutionary successful taxa and (ii) species that had diverged early from the taxa of evolutionary successful r-strategists. Such taxa are characterized by the emergence of traits that give them an advantage (e.g., eusociality, ability to fly, position at the top of the food chain, etc.) and can often be found together (positive covariation).

Thus, it is assumed that a species-specific LS has a close functional relationship with other anatomical and physiological characteristics of the species, similar in nature to the allometric relationships between body size or metabolic rate and body mass [89].

Different traits demonstrate a varying degree of impact on the LS. Therefore, it is important to distinguish between the following two categories of aging/longevity factors.

(1) Physiological/biochemical/molecular factors with a direct effect on the aging rate [the rate of ROS generation, efficiency of ROS control, activity of particular biochemical pathways and repair enzymes, etc.]. Such factors directly cause acceleration or slowing of aging; they are results of previous selection for longevity, which could be more or less intense depending on the factors from category 2.

(2) Evolutionary factors [sociality, safety, low level of external nonselective (age-independent) mortality; most likely, size also belongs here because large size does not automatically make an animal long-lived but only creates prerequisites for a stronger selection for longevity]. These factors determine the intensity of selection for longevity (or *vice versa*, for a short life), which can be assessed using approaches developed to analyze the dispersion of LS values as a measure of disorder (LS inequality, Gini coefficient, Keyfitz entropy, etc.) [34].

Although there might be many traits promoting longevity, but their effect will be negligible. The relative rate of increase in the LS per unit of increase in any trait evolving in a given taxon (e.g., per unit of weight gain) will indicate the efficiency of this trait in terms of longevity (gerontological success). The same can be said about the rate of evolution of genes responsible for these traits. The presence in a given taxon of genes determining longevity (genes for DNA repair, cancer resistance, antioxidant defense, etc.)

is often associated with the appearance of isoforms of gene products typical for the long-lived species of this taxon. Tortoise shell or sociality of naked mole-rats do not slow aging *per se*. However, these factors increase a probability that the population will undergo more intense selection for longevity. As a result, some traits from category 1 will change, leading to an increase or decrease in longevity.

The traits that give an advantage to a particular taxon (e.g., cephalization in primates) will develop in such taxa more rapidly or to a greater extent compared to other taxa. Gerontologically successful taxa often include species successful even against the existing background (naked mole-rat among Bathyergidae and humans among Hominidae). In addition, due to the long-term stabilizing selection, gerontologically successful species are often relict species, such as the short-beaked echidna *Tachyglossus aculeatus*, platypus *Ornithorhynchus anatinus*, tuatara *Sphenodon punctatus*, crocodiles, including long-lived *C. porosus*, *Crocodylus niloticus*, and *Osteolaemus tetraspis*, olm *P. anguinus*, West Indian Ocean coelacanth *Latimeria chalumnae*, etc. A more complex body structure and faster metabolism can contribute to the occupation of new ecological niches and displacement of other animal groups from the old ones [90]. However, in terms of gerontological success, this might create new potentially vulnerable complex systems, whose probability of failure increases with age (the process of biological aging, "slow phenoptosis"). The latter will be counteracted by the improvement of body defense systems (anti-aging programs, according to Skulachev et al. [34]), which will be reflected in the evolutionary changes in the respective genes. The rate of evolution of genes responsible for the development of traits advantageous for a given taxon (large brain, sociality, shell, enzymes of venom synthesis pathway, etc.) can be compared with the rate of evolution of genes responsible for the anti-aging programs (first of all, DNA repair and antioxidant systems) [60, 91-95]. In addition, the problem of reducing the damage from ROS produced by the mitochondria (one of the most known aging factors) in long-lived species is often solved one way or another [34, 39, 40, 59, 96, 97]. The data on amphibians and reptiles make it possible to find differences in the patterns of LS evolution and aging rate in ectothermic tetrapods compared to endotherms. These parameters proved to be more diverse in amphibians and reptiles *vs*. mammals and birds. Each order of amphibians and reptiles contains non-aging species with almost no age-related increase in the probability of death [among endotherms, species with similar thermoregulation (mesotherms) are naked mole-rat and platypus]. Species with efficient physical or chemical defenses (hard scales, bony carapace, venom glands) tend to live longer and age more slowly than the unprotected species. This fact supports the classical evolutionary hypothesis stating that the age-independent mortality favors the evolution of rapid aging and short LS (strategy 1; see the "Combination of evolutionary success and longevity (evolutionary strategies)" section above). For example, *Drosophila* and nematode *C. elegans* live short lives, but their aging is very evident. Experiments performed by the Markov's group [98] showed that there may be a selection for both a decrease and increase in the LS (aging slows down). Also, there might be situations when a short LS is associated not with fast aging but with high mortality rate, which is sufficient, however, for some individuals to live until maturity and to leave enough offspring for the population to reproduce (e.g., great tit *P. major* in the study by Jones et al. [10]). The hypothesis of evolutionary trade-off between early reproduction and longevity has also been confirmed: species reaching sexual maturity early and producing numerous offspring each year live shorter lives and age faster.

Therefore, the species-specific LS established in the course of evolution results from the balance between several differently directed evolutionary forces. We are especially interested in the traits contributing to the long species-specific LS of tetrapods (traits of gerontological success) and the efficiency of their use. As we have discussed previously [15], the success of mammals as a taxon has been due to homeothermy, encephalization, increase in size, and, most importantly, sociality; however, such trends are generally not typical for tetrapods.

Long LS requires not only a gerontological success (the presence of traits promoting longevity), but also efficient use of these traits, i.e., how the species respond to aging and implement the anti-aging programs. Skulachev et al. [34] formulated this principle as the "multiplicity of aging [and anti-aging] pathways." Before that, there had been two extreme views prevalent in gerontological literature. The first one is the normal damage accumulation theory stating that aging and its rate (fast–slow aging continuum) depend only on the rates of damage appearance and its repair in the body. The other extreme view was represented by the evolutionary theories, first of all, the antagonistic pleiotropy theory (see above), implying that genes responsible for the growth/development/reproduction during the first part of life provide so many benefits that they outweigh their negative effect in the second part of life. In our opinion, these ideas do not contradict each other and can be correct at the same time. For example, if there is a mutation that increases early fecundity in a given species at the cost of accelerated damage accumulation with age, then selection can theoretically support this mutation because, for example, early fecundity in this species appears to be more important for general adaptability than accelerated

damage accumulation. This would be both a typical example of antagonistic pleiotropy and an illustration of the fact that aging depends on the rate of damage accumulation and repair [89]. Both theories seem to be compatible with each other. It is difficult to unambiguously identify such systems and signaling cascades, perhaps, with the exception of those responsible for the growth, proliferation, and regeneration.

In continuation of our work on mammals, here we compared the traits that promote longevity in the sister clades of amphibians and reptiles that include a large number of long-lived species, especially tortoises. The mathematical indicators used to assess a predisposition to longevity in different species include both standard indicators [mortality rate, basal mortality rate, its variance (CV_{LS})] and their derivatives. The protective phenotypes and life-history strategies provide further explanation for the macroevolutionary patterns of aging, while analysis of ectothermic tetrapods in a comparative context expands our understanding of the evolution of aging.

The evolution of longevity is associated with main evolutionary trends, whose criterion is biological progress. Longevity *per se* is very rarely relevant for the evolutionary success; therefore, there is not a single high-ranking taxon whose success is caused by the predisposition for longevity. Indeed, longer LS is rarely advantageous both in the intergroup and intragroup selection. While improving in the process of evolution and ensuring their evolutionary success, taxa can gain some traits contributing to longevity but lose some other traits. The evolution of these processes can be explained within the framework of the theory suggested by Skulachev et al. [34, 81] on the diversity of aging and anti-aging ontogenetic programs in animals in general and in reptiles and amphibians in particular. Thus, the level of external mortality, which determines the selection pressure on the late-onset harmful mutations, and the trade-off between a fast life and a long life (the two factors predicted by the evolutionary theory of aging) in all likelihood have a stronger impact on the evolution of longevity in terrestrial vertebrates than the intensity of metabolism. As regards encephalization, the high metabolic costs of the nervous tissue formation in ectothermic animals apparently exceed the cognitive benefits of developing a larger brain. This leads to the optimization of energy expenditures in the course of natural selection rather than to the development and improvement of cognitive functions.

Other two popular hypotheses suggesting that warm-blooded animals should age faster than cold-blooded animals because of higher metabolic rates and that cold-blooded animals living in the regions with a warm climate should age faster than those living in colder regions, have not been confirmed. This implies that the high metabolic rate leading to the accelerated accumulation of molecular damage is a less important factor in the evolution of aging than selection for the ability to repair this damage. The comment by Sacher [89] that it is not the metabolic rate that matters, but rather the quality of metabolism (i.e., how optimal it is), is in agreement with the theory of gerontological success proposed by us. Apparently, it has to be accepted that metabolic rate is not a crucial factor in the evolution of aging.

Molecular damage of any nature (generation of ROS, loss of telomeres, cytokine production by aging cells, or DNA damage) accumulate faster at a higher metabolic rate. However, the evolutionary fate of a species, i.e., the eventual rate of its aging, seems to be determined not so much by the rate of damage accumulation, but rather by the strength of selection for the ability to repair this damage, which includes, in addition to the DNA repair and antioxidant defense systems [91, 60, 92, 93, 97, 99, 100], the control of mitochondrial ROS production [39, 96] and the presence of extremely diverse (starting already from unicellular organisms) cell death pathways eliminating senescent and transformation-prone cells [34, 101, 102].

In this sense, evolution is stronger than biochemistry. For example, factors affecting the aging rate and LS in tetrapods are temperature, the presence of protective adaptations, and the age of the reproduction and fecundity onset. However, an exceptional longevity of tortoises (in contrast to mammals) seems to be primarily related not to the low metabolic rate, advanced brain, or sociality, but to the presence of defensive structures (shells) protecting them from predators.

However, here it is necessary to mention once again the concept of gerontological success efficiency: factors extremely favorable for the LS in some tetrapods will not necessarily be equally favorable in other tetrapods. Thus, in armadillos (Mammalia, Cingulata) protected with an armor of articulated osteoderms, the longevity quotient (LS adjusted for the body weight, one of the simplest indicators of gerontological success efficiency) varies within a range of 1.12 to 1.5. Only one species, the southern three-banded armadillo *Tolypeutes matacus*, has a relatively high longevity quotient (LQ) (2.46) that is approximately equal to the longevity quotient of the chimpanzee *Pan troglodytes* (2.70). Animals with the top longevity quotient values (calculated for mammals) include naked mole-rat (3.68), humans (4.63), and several species of common bats, with the highest longevity quotient found for the Brandt's bat *Myotis brandtii* (6.43). The improvement, first and foremost, of the mechanisms providing safety is consistent with the defense pathways of naked mole-rats (dwelling in burrows) and chiropterans (ability to fly, which is also one of the best defense adaptations).

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REFERENCES

1. Comfort, A. (1979) *The Biology of Senescence*, Churchill Livingstone, Edinburgh and London.
2. Austad, S. N. (1997) *Why We Age*, John Wiley and Sons, New York.
3. Finch, C. E. (2009) Update on slow aging and negligible senescence – a mini-review, *Gerontology*, **55**, 307-313, doi: 10.1159/000215589.
4. Medawar, P. B. (1952) *An Unsolved Problem of Biology*, H. C. Lewis & Co LTD, London.
5. Williams, G. C. (1957) Pleiotropy, natural selection and the evolution of senescence, *Evolution*, **11**, 398-411, doi: 10.1111/j.1558-5646.1957.tb02911.x.
6. Kirkwood, T. B. L. (1977) Evolution of ageing, *Nature*, **270**, 301-304, doi: 10.1038/270301a0.
7. Rando, T. A., and Chang, H. Y. (2012) Aging, rejuvenation, and epigenetic reprogramming: resetting the aging clock, *Cell*, **148**, 46-57, doi: 10.1016/j.cell.2012.01.003.
8. Skulachev, M. V., and Skulachev, V. P. (2014) New data on programmed aging – slow phenoptosis, *Biochemistry (Moscow)*, **79**, 977-993, doi: 10.1134/S0006297914100010.
9. Vaupel, J. W., Baudisch, A., Dölling, M., Roach, D. A., and Gampe, J. (2004) The case for negative senescence, *Theor. Popul. Biol.*, **65**, 339-351, doi: 10.1016/j.tpb.2003.12.003.
10. Jones, O. R., Scheuerlein, A., Salguero-Gómez, R., Camarda, C. G., Schaible, R., Schaible, R., Casper, B. B., Dahlgren, J. P., Ehrlén, J., García, M. B., Menges, E., Quintana-Ascencio, P. F., Caswell, H., Baudisch, A., and Vaupel, J. W. (2014) Diversity of ageing across the tree of life, *Nature*, **505**, 169-173, doi: 10.1038/nature12789.
11. Pascual-Torner, M., Carrero, D., Pérez-Silva, J. G., Álvarez-Puente, D., Roiz-Valle, D., Bretones, G., Rodríguez, D., Maeso, D., Mateo-González, E., Español, Y., Mariño, G., Acuña, J. L., Quesada, V., and López-Otín, C. (2022) Comparative genomics of mortal and immortal cnidarians unveils novel keys behind rejuvenation, *Proc. Natl. Acad. Sci. USA*, **119**, e2118763119, doi: 10.1073/pnas.2118763119.
12. Martínez, D. E. (1998) Mortality patterns suggest lack of senescence in hydra, *Exp. Gerontol.*, **33**, 217-225, doi: 10.1016/s0531-5565(97)00113-7.
13. Bilinski, T., Bylak, A., and Zadrag-Tecza, R. (2016) Principles of alternative gerontology, *Aging (Albany NY)*, **8**, 589-602, doi: 10.18632/aging.100931.
14. Bilinski, T., Bylak, A., Kukuła, K., and Zadrag-Tecza, R. (2021) Senescence as a trade-off between successful land colonisation and longevity: critical review and analysis of a hypothesis, *PeerJ*, **9**, e12286, doi: 10.7717/peerj.12286.
15. Shilovsky, G. A., Putyatina, T. S., and Markov, A. V. (2022) Evolution of longevity as a species-specific trait in mammals, *Biochemistry (Moscow)*, **87**, 1579-1599, doi: 10.1134/S0006297922120148.
16. Martinez, D. E., and Levinton, J. S. (1992) Asexual metazoans undergo senescence, *Proc. Natl. Acad. Sci. USA*, **89**, 9920-9923, doi: 10.1073/pnas.89.20.9920.
17. Healy, K., Ezard, T. H. G., Jones, O. R., Salguero-Gómez, R., and Buckley, Y. M. (2019) Animal life history is shaped by the pace of life and the distribution of age-specific mortality and reproduction, *Nat. Ecol. Evol.*, **3**, 1217-1224, doi: 10.1038/s41559-019-0938-7.
18. Hoekstra, L. A., Schwartz, T. S., Sparkman, A. M., Miller, D. A. W., and Bronikowski, A. M. (2020) The untapped potential of reptile biodiversity for understanding how and why animals age, *Funct. Ecol.*, **34**, 38-54, doi: 10.1111/1365-2435.13450.
19. Dart, A. (2022) Peto's paradox put to the test, *Nat. Rev. Cancer*, **22**, 129, doi: 10.1038/s41568-022-00447-4.
20. De Magalhães, J. P., and Costa, J. (2009) A database of vertebrate longevity records and their relation to other life–history traits, *J. Evol. Biol.*, **22**, 1770-1774, doi: 10.1111/j.1420-9101.2009.01783.x.
21. Martin, F. J., Amode, M. R., Aneja, A., Austine-Orimoloye, O., Azov, A. G., Azov, A. G., Barnes, I., Becker, A., Bennett, R., Berry, A., Bhai, J., Bhurji, S. K., Bignell, A., Boddu, S., Branco Lins, P. R., Brooks, L., Ramaraju, S. B., Charkhchi, M., Cockburn, A., Da Rin Fiorretto, L., Davidson, C., Dodiya, K., Donaldson, S., El Houdaigui, B., El Naboulsi, T., et al. (2023) Ensembl 2023, *Nucleic Acids Res.*, **51**, 933-941, doi: 10.1093/nar/gkac958.
22. Nielsen, J., Hedeholm, R. B., Heinemeier, J., Bushnell, P. G., Christiansen, J. S., Olsen, J., Ramsey, C. B., Brill, R. W., Simon, M., Steffensen, K. F., and Steffensen, J. F. (2016) Eye lens radiocarbon reveals centuries of longevity in the Greenland shark (*Somniosus microcephalus*), *Science*, **353**, 702-704, doi: 10.1126/science.aaf1703.
23. Congdon, J. D., Nagle, R. D., Kinney, O. M., van Loben Sels, R. C., Quinter, T., and Tinkle, D. W. (2003) Testing hypotheses of aging in long-lived painted turtles (*Chrysemys picta*), *Exp. Gerontol.*, **38**, 765772, doi: 10.1016/s0531-5565(03)00106-2.

24. Voituron, Y., De Fraipont, M., Issartel, J., Guillaume, O., and Clobert, J. (2011) Extreme lifespan of the human fish (*Proteus anguinus*): a challenge for ageing mechanisms, *Biol. Lett.*, 7, 105107, doi: 10.1098/rsbl.2010.0539.
25. Kostanjšek, R., Diderichsen, B., Recknagel, H., Gunde-Cimerman, N., Gostinčar, C., Fan, G., Kordiš, D., Trontelj, P., Jiang, H., Bolund, L., and Luo, Y. (2022) Toward the massive genome of *Proteus anguinus*-illuminating longevity, regeneration, convergent evolution, and metabolic disorders, *Ann. N. Y. Acad. Sci.*, **1507**, 5-11, doi: 10.1111/nyas.14686.
26. Voituron, Y., Guillaume, O., Dumet, A., Zahn, S., and Criscuolo, F. (2023) Temperature-independent telomere lengthening with age in the long-lived human fish (*Proteus anguinus*), *Proc. Biol. Sci.*, **290**, 20230503, doi: 10.1098/rspb.2023.0503.
27. Delhaye, J., Salamin, N., Roulin, A., Criscuolo, F., Bize, P., and Christe, P. (2016) Interspecific correlation between red blood cell mitochondrial ROS production, cardiolipin content and longevity in birds, *Age (Dordr)*, **38**, 433-443, doi: 10.1007/s11357-016-9940-z.
28. Amir, Y., Insler, M., Giller, A., Gutman, D., and Atzmon, G. (2020) Senescence and longevity of sea urchins, *Genes (Basel)*, **11**, 573, doi: 10.3390/genes11050573.
29. Medina-Feliciano, J. G., and García-Arrarás, J. E. (2021) Regeneration in echinoderms: molecular advancements, *Front. Cell. Dev. Biol.*, **9**, 768641, doi: 10.3389/fcell.2021.768641.
30. Korotkova, D. D., Lyubetsky, V. A., Ivanova, A. S., Rubanov, L. I., Seliverstov, A. V., Zverkov, O. A., Martynova, N. Y., Nesterenko, A. M., Tereshina, M. B., Peshkin, L., and Zaraisky, A. G. (2019) Bioinformatics screening of genes specific for well-regenerating vertebrates reveals c-answer, a regulator of brain development and regeneration, *Cell Rep.*, **29**, 1027-1040.e6, doi: 10.1016/j.celrep.2019.09.038.
31. Kolora, S. R. R., Owens, G. L., Vazquez, J. M., Stubbs, A., Chatla, K., Jainese, C., Seeto, K., McCrea, M., Sandel, M. W., Vianna, J. A., Maslenikov, K., Bachtrog, D., Orr, J. W., Love, M., and Sudmant, P. H. (2021) Origins and evolution of extreme life span in Pacific Ocean rockfishes, *Science*, **374**, 842-847, doi: 10.1126/science.abg5332.
32. Reinke, B. A., Cayuela, H., Janzen, F. J., Lemaître, J. F., Gaillard, J. M., Lawing, A. M., Iverson, J. B., Christiansen, D. G., Martínez-Solano, I., Sánchez-Montes, G., Gutiérrez-Rodríguez, J., Rose, F. L., Nelson, N., Keall, S., Crivelli, A. J., Nazirides, T., Grimm-Seyfarth, A., Henle, K., Mori, E., Guiller, G., Homan, R., Olivier, A., Muths, E., Hossack, B. R., Bonnet, X., et al. (2022) Diverse aging rates in ectothermic tetrapods provide insights for the evolution of aging and longevity, *Science*, **376**, 1459-1466, doi: 10.1126/science.abm0151.
33. Skulachev, V. P., Holtze, S., Vyssokikh, M. Y., Bakeeva, L. E., Skulachev, M. V., Markov, A. V., Hildebrandt, T. B., and Sadovnichii, V. A. (2017) Neoteny, prolongation of youth: From naked mole rats to "naked apes" (humans), *Physiol. Rev.*, **97**, 699-720, doi: 10.1152/physrev.00040.2015.
34. Skulachev, V. P., Shilovsky, G. A., Putyatina, T. S., Popov, N. A., Markov, A. V., Skulachev, M. V., and Sadovnichii, V. A. (2020) Perspectives of *Homo sapiens* lifespan extension: focus on external or internal resources? *Aging (Albany NY)*, **12**, 5566-5584, doi: 10.18632/aging.102981.
35. Wilkinson, P. M., Rainwater, T. R., Woodward, A. R., Leone, E. H., and Carter, C. (2016) Determinate growth and reproductive lifespan in the American alligator (*Alligator mississippiensis*): evidence from long-term recaptures, *Copeia*, **104**, 843-852, doi: 10.1643/CH-16-430.
36. Moreira, M. O., Qu, Y. F., and Wiens, J. J. (2021) Large-scale evolution of body temperatures in land vertebrates, *Evol. Lett.*, **5**, 484-494, doi: 10.1002/evl3.249.
37. Clarke, A., and Pörtner, H. O. (2010) Temperature, metabolic power and the evolution of endothermy, *Biol. Rev.*, **85**, 703-727, doi: 10.1111/j.1469-185X.2010.00122.x.
38. Skulachev, M. V., Severin, F. F., and Skulachev, V. P. (2015) Aging as an evolvability-increasing program which can be switched off by organism to mobilize additional resources for survival, *Curr. Aging Sci.*, **8**, 95-109, doi: 10.2174/1874609808666150422122401.
39. Skulachev, V. P., Vyssokikh, M. Y., Chernyak, B. V., Averina, O. A., Andreev-Andrievskiy, A. A., Zinovkin, R. A., Lyamzaev, K. G., Marey, M. V., Egorov, M. V., Frolova, O. J., Zorov, D. B., Skulachev, M. V., and Sadovnichii, V. A. (2023) Mitochondrion-targeted antioxidant SkQ1 prevents rapid animal death caused by highly diverse shocks, *Sci. Rep.*, **13**, 4326, doi: 10.1038/s41598-023-31281-31289.
40. Skulachev, V. P., Vyssokikh, M. Y., Chernyak, B. V., Mulkidjanian, A. Y., Skulachev, M. V., Shilovsky, G. A., Lyamzaev, K. G., Borisov, V. B., Severin, F. F., and Sadovnichii, V. A. (2023) Six functions of respiration: isn't it time to take control over ROS production in mitochondria, and aging along with it? *Int. J. Mol. Sci.*, **24**, 12540, doi: 10.3390/ijms241612540.
41. Patnaik, B. K. (1994) Ageing in reptiles, *Gerontology*, **40**, 200-220, doi: 10.1159/000213588.
42. Alvarez, J. A., and Vaupel, J. W. (2023) Mortality as a function of survival, *Demography*, **60**, 327-342, doi: 10.1215/00703370-10429097.
43. da Silva, R., Conde, D. A., Baudisch, A., and Colchero, F. (2022) Slow and negligible senescence among testudines challenges evolutionary theories of senescence, *Science*, **376**, 1466-1470, doi: 10.1126/science.abl7811.
44. Frýdlová, P., Mrzílková, J., Šeremeta, M., Křemen, J., Dudák, J., Žemlička, J., Minnich, B., Kverková, K., Němec, P., Zach, P., and Frynta, D. (2020) Determi-

nate growth is predominant and likely ancestral in squamate reptiles, *Proc. Biol. Sci.*, **287**, 20202737, doi: 10.1098/rspb.2020.2737.
45. Sparkman, A. M., Arnold, S. J., and Bronikowski, A. M. (2007) An empirical test of evolutionary theories for reproductive senescence and reproductive effort in the garter snake *Thamnophis elegans*, *Proc. Biol. Sci.*, **274**, 943-950, doi: 10.1098/rspb.2006.0072.
46. Kara, T. C. (1994) Ageing in amphibians, *Gerontology*, **40**, 161-173, doi: 10.1159/000213585.
47. Jiang, Y., Zhao, L., Luan, X., and Liao, W. (2022) Geographical variation in body size and the Bergmann's rule in Andrew's toad (*Bufo andrewsi*), *Biology (Basel)*, **11**, 1766, doi: 10.3390/biology11121766.
48. Miller, J. K. (2001) Escaping senescence: demographic data from the three-toed box turtle (*Terrapene carolina triunguis*), *Exp. Gerontol.*, **36**, 829-832.
49. Warner, D. A., Miller, D. A., Bronikowski, A. M., and Janzen, F. J. (2016) Decades of field data reveal that turtles senesce in the wild, *Proc. Natl. Acad. Sci. USA*, **113**, 6502-6507, doi: 10.1073/pnas.1600035113.
50. Bronikowski, A. M., Hedrick, A. R., Kutz, G. A., Holden, K. G., Reinke, B., and Iverson, J. B. (2023) Sex-specific innate immunity and ageing in long-lived fresh water turtles (*Kinosternon flavescens*: Kinosternidae), *Immun. Ageing*, **20**, 11, doi: 10.1186/s12979-023-00335-x.
51. Cayuela, H., Akani, G. C., Hema, E. M., Eniang, E. A., Amadi, N., Ajong, S. N., Dendi, D., Petrozzi, F., and Luiselli, L. (2019) Life history and age-dependent mortality processes in tropical reptiles, *Biol. J. Linn. Soc. Lond.*, **128**, 251-262, doi: 10.1093/biolinnean/blz103.
52. Shilovsky, G. A., Putyatina, T. S., Markov, A. V., and Skulachev, V. P. (2015) Contribution of quantitative methods of estimating mortality dynamics to explaining mechanisms of aging, *Biochemistry (Moscow)*, **80**, 1547-1559, doi: 10.1134/S0006297915120020.
53. Shilovsky, G. A., Putyatina, T. S., Ashapkin, V. V., Luchkina, O. S., and Markov, A. V. (2017) Coefficient of variation of lifespan across the tree of life: is it a signature of programmed aging? *Biochemistry (Moscow)*, **82**, 1480-1492, doi: 10.1134/S0006297917120070.
54. Gavrilova, N. S., Gavrilov, L. A., Severin, F. F., and Skulachev, V. P. (2012) Testing predictions of the programmed and stochastic theories of aging: comparison of variation in age at death, menopause, and sexual maturation, *Biochemistry (Moscow)*, **77**, 754-760, doi: 10.1134/S0006297912070085.
55. Finch, C. E., and Tanzi, R. E. (1997) Genetics of aging, *Science*, **278**, 407-411, doi: 10.1126/science.278.5337.407.
56. Bronikowski, A. M. (2008) The evolution of aging phenotypes in snakes: a review and synthesis with new data, *Age (Dordr)*, **30**, 169-176, doi: 10.1007/s11357-008-9060-5.
57. Robert, K. A., and Bronikowski, A. M. (2010) Evolution of senescence in nature: physiological evolution in populations of garter snake with divergent life histories, *Am. Nat.*, **175**, 147-159, doi: 10.1086/649595.
58. Olsson, M., Wapstra, E., and Friesen, C. (2018) Ectothermic telomeres: it's time they came in from the cold, *Philos. Trans. R. Soc. Lond. B Biol. Sci.*, **373**, 20160449, doi: 10.1098/rstb.2016.0449.
59. Holtze, S., Gorshkova, E., Braude, S., Cellerino, A., Dammann, P., Hildebrandt, T. B., Hoeflich, A., Hoffmann, S., Koch, P., Terzibasi Tozzini, E., Skulachev, M., Skulachev, V. P., and Sahm, A. (2021) Alternative animal models of aging research, *Front. Mol. Biosci.*, **8**, 660959, doi: 10.3389/fmolb.2021.660959.
60. Omotoso, O., Gladyshev, V. N., and Zhou, X. (2021) Lifespan extension in long-lived vertebrates rooted in ecological adaptation, *Front. Cell. Dev. Biol.*, **9**, 704966, doi: 10.3389/fcell.2021.704966.
61. Botha, J., Weiss, B. M., Dollman, K., Barrett, P. M., Benson, R. B. J., and Choiniere, J. N. (2023) Origins of slow growth on the crocodilian stem lineage, *Curr. Biol.*, **8**, 4261-4268.e3, doi: 10.1016/j.cub.2023.08.057.
62. Ripple, W. J., Newsome, T. M., Wolf, C., Dirzo, R., Everatt, K. T., Galetti, M., Hayward, M. W., Kerley, G. I., Levi, T., Lindsey, P. A., Macdonald, D. W., Malhi, Y., Painter, L. E., Sandom, C. J., Terborgh, J., and Van Valkenburgh, B. (2015) Collapse of the world's largest herbivores, *Sci. Adv.*, **1**, e1400103, doi: 10.1126/sciadv.1400103.
63. Fraser, D., Villasenor, A., Toth, A. B., Balk, M. A., Eronen, J. T., Andrew Barr, W., Behrensmeyer, A. K., Davis, M., Du, A., Tyler Faith, J., Graves, G. R., Gotelli, N. J., Jukar, A. M., Looy, C. V., McGill, B. J., Miller, J. H., Pineda-Munoz, S., Potts, R., Shupinski, A. B., Soul, L. C., and Kathleen Lyons, S. (2022) Late quaternary biotic homogenization of North American mammalian faunas, *Nat. Commun.*, **13**, 3940, doi: 10.1038/s41467-022-31595-8.
64. Stockdale, M. T., and Benton, M. J. (2021) Environmental drivers of body size evolution in crocodile-line archosaurs, *Commun. Biol.*, **4**, 38, doi: 10.1038/s42003-020-01561-5.
65. Legendre, L. J., Guénard, G., Botha-Brink, J., and Cubo, J. (2016) Palaeohistological evidence for ancestral high metabolic rate in archosaurs, *Syst. Biol.*, **65**, 989-996, doi: 10.1093/sysbio/syw033.
66. Wiemann, J., Menéndez, I., Crawford, J. M., Fabbri, M., Gauthier, J. A., Hull, P. M., Norell, M. A., and Briggs, D. E. G. (2022) Fossil biomolecules reveal an avian metabolism in the ancestral dinosaur, *Nature*, **606**, 522-526, doi: 10.1038/s41586-022-04770-6.
67. Schmalhausen, I. I. (1982) Organism as a whole in its individual and historic development, in *Izbrannye trudy (Selected works) [In Russian]*, Nauka, Moscow.
68. Edmonds, D., Dreslik, M. J., Lovich, J. E., Wilson, T. P., and Ernst, C. H. (2021) Growing as slow as a turtle: unexpected maturational differences in a small, long-lived species, *PLoS One*, **16**, e0259978, doi: 10.1371/journal.pone.0259978.

69. Omeyer, L. C. M., Fuller, W. J., Godley, B. J., Snape, R. T. E., and Broderick, A. C. (2018) Determinate or indeterminate growth? Revisiting the growth strategy of sea turtles, *Marine Ecol. Progr. Ser.*, **596**, 199-211, doi: 10.3354/meps12570.
70. Hariharan, I. K., Wake, D. B., and Wake, M. H. (2015) Indeterminate growth: could it represent the ancestral condition? *Cold Spring Harb. Perspect. Biol.*, **8**, a019174, doi: 10.1101/cshperspect.a019174.
71. Derocher, A. E., and Wiig, O. (2002) Postnatal growth in body length and mass of polar bears (*Ursus maritimus*) at Svalbard, *J. Zool.*, **256**, 343-349, doi: 10.1017/S0952836902000377.
72. McKenzie, J., Page, B., Goldsworthy, S. D., and Hindell, M. A. (2007) Growth strategies of New Zealand fur seals in southern Australia, *J. Zool.*, **272**, 377-389, doi: 10.1111/j.1469-7998.2006.00278.x.
73. Mumby, H. S., Chapman, S. N., Crawley, J. A. H., Mar, K. U., Htut, W., Soe, A. T., Aung, H. H., and Lummaa, V. (2015) Distinguishing between determinate and indeterminate growth in a long-lived mammal, *BMC Evol. Biol.*, **15**, 214, doi: 10.1186/s12862-015-0487-x.
74. Shine, R., and Charnov, E. L. (1992) Patterns of survival, growth, and maturation in snakes and lizards, *Am. Naturalist*, **139**, 1257-1269, doi: 10.1086/285385.
75. Shine, R., and Iverson, J. B. (1995) Patterns of survival, growth and maturation in turtles, *Oikos*, **72**, 343-348, doi: 10.2307/3546119.
76. Harris, R. J., and Arbuckle, K. (2016) Tempo and mode of the evolution of venom and poison in tetrapods, *Toxins (Basel)*, **8**, 193, doi: 10.3390/toxins8070193.
77. Stark, G. (2022) Large and expensive brain comes with a short lifespan: the relationship between brain size and longevity among fish taxa, *J. Fish. Biol.*, **101**, 92-99, doi: 10.1111/jfb.15074.
78. Stark, G., and Pincheira-Donoso, D. (2022) The evolution of brain size in ectothermic tetrapods: large brain mass trades-off with lifespan in reptiles, *Evol. Biol.*, **49**, 180-188, doi: 10.1007/s11692-022-09562-4.
79. Yu, X., Zhong, M. J., Li, D. Y., Jin, L., Liao, W. B., and Kotrschal, A. (2018) Large-brained frogs mature later and live longer, *Evolution*, **72**, 1174-1183, doi: 10.1111/evo.13478.
80. Skulachev, V. P. (1997) Aging is a specific biological function rather than the result of a disorder in complex living systems: biochemical evidence in support of Weismann's hypothesis, *Biochemistry (Moscow)*, **62**, 1191-1195.
81. Lidsky, P. V., Yuan, J., Rulison, J. M., and Andino-Pavlovsky, R. (2022) Is aging an inevitable characteristic of organic life or an evolutionary adaptation? *Biochemistry (Moscow)*, **87**, 1413-1445, doi: 10.1134/S0006297922120021.
82. Bronikowski, A., and Vleck, D. (2010) Metabolism, body size and life span: a case study in evolutionarily divergent populations of the garter snake (*Thamnophis elegans*), *Integr. Comp. Biol.*, **50**, 880-887, doi: 10.1093/icb/icq132.
83. Dammann, P., Šaffa, G., and Šumbera, R. (2022) Longevity of a solitary mole-rat species and its implications for the assumed link between sociality and longevity in African mole-rats (Bathyergidae), *Biol. Lett.*, **18**, 20220243, doi: 10.1098/rsbl.2022.0243.
84. Burgin, C. J., Colella, J. P., Kahn, P. L., and Upham, N. S. (2018) How many species of mammals are there? *J. Mammal.*, **99**, 1-14, doi: 10.1093/jmammal/gyx147.
85. Giaimo, S., and Traulsen, A. (2022) The selection force weakens with age because ageing evolves and not vice versa, *Nat. Commun.*, **13**, 686, doi: 10.1038/s41467-022-28254-3.
86. Prum, R. O., Berv, J. S., Dornburg, A., Field, D. J., Townsend, J. P., Lemmon, E. M., and Lemmon, A. R. (2015) A comprehensive phylogeny of birds (Aves) using targeted next-generation DNA sequencing, *Nature*, **526**, 569-573, doi: 10.1038/nature15697.
87. Rotger, A., Tenan, S., Igual, J. M., Bonner, S., and Tavecchia, G. (2023) Life span, growth, senescence and island syndrome: Accounting for imperfect detection and continuous growth, *J. Anim. Ecol.*, **9**, 183-194, doi: 10.1111/1365-2656.13842.
88. Van Schaik, C. P., Song, Z., Schuppli, C., Drobniak, S. M., Heldstab, S. A., and Griesser, M. (2023) Extended parental provisioning and variation in vertebrate brain sizes, *PLoS Biol.*, **21**, e3002016, doi: 10.1371/journal.pbio.3002016.
89. Sacher, G. A. (1968) Molecular versus systemic theories on the genesis of ageing, *Exp. Gerontol.*, **3**, 265-271, doi: 10.1016/0531-5565(68)90011-9.
90. Knope, M. L., Bush, A. M., Frishkoff, L. O., Heim, N. A., and Payne, J. L. (2020) Ecologically diverse clades dominate the oceans via extinction resistance, *Science*, **367**, 1035-1038, doi: 10.1126/science.aax6398.
91. Lewis, K. N., Wason, E., Edrey, Y. H., Kristan, D. M., Nevo, E., and Buffenstein, R. (2015) Regulation of Nrf2 signaling and longevity in naturally long-lived rodents, *Proc. Natl. Acad. Sci. USA*, **112**, 3722-3727, doi: 10.1073/pnas.1417566112.
92. Shilovsky, G. A., Shram, S. I., Morgunova, G. V., and Khokhlov, A. N. (2017) Protein poly(ADP-ribosyl)ation system: Changes in development and aging as well as due to restriction of cell proliferation, *Biochemistry (Moscow)*, **82**, 1391-1401, doi: 10.1134/S0006297917110177.
93. Shilovsky, G. A. (2022) Lability of the Nrf2/Keap/ARE cell defense system in different models of cell aging and age-related pathologies, *Biochemistry (Moscow)*, **87**, 70-85, doi: 10.1134/S0006297922010060.
94. Jové, M., Mota-Martorell, N., Fernàndez-Bernal, A., Portero-Otin, M., Barja, G., and Pamplona, R. (2023) Phenotypic molecular features of long-lived animal species, *Free Radic. Biol. Med.*, **208**, 728-747, doi: 10.1016/j.freeradbiomed.2023.09.023.

95. Rafikova, E., Nemirovich-Danchenko, N., Ogmen, A., Parfenenkova, A., Velikanova, A., Tikhonov, S., Peshkin, L., Rafikov, K., Spiridonova, O., Belova, Y., Glinin, T., Egorova, A., and Batin, M. (2023) Open Genes – a new comprehensive database of human genes associated with aging and longevity, *Nucleic Acids Res.*, **52**, gkad712, doi: 10.1093/nar/gkad712.
96. Vyssokikh, M. Y., Holtze, S., Averina, O. A., Lyamzaev, K. G., Panteleeva, A. A., Marey, M. V., Zinovkin, R. A., Severin, F. F., Skulachev, M. V., Fasel, N., Hildebrandt, T. B., and Skulachev, V. P. (2020) Mild depolarization of the inner mitochondrial membrane is a crucial component of an antiaging program, *Proc. Natl. Acad. Sci. USA*, **117**, 64916501, doi: 10.1073/pnas.1916414117.
97. Odeh, A., Eddini, H., Shawasha, L., Chaban, A., Avivi, A., Shams, I., and Manov, I. (2023) Senescent secretome of blind mole rat *Spalax* inhibits malignant behavior of human breast cancer cells triggering bystander senescence and targeting inflammatory response, *Int. J. Mol. Sci.*, **24**, 5132, doi: 10.3390/ijms24065132.
98. Yakovleva, E. U., Naimark, E. B., and Markov, A. V. (2016) Adaptation of *Drosophila melanogaster* to unfavorable growth medium affects lifespan and age-related fecundity, *Biochemistry (Moscow)*, **81**, 1445-1460, doi: 10.1134/S0006297916120063.
99. Jacobs, P. J., Hart, D. W., Merchant, H. N., Voigt, C., and Bennett, N. C. (2023) The evolution and ecology of oxidative and antioxidant status: a comparative approach in African mole-rats, *Antioxidants (Basel)*, **12**, 1486, doi: 10.3390/antiox12081486.
100. Tyshkovskiy, A., Ma, S., Shindyapina, A. V., Tikhonov, S., Lee, S. G., Bozaykut, P., Castro, J. P., Seluanov, A., Schork, N. J., Gorbunova, V., Dmitriev, S. E., Miller, R. A., and Gladyshev, V. N. (2023) Distinct longevity mechanisms across and within species and their association with aging, *Cell*, **186**, 2929-2949.e20, doi: 10.1016/j.cell.2023.05.002.
101. Grosfeld, E. V., Bidiuk, V. A., Mitkevich, O. V., Ghazy, E. S. M. O., Kushnirov, V. V., and Alexandrov, A. I. (2021) A systematic survey of characteristic features of yeast cell death triggered by external factors, *J. Fungi (Basel)*, **7**, 886, doi: 10.3390/jof7110886.
102. Khan, I., Yousif, A., Chesnokov, M., Hong, L., and Chefetz, I. (2021) A decade of cell death studies: breathing new life into necroptosis, *Pharmacol. Ther.*, **220**, 107717, doi: 10.1016/j.pharmthera.2020.107717.