Introduction

Aging in birds

Donna J. Holmes^{1,*} & Mary Ann Ottinger²

¹Department of Biological Sciences, University of Idaho, Moscow, ID 83844-3051, USA; ²AGNR-Department of Animal and Avian Sciences, University of Maryland, College Park, MD 20742-2311, USA;

*Author for correspondence (e-mail: electric@uidaho.edu; fax: 208-885-7905)

Received 5 September 2005; accepted in revised form 30 September 2005

In his classic 1957 paper exploring the forces shaping the diversity of aging patterns in nature, evolutionary theorist George Williams suggested that animals with special adaptations for avoiding death by predation, disease, or accident should be expected to evolve unusually long life spans, slower aging rates, and cellular mechanisms for prolonging somatic maintenance (Williams 1957). Some of the specific adaptations in this protective arsenal against mortality could include a subterranean life style, hard shells, prickly quills – and, of course, the ability to fly.

As we have illustrated in our reviews since 1995, birds as a group enjoy remarkably slow aging rates and long life spans for their size (see, for example, Holmes and Austad 1995; Holmes 2003; Holmes and Ottinger 2003, in press). The remarkably slow aging that characterizes many members of the class Aves relative to similar-sized, non-flying mammals appears, at least in part, to be correlated with an evolutionary history of low adult mortality rates. Even small (<100g) songbirds, like barn swallows (*Hirundo rustica*) often survive in the wild up to 5 years or more; captive zebra finches (15–20g) routinely live over 8 years. Hummingbirds weighing under 10g (e.g., the broad-tailed hummingbird, *Selasphorus platycercus*) have been banded and recaptured by field biologists for up to 15 years. Many wild seabirds survive and continue to reproduce very successfully for two or three decades or more, showing few overt signs of deterioration in fitness.

In this special issue, we have assembled a group of papers representing some of the best current research relevant to the field of biogerontology employing birds as animal models, including work on both wild and domestic species. Domestic birds are already well established as research models in developmental

biology, neurobiology, endocrinology and comparative physiology. A preliminary genome sequence of the domestic chicken has been completed, and this bird is well suited for studies of the molecular correlates of aging and cellular senescence (Swanberg and Delany, *this issue*). Another domestic galliform bird, the Japanese quail, has been used for over two decades for studies of reproductive biology and the neuroendocrine correlates of aging. Male quail show remarkable plasticity of aging-related changes in hypothalamic regulation of reproduction, and changes in reproductive behavior can serve as aging biomarkers or early predictors of later fertility declines (Ottinger 1998, 2001; Ottinger et al. 2004). Moreover, short-term caloric restriction has been used by the poultry industry for years to improve egg production and extend the reproductive life span of quail and chickens. Passerine songbirds – primarily canaries and zebra finches – are the focus of a growing body of work demonstrating the regenerative potential of neurons in brain centers controlling song learning (Schlinger and Saldanha, *this issue*). Since the phenomenon of avian adult neurogenesis has no direct counterpart in mammalian models, studies of the molecular basis for this kind of neuroregeneration could prove critically important for understanding the potential for therapeutic brain repair in humans.

The long life spans and slow aging rates of birds are even more remarkable when considered in light of their high gram-specific rates of energy expenditure. The oxidative damage hypothesis, currently a central theory in biogerontology, posits that reactive oxygen species (ROS) generated during normal oxidative metabolism are responsible for many of the molecular changes underlying aging-related physiological declines (Harman 1956). A corollary of this

hypothesis is that homeothermic vertebrates that age slowly *despite* high lifetime energy expenditures may have special ways of resisting ROS damage to their cells and molecules (Monnier 1990, 1991; Holmes and Austad 1995; Barja 1998). This prediction is now supported by a growing body of comparative biochemical evidence (*summarized by Pamplona and Barja, this issue*). Avian defenses against oxidative damage may include a complex array of mechanisms, including antioxidant enzymes and structural defenses, such as lower levels of saturated fatty acids in cell or mitochondrial membranes. Birds may also have superior forms of protection against – and repair of – damage to DNA and other cellular components by prooxidant molecules. Even more intriguing, however, is the possibility that bird mitochondria employ specialized alterations of the mitochondria ‘machinery’ itself, including adaptive proton leak that may result in the production of fewer ROS in the first place.

The aging research community has also shown a great deal of interest in the relationship between telomere length, telomerase activity and maximum life span in vertebrates, including birds. Telomeres, the conserved nucleotide sequences essential for replication of linear chromosomes, have been shown to shorten with age in somatic cells of humans, and are implicated in cellular senescence in mice (Harley 1995). In this issue, Delany and colleagues review the provocative and sometimes conflicting evidence from recent studies exploring the relationships among avian telomere structure and function, life span and aging.

Field ornithologists have been monitoring wild bird populations for decades, generating a wealth of information relevant to evolutionary aging and life-history theory. Wild bird populations are also excellent systems for identifying phenotypic predictors of successful aging in outbred vertebrates subject to natural evolutionary forces. In this issue, avian behavioral ecologists Anders Møller and colleagues use a retrospective statistical approach, similar to that employed in studies of human centenarians, for exploring the relationship between phenotype and longevity in free-living European barn swallows (*Møller et al., this issue*). The juxtaposition of ecology, avian biology, and lifetime reproductive strategies allows us to gain more understanding of the adaptations made by long-lived species. A series of studies have been conducted in the common tern. In this species, experienced older pairs have greater re-

productive success, thereby providing an opportunity to compare age-related differences in parenting and underlying behavioral adaptations (*Pearson et al., this issue*). Studies like these are particularly interesting when contrasted with those on short-lived species, both in captive and field settings (Ottinger et al. 1995; 2003).

Specific aging-related physiological declines, including immunosenescence, are well documented in laboratory rodents and humans. Recently, reliable aging-related changes in aspects of either cellular or humoral immunity have also been reported in wild populations of several bird species, including barn swallows, collared flycatchers, and ruffs (Holmes and Austad 2004). In this issue, LaVoie provides a thorough background on avian models of immune function, and reports the preliminary results of a study of aging-related changes in immune responses in laboratory quail intended to integrate aspects of both innate and acquired immunity (*LaVoie, this issue*).

In captivity under hospitable conditions, some bird species have postreproductive life spans of one third or more of the total life span (Woodard and Abplanalp 1971; Holmes et al. 2001). Since female birds and mammals both produce the vast majority of their primary oocytes, or developing eggs, before or shortly after birth, this fundamental reproductive trait sets homeotherms apart from most female fishes, amphibians and reptiles. New, long-lived avian models may be particularly relevant for studying the molecular basis for slow or reversible fertility loss, as well as the role of a finite oocyte pool in the timing of reproductive aging. To date, little research has focused on natural variability in ovarian aging in birds of different orders or divergent life-history patterns (for an exception, see Ricklefs et al. 2003).

As the field of aging has evolved, so has our understanding of the promise of ‘nontraditional’ vertebrate models for aging, including certain primates, exceptionally long-lived rodents like naked mole-rats, bats, and birds. A rigorous comparative approach, employing a variety of distantly related animal species, can be useful for identifying a range of potential molecular ‘solutions’ to the problem of long-term somatic maintenance and repair (Finch 1990; Austad 1993, 2005; Austad and Holmes 1999). But the development of new animal models – domestic or wild – is difficult. Biogerontologists and funding agencies are most comfortable with established animal models for which molecu- lar

tools have already been ‘mainstreamed’ into current research paradigms. There are also obvious methodological challenges. Development of genetic resources for long-lived birds, including basic information about genetic variability of domestic lines, as well as isogenic and transgenic strains, has lagged behind those of traditional short-lived laboratory animals. But new microarray resources for chicken and quail are continually being developed and, as the sequencing of the chicken genome is being completed, ongoing projects by a number of investigators will soon insure successful characterization of substantial segments of the zebra finch and canary genomes.

Additional, focused effort will be required to direct resources toward the development of novel, exceptionally long-lived models for aging studies. Well-conceived, longitudinal aging studies using birds will inevitably take longer than studies on most standard laboratory animals, and will require substantial financial investment if they are to be worthwhile. Accepted techniques for the measurement of aging biomarkers will need to be adapted and calibrated for judiciously selected bird models. This effort will require interdisciplinary collaboration between established biogerontologists and bird biologists. Breakthroughs in understanding fundamental biological processes are often attained by utilizing alternative animal systems uniquely suited to modeling phenomena of special interest. We hope that this special issue stimulates additional dialog and collaborations, as well as highlights the exquisite – and as yet poorly understood – adaptations that allow so many avian species to combat aging.

Donna J. Holmes
University of Idaho

Mary Ann Ottinger
University of Maryland – College Park

References

- Austad SN (1993) The comparative perspective and choice of animal models in aging research. *Aging (Milano)* 5: 259–267
- Austad SN (2005) Diverse aging rates in metazoans: targets for functional genomics. *Mech Ageing Dev* 126(1): 43–49
- Austad SN and Holmes DJ (1999) Evolutionary approaches to probing aging mechanisms. In: Yu BP (ed) *Methods in Aging Research*, pp 437–452. CRC Press, Boca Raton, FL
- Barja G (1998) Mitochondrial free radical production and aging in mammals and birds. *Ann NY Acad Sci* 854: 224–238
- Finch CE (1990) *Longevity, Senescence, and the Genome*. University of Chicago Press, Chicago, IL
- Harley CB (1995) Telomeres and aging. In: Blackburn EH and Greider CW (eds) *Telomeres*, pp 247–263. Cold Spring Harbor Laboratory Press, Cold Spring Harbor
- Harman D (1956) Aging: a theory based on free radical and radiation chemistry. *J Gerontol* 11: 289–300
- Holmes DJ (2003) Aging in birds. In: Osiewacz H (ed) *Aging in Organisms*, pp 201–219. Kluwer Press, Amsterdam
- Holmes DJ and Austad SN (1995) Birds as animal models for the comparative biology of aging: a prospectus. *J Gerontol Biol Sci* 50A: 59–66
- Holmes DJ and Austad SN (2004) Declining Immunity with Age in the Wild? Evidence from Bird Populations. *Science of Aging Knowledge Environment (SAGE KE)*, Science Online 21: pe22
- Holmes DJ and Ottinger MA (2003) Birds as long-lived animal models for the study of aging. *Exp Gerontol* 38: 1365–1375
- Holmes DJ and Fluckiger R et al. (2001) Comparative biology of aging in birds: an update. *Exp Gerontol* 36: 869–883
- Monnier VM (1990) Nonenzymatic glycosylation: the Maillard reaction and the aging process. *J Gerontol: Biol Sci* 45: B105–B111
- Monnier VM and Sell DR et al. (1991) Mechanisms of protection against damage mediated by the Maillard reaction in aging. *Gerontol* 37: 152–165
- Ottinger MA (1998) Male reproduction: testosterone, gonadotropins, and aging. In: Mobbs CV, Hof PR (eds) *Functional Endocrinology of Aging*, Vol 29, pp 105–126. Karger
- Ottinger MA (2001) Quail and other short-lived birds. *Exp Gerontol* 36: 859–868
- Ottinger MA, Nisbet ICT and Finch CE (1995) Aging and reproduction: comparative endocrinology of the common tern and Japanese quail. *Am Zool* 35: 299–306
- Ottinger MA., Reed E, Wu J, Thompson N and French JB (2003) Establishing appropriate measures for monitoring aging in birds: comparing short and long lived species. *Exp Gerontol* 38(7): 747–750
- Ottinger MA, Abdelnabi M, Li Q, Chen K, Thompson N, Harada M et al. (2004) The Japanese quail: a model for studying reproductive aging of hypothalamic systems. *Exp Gerontol* 39: 1679–1693
- Ricklefs R and Scheuerlein A et al. (2003) Age-related patterns of fertility in captive populations of birds and mammals. *Exp Gerontol* 38(7): 741–746
- Williams GC (1957) Pleiotropy, natural selection and the evolution of senescence. *Evolution* 11: 398–411
- Woodard AE and Abplanalp H (1971) Longevity and reproduction in Japanese quail maintained under stimulatory lighting. *Poult Sci* 50: 688–692