Aging Pathobiology and Therapeutics 2026; 8(1): 01-02 ***01***
DOI: 10.31491/APT.2026.03.202

EDITORIAL

Geropathology is a common denominator for multispecies research in geroscience, from insects to nonhuman primates

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Abstract

Geropathology embraces geroscience by defining anatomic and molecular aspects of aging as a basis for gaining a better understanding of how we age, and embellishes the identification of specific targets for gerotherapeutic intervention. Anatomic geropathology in various animal models of aging is based on microscopic evaluation of all age-related lesions so that lesion severity can be assigned a score as a quantitative value in a specific organ. Laboratory mice, nonhuman primates, pet cats, and house crickets have all been shown to develop similar age-related lesions that increase in severity with increasing age. These observations suggest that geropathology serves as a common denominator involving the cellular deterioration of tissues with increasing age in a diverse animal population from insects to high order mammals such as nonhuman primates. Geroscience, as an evolutionary-conserved approach to prevent the rapid progression of aging and age-related conditions in older people, is therefore supported by geropathological interrogation.

Keywords: Geroscience, geropathology, age-related lesions, laboratory mice, nonhuman primates, pet cats, house crickets

Geroscience assumes all diseases that affect primarily older adults have a common and major underlying cause of declining function and resilience that is part of the aging process. Geropathology embraces geroscience by defining anatomic and molecular aspects of aging as a basis for gaining a better understanding of how we age, how we develop age-related diseases, and the emergence of specific targets for gerotherapeutic intervention [1].

Anatomic geropathology is based on microscopic evaluation of all age-related lesions so that lesion severity can be assigned a score as a quantitative value in a specific organ. Therefore, increases in lesion severity in individual organs can be followed with increasing age. This approach is in line with the geroscience concept that manipulation of aging will simultaneously delay the appearance or severity of major diseases with a decrease in the severity of histological lesions because of the same underlying major risk factor: aging and the multiple processes involved in aging. Ideally, studies to advance a geropathology lesion grading approach would be carried out in humans. However, from a geropathology perspective, clinical studies can be challenging because of a lengthy lifespan and lack of access to tissues from human organs. Therefore, animal models are being relied on to partially overcome these challenges. An ideal animal model of human aging should exhibit comparable naturally occurring diseases, share the same environment, have a heterogeneous background, and be amenable to therapeutic intervention studies that would accurately predict positive results in people. Rodents, and to a lesser extent, nonhuman primates, are used extensively in geroscience research studies. These species have many advantages for modeling a wide variety of age-related conditions and biology of aging concepts.

The mouse is one the most widely used mammalian species in geroscience research. An anatomic geropathology grading approach has been developed and validated in mice as a useful tool to study aging and the relationship of age-related histopathologic lesions in specific organs to age related disease [2]. Geropathological interrogation of individual mouse organs provides a powerful look at the morphologic changes associated with increasing age in an organ-dependent manner [3]. In addition, lesion grading provides insights into how different organs respond to

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Received: 25 March 2026
Accepted: 25 March 2026 / Published: 31 March 2026

therapeutic drugs based on changes in severity of lesion scores.

Even though mice develop a number of age-related conditions, some are still not well aligned with several common age-related ailments observed in people. Nonhuman primates (NHPs) share more similarities in aging and spontaneous chronic diseases with humans than mice, so are considered an excellent translational model of aging. A preliminary geropathology grading platform has been described for rhesus macaques and common marmosets [4]. Lesion severity in specific organs has been shown to increase with increasing age in both species similar to the mouse.

Several species are not as commonly used in geroscience research as mice and NHPs, but have outstanding characteristics for modeling aging in humans. Pet cats share the same environment and are exposed to the same environmental conditions as humans. In addition, comorbidities occurring in humans are common in pet cats and provide a rich venue for investigating the impact of aging on risk for developing chronic disease conditions and the role multiple pathways of aging may be playing [5]. Lesion severity in specific organs has been shown to increase with increasing age in pet cats similar to mice and NHPs.

Another species that is just being developed as an animal model of aging is the house cricket [6]. The house cricket has a relatively short lifespan of 10 to 12 weeks, with distinct developmental stages that can be compared to life stages of humans. Physiological processes are well-characterized and maintenance in laboratory settings is straightforward and inexpensive. Therefore, the house cricket is a practical model for studying morphological and functional deterioration associated with aging. Interestingly, geropathological assessment shows that house crickets develop lesion severity with increasing age just like pet cats, NHPs and mice (Klug, Liao, and Ladiges, unpublished observations). Organs are rudimentary but well compartmentalized, and in older crickets show a number of the same lesions seen in mammals.

These published and unpublished observations suggest there is a common thread involving the cellular deterioration of tissues with increasing age in a diverse animal population from insects to high order mammals such as NHPs. Therefore, geropathology is a base-line denominator for helping establish geroscience as an evolutionary-conserved approach to prevent the rapid progression of aging and age-related conditions in older people.

Declarations

Availability of data and materials: Not applicable.

Financial support and sponsorship: None.

Conflicts of interest: Warren Ladiges is a member of the editorial board of *Aging Pathobiology and Therapeutics*. The authors declare that they have no conflicts and were not involved in the journal's review or decision regarding this manuscript.

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Cite this article as: Klug J, & Ladiges W. Geropathology is a common denominator for multispecies research in geroscience, from insects to nonhuman primates. *Aging Pathobiol Ther*, 2026, 8(1): 01-02. doi: 10.31491/APT.2026.03.202