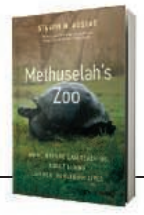
AGING

Longevity lessons

Animal aging could hold clues to healthier human life spans

Methuselah's Zoo: What Nature Can Teach Us About Living Longer, Healthier Lives
Steven N. Austad
MIT Press, 2022. 320 pp.



By **Charles Brenner**

Readers of several recently published books about longevity have been told that human aging is a solved problem. One recent book argues, for example, that dominantly acting longevity genes, identified in yeast, are conserved in animals including humans and can be activated by natural products such that we do not have to age (*1*). Given that the most powerful animal "longevity genes" are actually recessive alleles of genes required for growth and fertility, the certainty with which such claims have been made is astonishing.

It was therefore refreshing to read *Methuselah's Zoo*, the latest book from biologist Steven Austad, who expresses with clarity what we know and what we don't know about aging. Austad does not believe that aging is a solved problem, citing uncertainty about phenomena as fundamental as the timing of menopause with respect to women's life span. However, he believes that by dissecting the mechanisms by which particular animals age well, we will be able to develop medicines that promote longevity in the future.

Indeed, Austad is so confident of this assertion that in 2001, he bet gerontologist Jay Olshansky that the first person who will live to 150 had already been born. Their heirs will settle this wager no later than 2150.

Definitions matter in aging, so I appreciated that Austad establishes some boundaries early on. While he tips his hat to trees that are thousands of years old, he reasons that the ability of plants to expand clonally puts them in a different category than nearly every animal.

A former professional lion trainer and someone who spent decades studying animals in wild habitats, Austad introduces the longevity quotient (LQ) as a general system of classification that indicates whether a species' life span is above or below a trend line that adjusts for its size. (Big animals generally live longer than little animals, so a species' absolute life span does not capture whether it really is adept at aging.)

Scoring longevity on a size-normalized scale thus allows Austad to characterize mice as poor agers and to identify tuataras, Greenland sharks, rougheye rockfish, and olms (a type of salamander) as extraordinarily good agers. Although their estimated LQ is not as high as these four species, naked mole rats appear to age better than humans and, indeed, they are the only animal model organism to have a higher LQ than humans. (Note that the longest-lived whales, which outlive humans by a century, have a lower LQ than humans because their size goes in the denominator.)

Wisdom, the oldest known wild bird, is shown just shy of 68 years old.

Having established these terms, Austad argues that it is unfortunate that we depend on the laboratory mouse as much as we do to learn how to extend a healthy life span. He quips that humans have much to teach mice about longevity, rather than vice versa, and suggests broadening geroscience to animals with higher LQs in order to identify ways that organisms are able to remain cancer-free, physically active, and mentally astute into later decades. Cellular or organoid models of tissue resiliency and repair could potentially make up for our inability to cultivate the longest-lived animals as laboratory aging models, he argues.

I agree that we will find mechanisms of resiliency in animals of high LQ, but I would make a distinction between extended life span and extended health span. In large part, the selective pressures that formed animal gene sets are bottlenecks that optimized successful reproduction, which integrates many complex functions, including the ability to acquire food, avoid predation, attract a mate, and—in some cases—care for offspring until they can accomplish these functions themselves. These abilities require thousands of gene functions in the nervous, musculoskeletal, respiratory, and circulatory systems, and more.

Because animals that succeed in reproducing multiple times pass on the most genes, there is an indirect selection for longevity. However, clever as evolution is, it doesn't produce something for which there isn't a selection, namely postreproductive vigor, unless, for example, grandmothering sufficiently improves the reproductive success of an individual's offspring, as has been suggested in human longevity research (*2*).

If I were refereeing a debate between Austad and Olshansky, I'd imagine Olshansky would argue that any potential longevity medicine is more likely to help more people get to 100-plus years—that is, closer to a genetically encoded longevity maximum—than to extend the observed maximum (*3*). In this case, the mouse being a poor ager might make it a good model for health-span research, with end points such as improved wound healing and infection resistance in 20-month-old mice rather than extending the average life span of a mouse from 2 years to 2.5. If, however, we someday derive longevity medicine from the cave-dwelling olm, Steven Austad will deserve an assist. ■

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REFERENCES AND NOTES

1. D. A. Sinclair, M. D. LaPlante, *Lifespan: Why We Age—and Why We Don't Have To* (Atria Books, 2019).
2. K. Hawkes, J. E. Coxworth, *Evol. Anthropol.* **22**, 294 (2013).
3. S. J. Olshansky, *JAMA* **320**, 1323 (2018).

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