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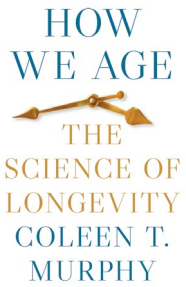
The science of longevity and the quest to solve an age-old problem



How We Age: The Science of Longevity
By Coleen T. Murphy
Princeton University Press: 2023. 464 PP. $35.00/£30.00.

How can we slow aging and enjoy a healthy lifespan? This outstanding question has long taunted humanity, as shown by the search for the 'fountain of youth'. Whereas explorers such as Ponce de Leon might have looked for a mythical spring in then-exotic locations (Florida), we now know that science (rather than drinking one's way around far-off lands) is how we can understand aging and improve our healthspan — that is, the youthful, healthy part of life. In particular, the past two decades have led to landmark discoveries in aging research[1]: Coleen Murphy's upcoming book *How We Age: The Science of Longevity* tells the story of these remarkable discoveries through the words of a protagonist in this field.

The book starts by highlighting the socioeconomic importance of studying gerontology. Essentially, because aging is the main risk factor for many diseases, a better understanding of the aging process has the potential to deliver preventive measures and cures for age-related diseases. The subsequent chapters introduce the reader to key areas of aging research. Chapters 3 and 4 discuss the remarkable difference in lifespan and healthspan of human centenarians as compared to the average population, as well as among animal species, including long-lived animals with high disease resistance such as the naked mole rat and the Greenland shark. Chapter 5 introduces the molecular biomarkers of aging and lays the foundation for the reader to understand the subsequent chapters, in which key landmark findings in aging research are reported. These discoveries include the key role of the insulin receptor–FoxO signaling pathway in regulating longevity (chapter 6), thus demonstrating that aging is a malleable process that is under the control of genetic pathways, and the remarkable discovery that different types of dietary restrictions act through distinct, yet interconnected pathways to fend off aging across animal species (chapter 7). The subsequent chapters examine the cellular and molecular mechanisms of aging, including the mechanisms that are responsible for the disposal of misfolded proteins and faulty organelles, the role of mitochondria and DNA repair, and the importance of stem cells in promoting tissue regeneration and in maintaining tissue function with aging[2] (chapters 8–10). Chapters 11 to 16 examine how aging is regulated by intercellular and intertissue crosstalk, and how the aging of certain sentinel tissues and the microbiota affects the aging of other tissues and of the organism via endocrine factors and long-distance signaling. Extending the notion of communication as a leitmotif of aging, the author reports the exciting findings that interindividual and intergenerational interactions govern aging, and that neuronal sensory systems[3] and transgenerational epigenetic inheritance[4] are responsible for these novel layers of longevity regulation. Lastly, chapter 17 describes the prospect of treating aging pharmacologically as a single intervention to prevent and/or simultaneously cure multiple diseases that arise with aging.

Throughout the book, the author alternates personal recounts of her witnessing and contributing to landmark discoveries[5] with a comprehensive overview of key areas of aging research. This includes not only studies of human centenarians but also those done in simple model organisms from the worm *Caenorhabditis elegans* and the fruit fly *Drosophila* to mice, which have provided fundamental new insights into aging because of their powerful genetic tools and short lifespans. Many examples are shown of how new technologies have been used to test long-held theories about aging. For example, the author recalls her work as postdoctoral fellow in the laboratory of Cynthia Kenyon, where she tackled the pressing problem of defining the transcriptional responses induced by the daf-2–daf-16 pathway in worms (corresponding to the insulin receptor–FoxO pathway in mammals). By using an innovative technology (by actually printing and analyzing her own custom-made microarrays), Murphy was able for the first time to identify the genes regulated by *daf-2–daf-16*, which included the antioxidant enzyme sod-3 (a superoxide dismutase). By using the first-ever available RNA interference library for functional studies in *C. elegans*, she found that many of these genes (and not simply *sod-3* upregulation) contributed to the longevity of *daf-2* mutants, thus disputing the centrality of the 'free radical' theory of aging that was popular at that time.

Altogether, the book provides an up-to-date overview of aging research that is told in a simple-to-read, yet authoritative manner by a leading expert in aging research. The author does an excellent job in conveying an explanation of the molecular and cellular mechanisms of aging that is accessible to the general public. Because the book is written with clarity and is enjoyable to read, it is an excellent way for any layperson to understand the latest developments and future challenges that await aging research. This book is also an outstanding resource for any scientist who wants to enter the aging field and for scientists already working in this area, who may enjoy seeing the developments in aging research through the eyes of a pioneer.

By retelling the latest fundamental discoveries in aging research, the author shows the reader how an arsenal of model organisms and experimental approaches is leading the way to extend longevity. The quest for healthy aging is fast-advancing and exciting times are ahead.

Reviewed by Fabio Demontis
St. Jude Children's Research Hospital, Memphis, TN, USA.
e-mail: fabio.demontis@stjude.org

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Competing interests

The author declares no competing interests.