Book Review


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In his time with the National Institute on Aging, the International Biogerontology Resource Institute, and Ellison Medical Foundation, Dr. Richard L. Sprott has become an esteemed researcher in the biology of aging. In this volume, he has assembled 27 researchers focusing on the genetics of aging. The ten chapters review an array of topics regarding the genetics of longevity and disease processes associated with aging. For biologists and those with a background in genetics, this volume provides an informative review of contemporary studies revolving around the biology of aging. For non-geneticists, the chapters provide a somewhat jargon-heavy primer to genetic aging. Many of the genetic processes correlated to longevity, however, will reappear throughout this book and allow those without biological research leanings to appreciate the spectrum of physiological and genetic pathways associated with aging. Dr. Sprott has assembled a review of substantial use to researchers, anthropologists, and clinicians alike.

The first chapter reviews foundations of aging at the cellular level using the lens of contemporary genetic research on organisms ranging from yeast to mammals. Key questions revolve around the difference between adult and embryonic stem cells, and differential preservation of both during aging. The authors focus on longevity pathways that are critical to cell regeneration and repair, cellular reprogramming, and metabolic enzymes essential to life span and morbidity studies. The second chapter deals with longevity regulators that are common across phylogeny, responsible for both development and inhibiting longevity. Termed ‘antagonistic pleiotropy’ due to their dual functions both in early development and in aging, these genetic processes are beneficial during development for their contributions to rapid cell proliferation and growth, yet detrimental later in life as they affect tumor growth and other diseases of aging.

Chapter 3 begins to look at environmental factors related to longevity, focusing on the role of oxygen. Despite being essential to the survival of all mammals, the metabolism of oxygen leads to the release of highly reactive oxygen species, which in turn lead to the alteration of cell structure during aging. Environmental oxygen level is therefore a natural avenue of research, and this chapter centers on hypoxia-inducible factor (HIF), a transcription factor responsible for cellular response to low oxygen, that has been extensively studied in animal models and linked to vascular health and overall longevity. However, HIF may prove to be a double-edged sword, as cancer cells can “hijack” it, detrimentally affecting long-term health. HIF has also been linked to diseases of the brain (e.g., Parkinson’s, Alzheimer’s), which can actually worsen in hypoxic conditions. The chapter authors rightfully call for further research and standardization on the topic, and this call is mirrored in Chapter 4, which reviews the intersection of dietary changes, gene mutations, and medical intervention and their effect on longevity. At the crux of this chapter is the question of exactly how these interventions increase longevity: by extending lifespan, or by postponing diseases of aging? Is longevity as “simple” as a decrease in early life hazards? This also chapter provides a fantastic set of guidelines for evaluating longevity data with a critical eye towards statistical power and over-assumptions.
Chapter 5 takes a departure from the nuances of genetics to look at primate models of aging. As the longest-lived of the primate species, humans face neurological degradation that other primates do not. It is interesting that human-like patterns of neurodegradation are only apparent in more distant primate species, and not our closest genetic relatives (bonobos or chimpanzees), therefore providing a promising research direction. Chapter 6 continues the theme of effective study models, focusing instead on exceptionally old-aged humans. Conserved pathways may be related to longevity in all species, and therefore selected for by natural selection. Genes for specific diseases, such as Alzheimer’s, metabolic syndromes, and cancer should be studied in centenarians to help tease out precisely how extremely old individuals are protected from such maladies.

The role of genes in the effective health-span is further evaluated in Chapter 7, which focuses on subjective (e.g., self-rated health) and objective (blood pressure) health markers and their relationship to stress and frailty. Using a wealth of data from numerous genetic and sibling studies, this chapter highlights the complex role of gene-environment interactions on successful aging. This theme is continued in Chapter 8, which demonstrates the extreme complexities of genetic and environmental interactions found even in a “simpler” mouse model. Using end-of-life as a single phenotypic marker for longevity, the authors use mice and popular candidate genes to evaluate the causative factors behind gerontological phenotypes, concluding that there are no “best” group, environment, or level of variable that can single-handedly answer the complex processes of aging.

The final two chapters highlight the recurring theme of complexity of the aging process using broader and more theoretical evaluations. Focusing on molecular networks, Chapter 9 discusses the aging process across numerous genetic pathways before moving on to more overarching metabolic and physiological processes (and corresponding failures thereof) associated with longevity. What develops is a cogent call for future research on these networks, not only in how they shape the aging process, but also how the aging process in turn shapes them. The final chapter of the volume uses the notion of “Nature and Nurture” as an explanatory mechanism for the complex aging process, but also summons the oft-overlooked element of “Chance” to the grand scheme of evolutionary processes that have shaped aging and longevity. The authors demonstrate that, between different species, variations in lifespan and health-span are largely governed by genotypes; however, within the same species, variations in these processes are shaped by stochastic events. These events, the author argues, likely evolved as a response to unpredictable environments during growth and development that resulted in detrimental effects later in life (antagonistic pleiotropy).

Overall, Dr. Sprott has assembled an admirable compilation of genetic studies of health and aging. While the biological data is dense at times, especially for non-biologists, this volume represents a necessary and valuable tool for researchers looking for a stepping-stone towards future research regarding the complex processes of genetic aging.