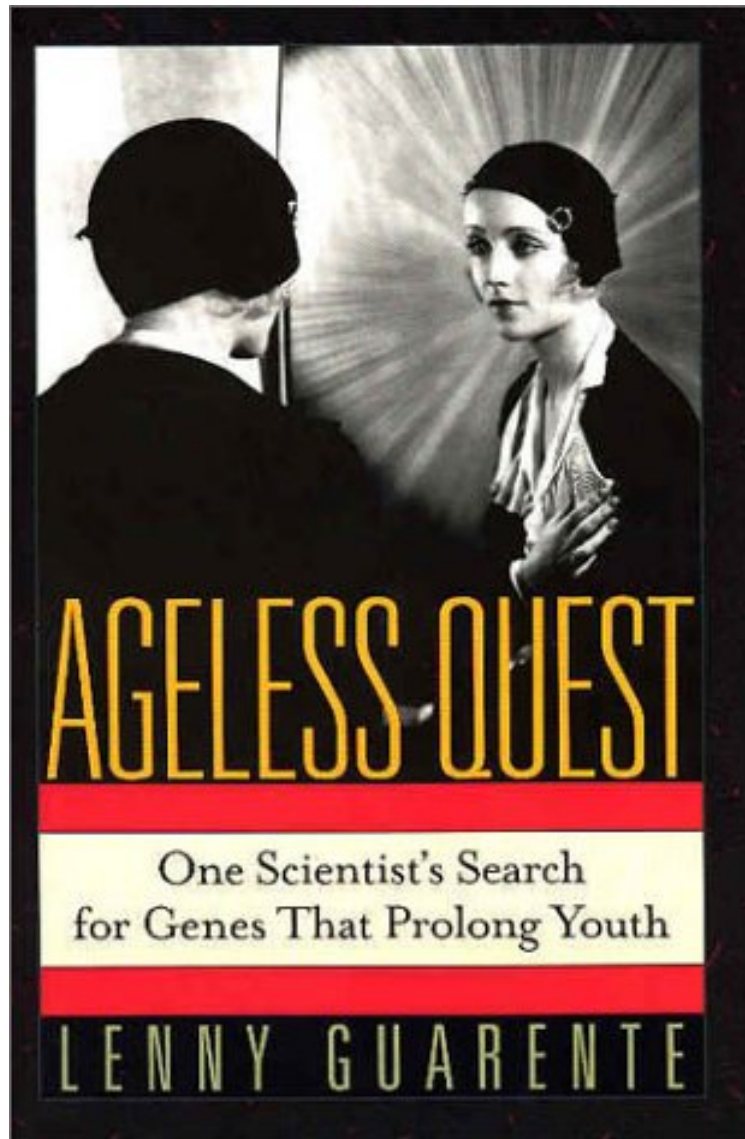


(Mobile ebook) Ageless Quest: One Scientist's Search for the Genes That Prolong Youth

# Ageless Quest: One Scientist's Search for the Genes That Prolong Youth

*Leonard Guarente*

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**Leonard Guarente : Ageless Quest: One Scientist's Search for the Genes That Prolong Youth** before purchasing it in order to gage whether or not it would be worth my time, and all praised Ageless Quest: One Scientist's Search for the Genes That Prolong Youth:

2 of 2 people found the following review helpful. Very Interesting StoryBy FernandoThe book has a very interesting story about this scientist (the author) and how did he performed his researches. I like it because it is the point of view

if a real scientist... It is a very good reading for beginners in this area. 17 of 20 people found the following review helpful. Great behind the scenes view of scientific research By Gary W. As a non-scientist with an interest on what the future may hold for us, I found *Ageless Quest* to be exceptionally informative, easy to understand, and thought provoking. I had always wondered what went on in those biology research labs, and was grateful to have the "behind the scenes" peek that this book provided. Extremely interesting and enjoyable reading; recommended for all. 1 of 10 people found the following review helpful. --By A Customer I picked up this book because of the cover. If you care about the scientific story, read it in the review literature. If you want a good read, look elsewhere.

*Ageless Quest* is a personal, sometimes controversial, account of the pursuit of a genetic 'cure' for aging by an expert in the field. The author is the Novartis Professor of Biology at the Massachusetts Institute of Technology. Aging has always been regarded as a highly complex process with many degenerative changes leading to the cessation of life. But recent research has identified a relatively simple mechanism that governs the pace of aging. Lenny Guarente's *Ageless Quest* is a scientific detective story for the baby boom generation. It offers an insider's view of an area of potentially astonishing high reward--and equally high risk.

From Publishers Weekly Science can be like sausage--sure, you like it, but you're better off not knowing how it's made. But with the arrival this year of a number of tell-all science memoirs, readers can't help but take a peek, deriving a certain lurid thrill. Given the potentially explosive subject matter, one would expect Guarente's account of his pursuit of a genetic "cure" for aging to dish up controversy, but it doesn't. Rather, this slim book delivers pure work-a-day science, without any insider dramatics. Guarente, a biologist at MIT whose work on aging has been featured in the *Wall Street Journal*, the *New York Times* and the *Boston Globe*, does gripe now and again about such things as the hardships of the tenure track. But the balance of the book details the author's intellectual adventure, touching along the way on theories of aging and the workings of the biotech industry. At the heart of his story is a gene called SIR2, which has been found to slow aging in yeast in animals. Could it eventually be used on humans? Possibly. Guarente views aging as a disease that someday might be treatable with new drugs, which raises further provocative questions about the ripple effect treatment could have on population, economics and other social factors. But the author, who excels as a diarist but less as a popular-science pitchman, leaves these questions largely untapped. This, admittedly, makes for sedate though quite amiable, utilitarian reading. Copyright 2003 Reed Business Information, Inc. Part autobiography, part social commentary, part science, [*Ageless Quest*] does an excellent job of explaining and extolling the use of model organisms for research into ageing... *Ageless Quest* conveys some quite difficult ideas and complex experimental results with a clarity and freshness that deserve to make it widely read. Nature *Ageless Quest* is a personal account of a rich and active academic life, in which descriptions of the scientific work that led to the discovery of Sir2, a potentially important biochemical factor that influences life's clock, are mixed with autobiographical sketches. The book is reminiscent in more than one way of Jim Watson's classic, *The Double Helix*, in that it paints an accurate picture of how scientific research was, and is, done: the excitement, the frustrations, the fear of competitors and the race for 'high-impact' publications. *Ageless Quest* is, therefore, not just a book about ageing, nor just about genes and proteins; it is also about people, and the nitty-gritty of doing science at the end of the twentieth century. One of the most endearing features of this little book, which can be read over the course of a weekend (or during a lengthy run of a native gel, to put it in scientists' time-units as well), is that its author pays tribute to the many people he has worked with over the years; or, to be more precise, to the dedicated and eager young scientists who have worked for him - a noteworthy difference. EMBO reports Basically a personal account of research into aging, including descriptions of his students and postdocs and their work at the laboratory bench, the book is a pleasure to read. The author writes with the clarity of a first-class journalist, an infectious enthusiasm and an eye for the revealing anecdote. Although the relevance of Sir2 and survival mechanisms discovered in short-lived laboratory organisms to aging in mammals is still questionable, I am convinced that by opening this avenue of research, Guarente and kindred spirits have done much to draw outstanding scientists into aging research, thereby shaking this field out of its stuffy reputation. That alone makes *Ageless Quest* and the story of its simple pursuit a timely contribution to the growing literature on why and how we age. Nature Genetics --Cold Spring Harbor Laboratory Press From the Publisher From Nature (February 20, 2003): Scientists in their later years sometimes enter a philosophypause, characterized by armchair speculations and the writing of autobiographies. *Ageless Quest*, although having this appearance, is an interesting exception, because it is written by a scientist at the peak of his powers. Part autobiography, part social commentary, part science, the book does an excellent job of explaining and extolling the use of model organisms for research into ageing. The common features of ageing are a decline in fecundity and increased vulnerability to death during adulthood. Many different kinds of damage and pathology accumulate with age, the precise spectrum varying between individuals. The complexity and variability of the ageing process have often led it to be regarded not as one process, but as many. For these reasons, ageing has seemed intractable, both to experimental analysis and to medical amelioration. Although many researchers studying ageing would not sign up to an agenda that aimed to increase lifespan per se, they would agree that their aim is to improve health in old age. The message of

Ageless Quest is that the prospects for improving health in the elderly are far greater than has been supposed, and that these improvements are, in turn, likely to extend lifespan. The recent history of scientific thinking about ageing is mirrored in the choices that Lenny Guarente has made in his own research career, a story that he tells with candour and insight. Initially he played safe, focusing his research on the regulation of gene expression, to win tenure at the Massachusetts Institute of Technology, a process akin to dodging a carefully aimed bullet. After tenure and security, he cast around for a riskier, less mature research area, and considered working both on AIDS (too crowded) and the human brain (too difficult). Several straws in the wind suggested that ageing could be amenable to the standard methods of genetic analysis. Slow-ageing, mutant strains of yeast and the nematode worm *Caenorhabditis elegans* had been described. And caloric restriction, in which food intake is reduced to about half of normal levels, had long been known to slow down ageing in rodents and other organisms, a phenomenon that is presumably mediated by altered gene expression. So graduate students Brian Kennedy and Nick Austriaco were given a year to establish the yeast ageing system in Guarente's lab. (An engaging feature of the book is the prominence given to the role of successive graduate students in shaping the science, along with Guarente's thumbnail sketches of their characters.) Kennedy and Austriaco found that different yeast strains aged at characteristically different rates. The team isolated four long-lived mutant yeast strains, one of which was also unable to mate, which allowed the mutation to be pinpointed to a gene whose protein product was already known to be involved in the regulation of gene expression. The quest to understand how this mutation slows ageing required tenacity, technical ingenuity and considerable thought. It wasn't the mutated gene itself that turned out to be critical, but a partner gene called SIR2. The original mutation had resulted in over- rather than under-activity of SIR2. The SIR2 gene therefore acts to promote the survival of the yeast. SIR2 turned out to have two telling characteristics. First, a homologue in *C. elegans* also increased lifespan, suggesting that the effect of SIR2 on ageing is conserved over huge evolutionary distances. Guarente has had what he terms "consistent mentoring" from successive departmental chairmen, and this latest discovery was greeted with: "Just what we need, a long-lived worm." Second, SIR2 encodes an enzyme (NAD-dependent histone deacetylase) that is involved in chromosomal compaction; when a chromosomal region is condensed, its genes become inaccessible and are turned off. As the enzyme requires NAD, high levels of which may indicate that cellular nutrient supplies are low, it would probably be most active when energy is in short supply. In accordance with this idea, the lifespan of yeast that overexpress SIR2 is not extended by reduced glucose availability, as it is in wild-type yeast. Writing about caloric restriction in the late 1980s, David Harrison and Robin Holliday pointed out that mammals and other animals have evolved methods of surviving hard times, particularly food shortage. Starved organisms can suppress processes that lead to reproduction, and enhance processes that protect against environmental stress. These changes may in turn slow down ageing, increasing the likelihood of successful reproduction when the food supply is restored. Guarente makes a good case that SIR2 epitomizes one kind of gene action of the sort that Harrison and Holliday envisaged. It is responsive to cellular nutrient status, and reacts to high NAD levels (and hence food shortage) by shutting down gene activity. Precisely which genes are turned off may differ between organisms. Genes in the insulin/IGF-like pathway, of which SIR2 may be part, are also nutrient-sensitive regulators of gene expression, and affect the rate of ageing in worm, fruitfly and mouse. The indications so far from model organisms are that interventions that slow down ageing can also improve age-specific health. Caloric restriction, for example, slows down the accumulation of multiple forms of age-related damage and pathology in rodents. Guarente is an optimist. He thinks that drugs targeted at products of genes such as SIR2 will become available in the next 10 or 20 years to improve age-specific health and slow down ageing. Although voluntary caloric restriction is not a feasible approach to improving human health, it may be possible to target the pathway that mediates the response. Indeed, Guarente devotes much of his time to his biotech company Elixir, and has much of interest to say about the synergies and conflicts of interest between academia and business. Ageless Quest conveys some quite difficult ideas and complex experimental results with a clarity and freshness that deserve to make it widely read.