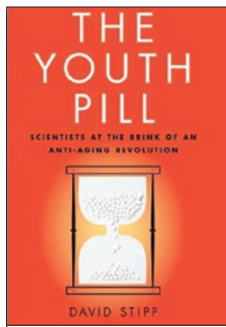


BOOK REVIEW

That obscure object of desire



The Youth Pill: Scientists at the Brink of an Anti-Aging Revolution

David Stipp

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Reviewed by Jan Vijg

Demographic shifts will soon have a major impact on the world economy. Fifteen years from now, there will be almost 70 million Americans over the age of 65. In China, home to the most extraordinary economic growth spurt in history, there will soon be a ratio of only one working-age adult to every six people over age 65. In Europe the situation is grimly similar. As the incidence of virtually all major chronic diseases increases with age, lower birth rates and the ever-decreasing mortality rate among the elderly will require a steep boost in healthcare expenditures.

Is there a reason to make the situation even worse by developing treatments to extend life span even further? In his new book, *The Youth Pill: Scientists at the Brink of an Anti-Aging Revolution*, David Stipp emphatically thinks there is. The reasoning behind this is simple: any intervention that genuinely slows down the aging process must inevitably also delay, ameliorate or prevent the diseases that are inextricably intertwined with the causes of aging. Unfortunately, we do not know what these causes are, and the aging-disease relationship is at present incompletely understood. Nevertheless, as shown in this book, successful interventions can be developed even in the absence of detailed knowledge as to how the increasing disease risk over time is anchored in the basic processes of cellular degeneration and death that we call aging.

The purpose of the book is to explain to nonscientists how recent progress in the science of aging has led to the development of experimental interventions that can, for the first time in history, add quality years to our lives. Infused with narrative—and with the occasional journalistic clichés and obligatory jokes—Stipp expertly and entertainingly describes some of the basic biology of aging, with its probable evolutionary roots and the dramatic diversity in aging rate among animal species. His subsequent description of the discovery that single-gene mutations can extend life span in the nematode and how this led to the recognition of evolutionarily conserved survival or longevity pathways is excellent. He provides a balanced description of almost all the issues that make the science of aging so exciting. This discussion is followed by chapters that deal with the issue that really fascinates Stipp and is central to this book: life extension.

As suggested by the book's title, the type of antiaging treatment that Stipp is primarily interested in would be delivered by a pill. The book

is focused almost exclusively on recently identified drugs that mimic dietary restriction. Dietary restriction involves strict food rationing, sometimes down to 40% of what animals normally eat, while avoiding malnutrition. It has been shown to extend healthy life span in a host of laboratory animals, from worms and flies to mice and dogs. The most publicized dietary restriction mimetic is resveratrol, a plant polyphenol and component of red wine. Resveratrol has many targets but is thought to act primarily by activating sirtuins, enzymes with protein deacetylase or monoribosyltransferase activity. Although beneficial in correcting metabolic problems associated with high-fat diets, there is thus far no evidence that resveratrol also extends normal life span. This is in striking contrast with the effect of another compound, rapamycin, which specifically suppresses the mammalian target of rapamycin complex 1 (mTORC1), thereby activating a number of beneficial, downstream processes.

The potential of rapamycin to extend healthy life span in mice was recently independently tested in three different laboratories. At all three sites, rapamycin significantly extended maximal life span in mice even when treatment began at the ripe old age of 20 months (corresponding to about 60 years of age in humans). As far as I know this is the first compound shown conclusively to promote longevity in a mammal, which makes it a good candidate for testing its effects on longevity in humans. Although not the elixir of immortality, this is an accomplishment that alchemists of yore would have been proud of! To his credit, Stipp discusses these findings critically, noting the potential downsides.

On the basis of this watershed moment of increasing maximal life span through a simple drug, Stipp discusses the implications of interventions that can extend life. It is especially these sections of the book that make good reading for professional scientists. How do people look at science that has the potential to affect their lives so dramatically? Is the desire to live longer, possibly very much longer, something that we should not want? Although Stipp shares some of the concerns raised by those who view the prospect of life extension as a threat rather than a benefit to society, he wants none of their defeatist objections. In his view, the benefits of dietary restriction mimetics in postponing the onset of disease and perhaps increasing maximal life span by 5 years far outweigh the potential disadvantages that have been raised, such as the effects of life extension on anomie and frailty, and from a wider perspective, on resource depletion. And I agree with him that little of what the naysayers argue is supported by solid evidence.

Although overall the book is eminently readable, a weakness is the overdose of panegyric in the discussion of resveratrol. Stipp's extraordinary attention to the company Sirtris, with a whole chapter devoted to what basically amounts to how to run a biotech business, is especially irksome and distracts attention from the science.

Notwithstanding, the book as a whole is both entertaining and informative. Although it is primarily a book for the lay public, and for the insider the science is undoubtedly superficial, scientists not familiar with research on longevity and aging will learn a lot.

COMPETING FINANCIAL INTERESTS

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