Live fast, die young

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Ageless Quest: One Scientist's Search for Genes That Prolong Youth
by Lenny Guarente
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The realization that all life is finite must have been one of the most disconcerting events during the evolution of human cognition. The invention of comforting ideas of an afterlife in another world, or rebirth in this one, with or without transfiguration, may be a direct consequence of the shocking realization of our inevitable mortality. Myths about fountains of youth, as well as works such as 'The Picture of Dorian Grey' by Oscar Wilde, are tell-tale signs that we have never fully come to grips with the fact that ageing and death is the fate that befalls even the most beautiful and strongest among us. It is hardly a surprise, therefore, that scientists have turned their inquisitive minds to understanding, and possibly overcoming, this intriguing biological phenomenon.

One such scientist is yeast geneticist Lenny Guarente, who has gathered his recollections of his "quest for genes that prolong youth" into a slim volume. *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 excite-

ment, 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.

What I found particularly fascinating about Guarente's book were the snippets that give us a glimpse of the inner secrets of how science as a whole works, as related by an insider. To those who are able to read between the lines, these snapshots contain useful advice, particularly for the young and inexperienced, on how to survive, and maybe even prosper, in the world of ivory towers. But it is also confirming and sobering for the 'old lab rat'. Take, for example, the anxious question "Did I make any enemies?" asked rhetorically by the author as early as page 2, when he describes his run for tenure. A bright mind may be a prerequisite for success, but in the business of modern science it is by no means sufficient. Indeed, while the excitement of scientific research and the hunt that precedes a seminal discovery can be felt throughout *Ageless Quest*, the impartial observer cannot help but notice that the romance of science, which emanates from the accounts of past naturalists, such as Darwin's *The Voyage of the Beagle*, has long since gone. The last remnant of this spirit was driven out of academia when the president of a well-known elite American university coined the phrase "Publish or perish", after which universities turned into 'think tanks'.

As far as the 'results sections' of *Ageless Quest* are concerned, Guarente has every reason to be justifiably proud of

his important and probably wide-reaching insights into the control of ageing and anti-ageing. The deacetylase Sir2 has been shown to occupy a pivotal position at this basic level of physiological control, presumably acting as a relay station between the genome and the metabolic status of the organism. With the master regulator of ageing seemingly having been found, this sounds like the end of the story. But is it? Can what may well be the whole, or a large part, of the solution to the riddle of ageing in a single-celled fungus and a lowly nematode be transferred fully to much more complex multicellular beings such as ourselves? Is our biological decline, once we are past our prime, governed by Sir2 alone? Other theories assign much of the blame for our deterioration to free radicals and telomere shortening; how these fit into the picture, and whether they are entangled with Sir2 activity, remains to be seen. *Ageless Quest* can be understood by lay readers with a general scientific background that includes traces of fundamental biochemistry—at least if one attempts to keep up with the finer details of the author's line of argument. In any case, Guarente brings his science to life by taking it out into the real world, and by taking the reader into the smelly air of the strange world of high-tech laboratories.

Being concerned with the attempt to push the upper limits of average life expectancy into the three-digit region, in the light of an exploding human population, half of whom are malnourished and have a total lack of medical care, does seem like an act of Hollywood-style vanity. But, from a healthily cynical point of view, the mere prospect of a cure for the eventually inevitable seems to be a very promising business. The fear of death that hides in most of us is a bonanza waiting to be mined.

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