
References

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Recipe for Imortality

An expert in synthetic biology explains how people could soon live for centuries

THE YEARNING FOR immortality dates back at least to ancient times. As human brain size increased rapidly over the past million years, our ancestors began to think increasingly about the inevitability of death and the redemptive possibility of everlasting life. Ancient pha-raohs, queens, and kings used every means to ensure their vestigial persistence through future ages. They had themselves enshrined in legends, songs, and poems; they had their remains preserved in vast pyramids.

Part of the reason for that yearning may lie in the fact that people already live so long and with such self-awareness. Our species is distinctive in its ability to remember and to predict future events based upon past experience. Before the invention of writing, and even afterward, reliable predictions required the presence of memories in a living person. People well past their reproductive years could add value to their tribe by remembering early warning signs of rare phenomena, such as drought, locusts, and disease.

In modern times our learning extends even further. It includes postdoctoral studies and on-the-job training that may continue well into our 60s. Like our ancient predecessors, we enshrine the most important bits of our collective knowledge, only in more sophisticated embodiments: scientific publications, books, music, video, websites. Nevertheless, when people die, their wisdom -- the memories and mental processes that produced that knowledge -- dies too.

Throughout history, death was associated with assaults, sickness, and privation. Now an increasingly common cause of death is aging. As the wealth of nations increases and exposure to toxins and infectious agents drops, aging will become the cause of most disease, debility, and death. At the same time, many more people will remain active beyond the age of 100. So, beyond the fear of death, there are practical reasons to explore extending our healthy years.

Scientists have much to learn from the longest-lived humans, many of whom will have their DNA sequenced in the next two years. The effort to extend life -- and, even more, to extend life's youthful, vigorous phase-is a clear opportunity for synthetic biology, the technique of extensively engineering the genome. [George Church is a leading researcher in this emerging field.] The cure for aging will probably require a thorough redo of our genome.

We can scour the best of the biosphere for ideas. Species run the gamut when it comes to longevity. Some adult mayflies live, dance, and mate for all of three hours. At the other extreme, some specimens of bowhead whale appear to be more than 120 years old, judging from the age of harpoons lodged in their flesh. The oldest known fish, a koi, was a scarlet female named Hanako, who reportedly died at the age of 226 years on the memorable date 7/7/77. The hard-shell clam Arctica islandica can live more than 400 years (judging from annual shell rings) in nearly freezing water, where rates of metabolism are very low.

But it might be possible to evade aging entirely. In one widely cited publication from 1998 ("Mortality Patterns Suggest Lack of Senescence in Hydra," published in Experimental Gerontology), Daniel Martinez claimed that hydras -- small aquatic animals that look a bit like cacti -- may not undergo senescence at all and may be biologically immortal. More astonishing yet is an organism that appears to do something otherwise unheard-of in the animal kingdom: It gets younger. This ability is possessed by Tur-ritopsis nutricula, a jellyfish that can return from its sexually mature (medusa) state back to a younger (polyp) state. An entire population of such organisms can do this repeatedly and swiftly, escaping biological death through aging, although members of the species can still be killed through predation, accident, and disease.

This bizarre menagerie of extremely long-lived, possibly immortal, and fountain-of-youth organisms leads us to consider humans. Like these organisms, we are built of cells, and some of those cells can be immortal too.

The possibility of cellular immortality is also suggested by the case of Henrietta Lacks, an African American woman who suffered from cervical cancer and died on October 4,1951, at Johns Hopkins Hospital at the age of 31. For research purposes, cell samples had been taken from her cervix. They were code-named HeLa cells, using the first two letters of her first and last names.

Prior to Lacks's death, Hopkins researcher George Gey found that HeLa cells could easily be grown in lab glassware and kept alive indefinitely. As other researchers asked for samples, the cells replicated, grew, and proliferated so wildly that they often took over and wiped out cell lines of any kind with which they happened to come in contact. Descendants of the original HeLa cells are still alive today, more than 60 years after they were removed from Henrietta Lacks. HeLa cells are so biologically aberrant in their chromosome makeup that they could never be used to model immortal human life, but they nevertheless point the way.

The healthy cells most capable of making at least some aspects of individuals immortal are germ cells. The germ line, produced by egg and sperm, is the only part of us that naturally survives us in our offspring. Germ-line cells are the all-time champions of cellular survival. We can trace their dna back through billions, possibly trillions, of binary divisions, back to the dawn of life itself.

Cloning germ cells, then, looks like one possible path to human immortality. Germ cells from a mature animal can be reset to embryonic form; these are the famous "embryonic stem cells." The embryonic cells can develop into replacement organs in the lab or be injected into an egg, where they develop as a viable embryo and are literally born. We can also freeze such cells to keep them healthy and youthful; when the aging donor needs repairs to a damaged genome, the cells could be tapped. Scientists have already cloned more than 20 species, including carp, mice, sheep, monkeys, cattle, cats, dogs, and horses. Cloning is sometimes viewed as dangerous or unethical, but many new technologies are initially perceived that way, then accepted and finally widely embraced -- airplanes, for example, or in vitro fertilization.

At present, the main argument against human cloning is that occasional difficulties observed in cloning other animals suggest that human clones would sometimes be born with medical abnormalities. This is a serious concern, but it doesn't mean human cloning can never happen. In one plausible path to that end, veterinary scientists continue to get better at cloning agricultural mammals until the success rate is extremely high. When the chance of error in animal cloning becomes lower than the error rates of natural reproduction, human cloning trials could become socially and ethically acceptable or even recommended.

But even without cloning, life extension could be achieved. For instance, medical researchers might succeed in creating complex tissues and organs derived from patients' own stem cells. These so-called pluripotent stem cells can be derived from a variety of adult cells and be guided into almost any other tissue type. Synthetic biocircuits made of dna and encoded proteins could be inserted to detect and repair (or kill) cells with mutations known to cause cancer or aging.

In a related approach, new translational codes in the genome -- which define how a cell uses dna to construct proteins -- could make organisms resistant to all viruses. Viruses do their damage by entering cells and using the cellular machinery to replicate themselves. They are able to do this because both the viruses and the host cells make use of the same genetic code. But if we changed the code of the host cells, it would thwart the virus's ability to replicate, and so make the host immune.

That may sound like science fiction, but the Church lab at Harvard has already changed portions of the genetic code of E. coli bacteria to repel viral attacks. Beyond this, we could take the DNA repair abilities from Polypedilum vanderplanki, a fly whose larvae can survive complete desiccation and extremes of heat and cold, and transplant them into human cells.

Ultimately, synthetic biology could free us from obsolete limits set by evolution. We could repair damaged tissue and direct the growth of new tissues to create built-in body and brain parts that could interface with electronic devices. For example, some cells could be engineered to light up and signal if a person is experiencing inflammation, unusual neuronal activity, etc., functioning as noninvasive diagnostic devices.

Globally, life expectancy and the onset of old-age symptoms have been steadily improving at a rate of three months per year. A nearly perfect straight line for the past 170 years! Impressive, but some biotechnologies are improving at up to a tenfold rate per year, meaning that a dramatic change in the slope of that line could happen soon.

The route to long-lived humans will arrive via milestones that we can only guess at. Genome engineering in clinical trials today may become routine by 2014. By 2016 we may have ways to rejuvenate neurons, such as by injecting them with fresh nuclei from engineered stem cells, to make them young again. Or we may have developed miniature electronic circuits capable of monitoring and stimulating neurons, which might be used to augment memory or maintain neural functions during the replacement of neuronal nuclei. Within a decade, we should be able to use these technologies to read and alter the state of neurons for an enormous fraction of the cells in human brains. (We can already do this for dozens of neurons in humans with epilepsy.) This could lead to much longer life spans -- semi-immortality, extending progressively toward an unknown limit -- both for our cells and for our minds.

With such breakthroughs potentially less than a decade away, now is the time to consider what a world of semi-immortals would look like. One of the most commonly expressed objections to the prospect of human immortality is the unintended consequences of overpopulation, including the fear that long-lived individuals would take away jobs from younger people. Yet our resources have kept expanding.

Thomas Malthus died in 1834, worried about the survival of the world population, which then numbered 1 billion people and was growing by 5 million per year. Today the population stands at 7 billion and is growing by 75 million people per year. But instead of the global starvation and misery that Malthus envisioned, we have seen widespread rises in wealth, standards of living, health, and life expectancy. As economist Julian Simon once explained, "Resources come out of people's minds more than out of the ground or air. Minds matter economically as much as or more than hands or mouths. Human beings create more than they use, on average. It had to be so, or we would be an extinct species." Fertility rates tend to decrease with increasing life span even if the number of fertile years per person increases, which counters the trend toward population increase associated with increased life span.

The vision of a nearly immortal populace squelching the job prospects of youth is reminiscent of 19th-century Luddite concerns about machines' taking over jobs from humans. The likelier scenario is a population implosion marked by increasing numbers of older, healthier citizens, and more women in positions of power, a situation that could be beneficial for child rearing, philanthropy, diplomacy, and other aspects of our civilized life. Look for our values to change: With children a rarer resource, educators may become among the highest-paid workers in the world. Instead of teachers, grammar school kids might be coached by personal tutors on the model of the British university system.

One thing that makes for a robust and long-lived species is diversity among the population. That is as true for Homo sapiens as for any other. Personalized tutorial education might yield the advantages of greater human diversity, allowing us to embrace larger spectra of personality types, perceptual and cognitive idiosyncrasies, and high-functioning autistics, bipolars, ADHDS, and hyper-thymesiacs (who can recall autobiographical events in extraordinary detail). People with such traits occasionally succeed today, but in the future could do so more often.

Our new semi-immortals, people of indefinite and unknown longevity, would be a diverse population resistant to all viruses, known and unknown, all other pathogens, and all forms of cancer, autoimmune diseases, environmental toxins, and even radiation -- that last attribute particularly handy for space travel. We can acquire such abilities by importing into the human genome the genetic sequences from other organisms that already possess such attributes. Think of it as genetic data mining. We could get radiation-resistance genes, for example, from the Bdelloid rotifer, a class of small invertebrates that live in freshwater pools and survive megadoses of ionizing radiation. We will acquire other life-span-enhancing attributes by combining the best of all genomes of people who are comparatively youthful even though they are older than 100. The Church lab is currently analyzing the genomes of centenarians.

Semi-immortals could combine the best aspects of youthful dynamism with the wisdom of long experience. Such people in abundance would be of great benefit to society. If most of us expect to live possibly indefinitely in good health, there is a strong motivation to help protect humanity from long-term risks like extinction from a new pandemic, the exhaustion of key nonrenewable resources, global nuclear warfare -- or a meteor strike. After all, the survival of Earth itself is a prerequisite for the survival of individuals, whether mortal or potentially immortal. One does not want to go to all the trouble of reaching for immortality only to be wiped out by a flying rock.

"The cure for aging will probably require a thorough redo of the human genome."

"Like a species of jellyfish that reverts to youth, we may one day evade old age."

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