The Future of Aging

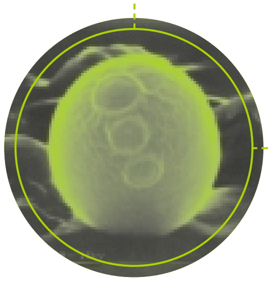
The aging boom is upon us. Life expectancy nearly doubled in the 20th century. Since 1900, the number of Americans age 65 and older has increased 10-fold. The oldest-old—people age 85 and older—constitute the fastest growing segment of the U.S. population. By 2050, this population— currently about 4 million people—could top 19 million. Living to 100 likely will become more commonplace. In 1950, only about 3,000 Americans were centenarians; by 2050, there could be nearly one million.

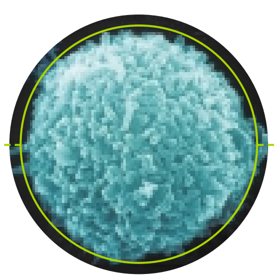
This remarkable burst of longevity, unprecedented in human history, has been possible because of equally remarkable improvements in sanitation, health care, and lifestyle. These advances have led to much conjecture about how aging will evolve in the 21st century. Some gerontologists suspect an average life expectancy of 85 years or more may be possible in the not-so-distant future. Others have speculated that the first person destined to live 130 years or more is alive today. Still others predict that robust health in later life will be more common as fewer and fewer older Americans live with disabilities. Whether any of these visions become reality will greatly depend on the emerging science of aging.

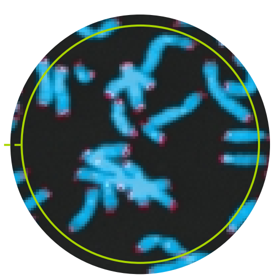
As investigators delve more deeply into how and why we age, its secrets are being deciphered at an unparalleled rate. Scientific understanding of the genetic, biochemical, and physiological aspects of this dynamic process has never been greater. Microarray technology has enabled gerontologists to characterize the expression of vast numbers of genes potentially important in human aging and longevity determination. Experiments involving yeast, fruit flies, nematodes, mice, and primates continue to yield insights into various aspects of aging that could one day be applicable to humans.

Still, many of the fundamental underpinnings of aging and longevity determination remain elusive. The role of telomeres in cellular senescence and aging, for instance, is poorly understood. It is unclear what, if any, effects diminishing hormone levels in later life have on aging, longevity, and health.

Gerontologists have unraveled many of the secrets of aging thanks to experiments with simple organisms such as yeast (below, left). Still, much remains unknown about the processes that underlie the journey from young to old, including the roles that macrophages, a part of the immune system (center) and telomeres (right) may play.







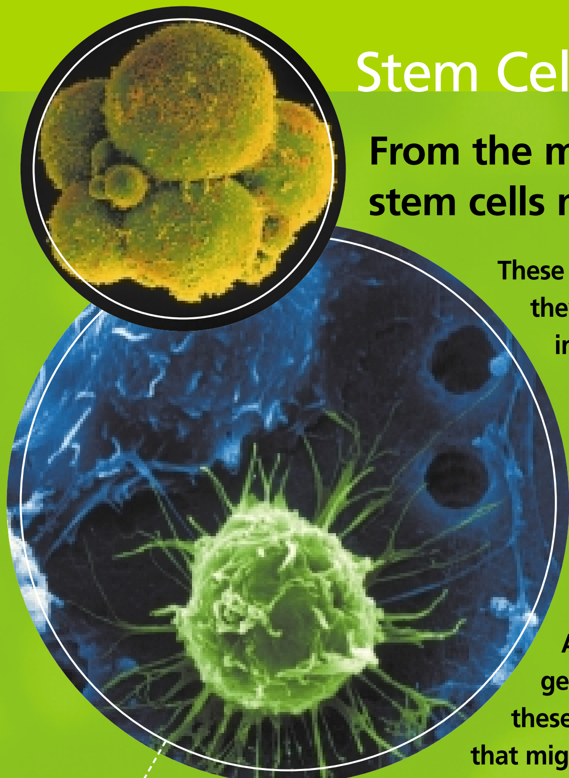
The question has been asked countless times in the 12 months since her 100th birthday…"What's the secret?"

– The Independence (Mo.) Examiner on centenarian Audrey Stubbart's 101st birthday.

Audrey Stubbart, shown at right in 1920, and below with her great-great granddaughter, told friends work kept her alive. During her long life, she taught school, raised five children, and operated a 2,000-acre sheep ranch in Wyoming with her husband. At 66, she took a job at the Independence (Mo.) Examiner, where she was a copy editor and columnist for nearly 40 years. She retired shortly before her death at age 105.

Stem Cells: Great Expectations, but Many Barriers Remain

From the moment they were first isolated in the late 1990s, human stem cells mesmerized gerontologists. And for good reason.



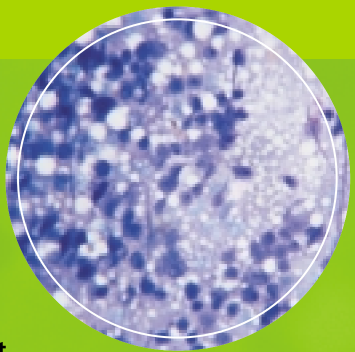
Colorized scanning electron micrograph of stem cells collected from human bone marrow. Stem cells are primitive cells that can multiply indefinitely, migrate to different parts of the body, and develop into different types of tissue. Bone marrow retains the ability to generate stem cells throughout life. Bone marrow stem cells typically give rise to bone, blood, and cartilage.

These versatile cells intrigue investigators because they are capable of transforming themselves into many different kinds of body tissue. Because of this flexibility, stem cells hold enormous potential for cell replacement or tissue repair in many age-associated degenerative disorders where loss of cells is currently irreversible, including diabetes, stroke, heart disease, and Alzheimer's and Parkinson's disease. With millions of older Americans suffering from these conditions, gerontologists are scrambling to find out if these cells will yield any practical interventions that might help promote healthy aging.

Stem cells can be derived from an embryo or an adult. Unlike most cells in the body, such as skin or heart cells, which are dedicated to perform a specific function, stem cells are not specialists. But under certain circumstances, they can differentiate into specialized cells. Another unique characteristic of stem cells is their ability to replicate for indefinite periods without becoming senescent.

Investigators suspect that embryonic stem cells can develop into almost any of the many known specialized cell types in the body, including bone, blood, and brain cells. However, these stem cells are not embryos, and cannot themselves develop into embryos. Adult stem cells apparently help repair or replace those tissues lost through natural attrition, or when they are damaged by injury or disease. Adult stem cells in bone marrow, for instance, regularly replenish the body's supply of red blood cells. Similarly, intestinal stem cells help maintain the lining of the intestines, which is frequently sloughed off in a natural process.

It is not clear, however, if adult stem cells can fully match embryonic stem cells' capacity to differentiate into vast arrays of replacement cells and tissues. In animal studies, certain adult stem cells have shown some potential to develop into multiple cell types, suggesting that both embryonic and adult stem cells could have therapeutic applications. NIA-supported investigators who injected adult mouse bone marrow cells into the circulatory systems of mice, for instance, discovered that these cells found their way into the



brains of the rodents and within 1-to-6 months became neuronal cells. A second study showed that adult mouse bone marrow cells could also develop into heart cells and vascular structures, resulting in the substantial replacement of damaged heart tissue within 2 weeks.

Despite these preliminary successes, many formidable hurdles must be overcome. Investigators still understand very little about how stem cells work, so determining how to get stem cells to do what investigators want them to do in the body remains a mystery. In adults, stem cells appear to become less spontaneously active with age, and some gerontologists suspect that inactivation of these cells may play a prominent role in the normal aging process. For investigators, finding ways to reactivate these cells and get them to where they are needed in the body are significant challenges.

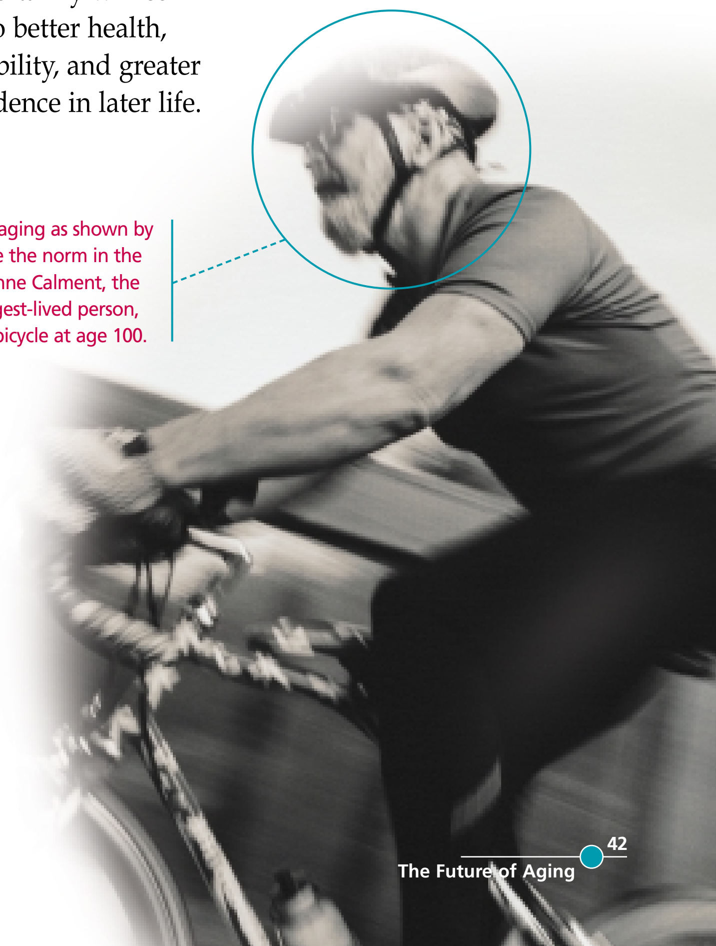
Still, the discovery of human stem cells is an important scientific breakthrough that clearly has the potential to improve the quality and length of life.

"For the first time in human history the prospect of living a long, healthy and productive life has become a reality for the majority of people... What was the privilege of the few has become the destiny of the many."

– Robert Butler, M.D., Gerontologist

Further study is needed to clarify how caloric restriction works, and to determine whether this intervention—or drugs that mimic its effects—might be effective and safe for humans.

These and other lingering research challenges underscore the enormity of the quest facing gerontologists. It is becoming increasingly clear that aging is an intricate bundle of interdependent processes, some of which are better understood than others. As gerontologists untangle these interconnecting genetic, biochemical, and physiological processes, they will likely uncover many more secrets of aging. These discoveries may lead to extended life-spans, and almost certainly will contribute to better health, less disability, and greater independence in later life.



Will robust aging as shown by this man, be the norm in the future? Jeanne Calment, the world's longest-lived person, still rode a bicycle at age 100.