Aging Research Grows Up

Drawing on insights from diverse disciplines such as evolutionary biology and food science, experts on aging are resolving the mysteries of growing old

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Long viewed as an insoluble enigma, aging is shedding its cloak of mystery as scientists start to understand why and how we age. Many studies support the theoretical argument that aging occurs because natural selection weakens with age, leaving us vulnerable to harmful, late-acting genes. As for what causes aging, scientists have narrowed the pack of candidates to a handful, including free radicals and reactions between glucose and proteins. In recent decades, many mechanisms for lengthening life in animals have come to light. By extending this research, scientists may be closing in on ways to lengthen the human life-span.

“Every man desires to live long; but no man would be old.” —Jonathan Swift in 1727, at age 60.

Unraveling the Riddle of Aging

The final 18 years of Swift’s life cruelly proved the truth of his words, as he fell victim to one ailment after another. Despite walking up to 10 hours a day, he grew frail and emaciated, complaining to a friend that “my skin comes off in ten miles riding because the skin and bone cannot agree together.” Fierce boils, some as big as an egg, erupted over his face, arms, and legs. And worst of all, dementia purloined his wit and his wits. The writer renowned for his slashing intelligence and scathing satire died not long after a Dublin “Commission on Lunacy” declared him mentally incompetent.

Eat a spartan diet, run 8 kilometers every day, pop vitamins by the handful, drink only the purest spring water—and you too will deteriorate and die. Although some species seem to elude the ravages of growing old (1, 2), aging is inescapable for humans and many other organisms—unless they die young from other causes. Aging, or senescence, has always been one of life’s cruel mysteries, flummoxing poets, philosophers, and scientists alike. Why would an orderly, well-regulated, vigorous body gradually weaken and fall to pieces? What drives this relentless decay? Not so long ago, the best anyone could do was guess.

But over the last couple of decades, the puzzles of aging have been clearing up like wrinkles under a plastic surgeon’s laser. Scientists have narrowed the causes of aging to a few likely candidates. “I think that we are at a very exciting time in aging research,” says human geneticist Douglas Wallace of Emory University in Atlanta. “For the first time, we have very robust experimental hypotheses to test.” And most researchers are confident that they’ve cracked the deepest enigma of aging. “I think the question of why we age is pretty much solved,” says Steven Austad, an evolutionary biologist at the University of Idaho in Moscow. Aging occurs, the theory goes, because natural selection’s power wanes as organisms get older, and it can’t halt their deterioration.

The best measure of our growing understanding of aging is the ability to manipulate the process in a variety of organisms. Already, scientists have found that genetic tinkering, enzyme mimics, selective breeding, and stringent diets can confer long life on lab inhabitants. For better or for worse, extensions of this research may soon allow us to postpone human aging (see “Life Extension—Our Salvation or Our Ruin?”).

Aging and Natural Selection

Arthritis, atherosclerosis, cancer, diabetes, Alzheimer’s (see “Detangling Alzheimer’s Disease”), and many other dread diseases plague our declining years. Many people mistakenly equate these diseases with aging. But demographer S. Jay Olshansky of the University of Illinois, Chicago, has calculated that even eliminating major causes of mortality such as cancer and heart disease would boost life expectancy in industrialized countries to only about 90 years. We would still get old and die. Aging is not a particular malady. It’s a distinct process, a progressive decline in function that makes us more vulnerable to these crippling or fatal age-related illnesses.

So why do our bodies gradually fail? We might be tempted to think of aging as a bit like mandatory retirement. From this perspective, aging serves to cull the old and make way for the young, thus promoting the survival of the species (3). But this naïve argument, which still appears embarrassingly often in the literature, fails at every level (3, 4). On the practical side, aging causes little mortality in nature. What demographers call extrinsic mortality—death from predators, disease, starvation, adverse weather conditions, and mishaps—cuts down most wild animals before they reach old age (3). And at the theoretical level, the argument relies on a wrongheaded view of evolution, discredited decades ago, that natural selection works to benefit the species (4, 5, 6). Natural selection favors traits that enhance the fitness of indi-

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viduals, and it can even promote traits that harm the species in the long run (4). The interests of species and individual may be identical—for example, a gene that increases drought resistance helps both individual and species. But when they clash, the interest of the individual prevails.

At first glance, the individual-selection perspective doesn’t seem to clarify matters. How could failing eyesight, deafness, clogged arteries, and incontinence possibly boost an organism’s fitness? A key insight resolves the problem. Aging is non-adaptive deterioration that occurs beyond the reach of natural selection. Although we often imagine it as an all-powerful Grim Reaper, natural selection actually has little impact on older animals.

From that revelation, biologists have hammered together a comprehensive theory of the evolution of aging (7). Immunologist and Nobel laureate Peter Medawar (8) and evolutionary biologists George C. Williams (9), W. D. Hamilton (10), and Brian Charlesworth (11) did most of the heavy lifting.

They recognized that a gene’s impact on fitness depends on when it is expressed. A young animal’s entire reproductive life lies ahead, so genes that act during youth exert a powerful effect on the animal’s fitness. However, genes acting after the beginning of reproduction exert a diminishing effect because those genes have already been transmitted to offspring. The force of natural selection declines rapidly after reproduction commences (Fig. 1). As a consequence, natural selection cannot purge genes that express harmful effects later in life.

According to the theory, then, aging results from the injurious actions of these "untouchable" genes. To put it another way, we age because natural selection also grows feeble with age. "Natural selection is why your body works," says Michael Rose, an evolutionary biologist at the University of California (UC), Irvine. "So if natural selection becomes weak, medically speaking, you’re going to be screwed."

Williams and Medawar proposed that two kinds of genes could drive aging (8, 9). The first kind are pleiotropic genes that have different effects in early and late life; this form of pleiotropy is known as antagonistic pleiotropy. When we’re young, these genes help us, but when we’re old they stab us in the back—or in the heart, the kidneys, the brain, the knees. The second kind of genes are strictly harmful, but they act only after a certain age. Such genes continually arise through mutation, but unlike deleterious mutations that manifest early, they can’t be pruned by natural selection.

Descending from the airy realm of theory, lab and field studies back the argument that weakening natural selection “allows” aging. Working with a laboratory population of Drosophila, Rose and colleagues intensified selection on later ages (12). The scientists gathered only the eggs laid by old females and used them to found the next generation. Repeating the procedure for 15 generations produced a 21% increase in longevity (Fig. 2). Continuing the selection for 2 decades doubled the life-span of the flies, which began reproducing at an age when most of their short-lived ancestors would have died.

But these flies don’t just stick around longer. They are über-flies, superior to the control group in almost every respect (7). They can fly for a longer time without tucking out. They store more fat and glycogen and better resist desiccation, starvation, and stress (13, 14). And making Hugh Hefner envious, the males can mate with eight to 10 females a day. “I have the flies that everyone would like to be,” says Rose. A similar, independent experiment by Leo Luckinbill at Wayne State University in Detroit also yielded ancient flies (15), although some of the traits enhanced by selection differed. And selection favoring early reproduction reverses the changes in life-span and vigor (16).

Rose and Luckinbill manipulated reproduction; altering mortality can trigger similar changes. If the rate of extrinsic mortality declines, natural selection weakens more slowly and animals should remain vigorous longer, according to the theory. That’s exactly what Austad observed in his study of opossums that inhabit a predator-free island off the Georgia coast (17). Not only did the shuffling, ratlike marsupials live longer than mainland animals, they also appeared to senesce more slowly. For example, the flexibility of collagen in the tail—a gauge of aging rate—declined at a lower rate among the insular opossums.

Surveying the evidence, Rose is confident that we’ve solved the problem of why aging occurs. “I think that most of the really deep questions about aging have been answered,” he says. All that’s left to accomplish is working out the details, he adds. Caleb Finch, a molecular biologist at the University of Southern California in Los Angeles, dissenters. We may need to revise the theory, Finch says, if turtles and some fish really aren’t aging (2).

Nabbing the two-faced pleiotropic genes and late-acting mutations that hasten physical deterioration would bolster the theory. Most searches for these genes have used statistical analysis to infer their presence (18, 19). For example, Rose and Charlesworth (18) measured reproduction at different ages in Drosophila. Increases in late-life reproduction brought decreases in reproduction at younger ages. This inverse relationship suggests the presence of pleiotropic genes, the authors conclude.
ed, but they did not identify any of the genes responsible. Although almost everyone agrees that age-related pleiotropic genes exist, specific examples are rare (3, 20). Even harder to find are the late-acting mutations; so far, the evidence for these genes is equivocal (3, 21).

OK, we get old because natural selection lets us down. But that raises another question: How do we age? What erodes our cells, tissues, and organs until they fail? Although scores of hypotheses to explain the mechanisms of aging have surfaced over the years—from radiation exposure to parasite attack—most of them have sunk again. Today, scientists are closing in on a few biochemical assaults that are probably responsible. Although their details vary, all the mechanisms come down to trade-offs between current survival and longevity. As Austad puts it, “Life, no matter how it is lived, is damaging to our health.”

Unleash the Radicals
Every breath an animal takes hastens its own death (see “The Two Faces of Oxygen”†). Releasing energy through aerobic respiration spawns reactive oxygen species as inevitable byproducts (22, 23). Sometimes called free radicals, oxygen radicals, or oxidants, these molecular vandals can arise anywhere in the cell, but most are born within the cellular power stations called mitochondria. They are the smoke given off by the mitochondrial fireplace, says Emory’s Wallace.

The main culprits are superoxide anion (O$_2^-$), hydroxy radical (•OH), and hydrogen peroxide (H$_2$O$_2$). These greedy molecules swipe electrons from other molecules they encounter, including vital cellular components such as proteins, DNA, and fats. The reaction can wound the macromolecule and creates another oxygen radical, sparking a chain reaction of destruction.

Not all free radicals are rogues (22). Immune cells dose pathogens with hydrogen peroxide, for example, and other oxygen radicals carry messages in the signaling pathways that regulate cell division (24). Even so, organisms spend energy to produce antioxidants for combating these ravenous molecules, suggesting that free-radical damage poses a threat. The enzymes superoxide dismutase (SOD), catalase, and glutathione peroxidase sop up and neutralize free radicals (22). Other molecules, such as ascorbate, pyruvate, and the carotenoids, form another arm of the antioxidant defense system.

Research on free radicals—and speculation about their effects—is booming. But although almost everyone agrees that free radicals injure cells and promote aging, no one can say how significant they are or exactly how they make us old. “We need a greater emphasis on understanding the sources of free radicals and what targets are damaged by them,” says molecular gerontologist Simon Melov of the Buck Institute for Age Research in Novato, California.

So far, tantalizing but circumstantial evidence links free radicals to life-span. One study found that transgenic fruit flies with extra copies of the genes for SOD and catalase live about one-third longer than normal (25). By spraying the nematode Caenorhabditis elegans with synthetic antioxidants, Melov and colleagues boosted the worm’s life-span by 44% (26). And longer lived species of mice also produce more antioxidant enzymes and fewer free radicals in their mitochondria than do shorter lived species (27). Furthermore, heightened oxidant resistance characterizes many of the long-lived mutant flies, worms, and mice discovered over the last few years (see next section).

To fill in the missing details, many researchers are focusing on events in the mitochondria, which are veritable free-radical factories. Wallace believes that oxidative damage to mitochondrial DNA (mtDNA) may be one underlying cause of aging. In a study of knockout mice that generated excess free radicals (28), he and his colleagues found higher-than-normal rates of mtDNA rearrangements in some tissues. Accumulated mtDNA damage eventually leads to cell suicide, Wallace says, and this process of apoptosis may slowly winnow functional cells from our tissues and might account for some of the effects of aging (see “More Than a Sum of Our Cells”§). Gradual apoptosis of muscle cells, for instance, could explain the progressive decline in physical strength as we get older. But to confirm this hypothesis, “a lot of good, hard science still needs to be done,” he says.

Grow Old Like Your Breakfast
Free radicals have won many hearts and minds, but another kind of chemical reaction, in which glucose couples with and irreversibly alters proteins, may also drive the molecular disruption of aging. In the chemistry textbooks it’s known as the Maillard reaction. Food scientists prefer a more colorful name: the browning reaction, because the same chemical transformation occurs as food is cooked, producing the golden-brown coating on French toast, for instance. As biochemist Anthony Cerami first realized while working at Rockefeller University in New York City (29), this reaction occurs within the body because glucose, despite its sweet reputation, can be rather nasty.

The trouble begins when glucose sticks to a protein and then undergoes an irreversible transformation to a brownish or yellowish molecule known as an advanced glycosylation endproduct, or AGE (Fig. 3). To hard to remove, these cellular troublemakers can crimp a protein, change its solubility, or clog an active site (30), and thus interfere with function. The sticky ends of AGEs can also adhere to a neighboring protein, forming a permanent cross-link that may disable both. For example, AGEs may produce the increased cross-linking between collagen molecules that accounts for cartilage’s reduced flexibility with age. As a final insult, AGEs can fasten onto DNA and may fracture the strand or block the expression of genes (31). Accumulate enough of this damage, the argument goes, and you’re toast.

Unfortunately, food scientists know more about tweaking the Maillard reaction to make pleasantly browned pizza crust than gerontologists know about the action of AGEs in the body. As a result, the evidence linking AGEs to aging (29, 32, 33) remains scant and inconclusive.

Aging and Cancer Prevention
In 1961, cell biologist Leonard Hayflick discovered the Holy Grail of aging—or so it seemed at the time. Studying human fibroblasts growing in culture, Hayflick noticed that cells divide a limited number of times, usually between 50 and 80 replications. Later work revealed that telomeres, repeated DNA sequences at the tips of the chromosomes and their associated proteins, shorten with each division and act as a meter, counting the number of duplications. Once the telomeres wear down, the cell enters an altered state called replicative senescence. It loses the ability to divide, resists apoptosis, and undergoes other bio-
chemical changes (34). Hayflick’s observation inspired a seductive hypothesis: Maybe we age because more and more of our cells senesce, and our physical infirmities result from a reduced capacity to replace dead or worn-out cells (see “More Than a Sum of Our Cells”\(^1\)).

Although the “Hayflick limit” appears to operate in some types of cells removed from an animal’s body, its role in organismal aging remains controversial. Doubters such as Wallace point out that cells in many parts of the body, including the muscles and heart, stop dividing during development, long before they hit the duplication limit. And continuously regenerating tissues such as the skin and the gut lining contain plenty of cells capable of dividing—including in samples from the elderly. Even Hayflick, now at UC San Francisco (UCSF), no longer sees limited replication as the chief problem of aging.

However, losing the ability to divide may undermine tissues that must quickly churn out fresh cells, says cell and molecular biologist Judith Campisi of Lawrence Berkeley National Laboratory in Berkeley, California. It may hamstring the immune system’s capacity to respond to novel pathogens, she says, and it may underlie the slower wound healing of elderly folks.

Replicative senescence may also exact an unexpected, age-related cost by promoting cancer in older animals (see “Dangerous Liaisons”\(^2\)). The notion is paradoxical, says Campisi, because the changes in a senescent cell serve to thwart perpetual cell division. Her recent research (33) reveals that even prime candidates for cancerous transformation—young cells that show DNA damage or that overexpress oncogenes—senesce. “To my mind, this is some of the strongest evidence that the senescence response evolved to protect against cancer,” she says.

Sounds like those self-sacrificing cells deserve three cheers. But as we get older, arrested cells can make trouble, because they aren’t inert. At least some seem to ooze enzymes that dissolve the intercellular matrix—the gluelike stuff that holds cells together—and break up surrounding tissues. Whether a cell becomes cancerous depends not only on genetic damage but on signals from its surroundings, says Campisi. These signals can prevent a cell from dividing uncontrollably even if it has all the requisite mutations (35). As the tissue fragments, however, this restraint wanes, and the cell can begin its mad multiplication. This may be another example of antagonistic pleiotropy, Campisi points out. The price of early cancer prevention may be cancer later in life.

Although each of these mechanisms—oxidative damage, AGEs, and replicative senescence—has its champions, research so far hasn’t implicated any mechanism as “the” cause of aging. And in fact, there’s no reason why all of them, or some combination, can’t be operating in different organisms or even within the same organism. As neurobiologist David Greenberg of the Buck Institute emphasizes, different organs in the body may age differently, and two cells within a particular organ may age at different rates and for different reasons.

Fig. 3: Fatal attraction. Browning reactions begin when glucose sticks to a protein (A). The product of that reaction undergoes complex changes to become an advanced glycosylation end-product. AGEs may snare a neighboring protein to form a permanent crosslink between the strands. Chemists have worked out the structures of only a few AGEs and crosslinks. One crosslink whose structure is known is 2-furanyl-4(5)-(2-furanyl)-1H-imidazole, also known as FFI (B).
The diets provide all required vitamins and minerals, but the animals receive much less food than they want. If you’re thinking of trying this at home, take note: This austere diet hasn’t yet been proven to increase longevity in any primates, least of all humans (37). However, caloric restriction is just one of many ways of cheating death, at least temporarily. Over the last decade, for example, researchers have discovered a horde of genes that stretch life-span in mice (38), Drosophila (39, 40), yeast (41, 42), and nematodes (43) (see Genes/Interventions Database6). Death takes a holiday for these creatures, some of which can live four times longer than normal.

Scientists know the most about the connection between genes and long life in C. elegans. They are unraveling the biochemical pathways that influence aging in these minute worms (Fig. 4) (43, 44) and have uncovered a number of life-extending genes that participate in the insulin/insulin-like growth factor (IGF-1) pathway, which governs growth, development, and metabolism. Genes in the pathway can also nudge the worm into a stress-resistant, sporelike state known as a dauer.

The discovery that single genes could dramatically extend life shocked many biologists. Although these genes have provided a new perspective on aging (45), they’ve also stirred up trouble. If you want to have fun at an aging conference, stand up in the bar and shout, “Aging is programmed.” Then duck as glasses and curses start to fly. To some scientists, the discovery of genes that lengthen life is indisputable evidence that aging must be a programmed process akin to development. However, many biologists howl at the suggestion of programmed aging.

“Aging as a process is antidevelopment,” says evolutionary geneticist Marc Tatar of Brown University in Providence, Rhode Island. “Aging is the falling apart of things.” What’s more, programmed aging doesn’t square with evolutionary theory: Natural selection wouldn’t favor a self-destruct mechanism. Says molecular biologist Gordon Lithgow of the Buck Institute, “You’d almost have to rewrite the whole theory of evolution to accommodate programmed aging.”

The field might not need a marriage counselor. Cynthia Kenyon of UCSF, who has spearheaded the C. elegans genetic work, suggested several years ago that aging might be comparable to “programmed” processes such as embryonic development and the cell cycle. However, she now shies away from that inflammatory word, preferring the milder term “regulated.” “I believe that aging in animals proceeds at a certain rate because of gene regulation,” she says. And some scientists see a movement toward reconciliation that can explain the flexibility in life-span without violating the tenets of evolutionary theory. “I would say that what is programmed is a way to sense the environment and to make a decision on how rapidly aging should proceed,” says molecular biologist Leonard Guarente of the Massachusetts Institute of Technology in Cambridge. Facing hard times, an organism may be able to slow its aging by entering a stress-resistant, hardy life stage, he conjectures. C. elegans hunkers down as the nonfeeding dauer. In rodents and possibly other animals, he believes, caloric restriction may provoke a comparable state.

What’s surprising, says Guarente, is that the switching mechanism may be universal. He and his colleagues have fingered a gene silencer named SIR2 that increases life-span in yeast (41, 46). The same gene lengthens life in nematodes (47), even though worms and yeast age very differently. And a family of similar genes turns up in mammals, including humans, although their functions are unknown. Guarente thinks that the link between SIR2 and longevity is a molecule called NAD, which sops up electrons from chemical reactions throughout the cell—including those that break down food. SIR2 needs NAD to work, and, Guarente speculates, caloric restriction may boost available supplies of NAD by slowing metabolism. The extra NAD may ensure that SIR2 keeps its target genes shut down, preventing them from turning on at the wrong times.

Inappropriate gene activity could be an underlying cause of aging, Guarente says. Supporting the notion of a universal mechanism, many long-lived flies, mice, and worms have altered insulin/IGF-1 pathways (48). Ames dwarf mice, for instance, live about 50% longer.

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**Fig. 4: What turns the worm.** In nematodes, several genes and input from sensory organs and the reproductive system influence the pace of aging.
longer than normal-sized mice and have much lower IGF-1 levels (49). However, neuroendocrinologist William Sonntag of Wake Forest University in Winston-Salem, North Carolina, warns that we shouldn’t be too quick to generalize. He questions whether these mice are really comparable to elderly worms and flies. Ames dwarf mice are riddled with defects, including low levels of growth hormone and thyroid-stimulating hormone. With so many changes, no one can yet pinpoint which is responsible for the mice’s longevity, he says.

Whatever the mechanism, Tatar and Lithgow concur with Guarente that many organisms show life-span flexibility in the face of hostile conditions. A common theme is that nearly all life-extending mutations or conditions (such as caloric restriction) step up resistance to stresses such as heat and oxidants, says Lithgow. And individual selection would favor such a switching mechanism as a way to respond to an uncertain environment. If resources are bountiful, an organism can live large, whereas lean times would require a thrifter existence.

But everything isn’t hugs and kisses just yet. Another scuffle has erupted over whether slow-aging animals pay a price for their extra time on Earth. No one disputes that these animals live long. But do they prosper? According to Tatar, evolutionary theory predicts that increased longevity should come at some cost. No organism can maximize every aspect of its life, he asserts, so if life-span stretches, something else has to give—usually reproduction. If life extension didn’t exact a toll, the world would be swarming with antique worms and buzzing with ancient flies. That these Methuselahs are extremely rare argues that their fitness is lower than that of normal individuals, he says.

Experiments so far give contradictory results on this question. Kenyon argues that her studies and those of other scientists show that many of the mutant worms are fit, even though some do have problems (48). Supporting her view, geneticist David Gems of University College London and colleagues screened nematodes with different mutations in thedaf-2 gene, one of the longevity-promoting genes. They found that whereas many of the mutant strains showed abnormalities, such as reduced fecundity and physical deformities, some seemed to reproduce and live normally (50).

Tatar counters that the researchers simply didn’t investigate the right situations. Lithgow agrees: “I’ll bet that any long-lived mutant has something wrong with it.” For example, Lithgow and colleagues unveiled an unexpected cost to long life in some mutant worms. They tested the survival of a mixed population of wild-type worms and long-lived animals that carry a mutant form of the gene age-1. Although the mutant worms compete successfully with wild-type animals when food is readily available, periods of starvation (like the worms would encounter in nature) cause them to die out in only a few generations (51). “Their fertility is rubbish under starvation,” says Lithgow.

What’s more, many long-lived lab animals suffer from severe defects that would kill them in the wild. Rodents raised on short rations grow into stunted adults that are usually sterile. To survive outside the lab, they’d need tiny polar suits, because they can’t maintain their body temperature. Similarly, Ames dwarf mice are sterile without injections of the hormone prolactin, says Andrzej Bartke, an endocrinologist at Southern Illinois University in Carbondale, and they are less active than normal mice. And a controversial paper argues that the longevity of mutant worms results from reduced metabolism (52). If that’s true, these animals suddenly become humdrum, because scientists have known for decades that slowing the metabolism of ectotherms (say, by raising the animals at low temperature) increases life-span.

More is at stake here than the well-being of a few nematodes. Studies like these might carry an important message for researchers seeking ways to slow human aging. If longevity always comes with trade-offs, any attempt to extend human life-span might produce grizzly side effects. However, most researchers are confident that we can get greater longevity while avoiding or minimizing the costs. “We are going to find ways to improve human health,” says Sonntag, “but it’s going to take an awful lot of work to do it.”

Just about everyone agrees that human aging is the next frontier—and measures to slow our aging may not be far away. Austad is so sure that life-extending interventions are in the offing that he put money on it, wagering fellow researcher S. Jay Olshansky that someone will live to the age of 150 by the year 2150. (One of the winner’s descendants will collect on the bet.)

The prospect of changing such a basic and universal human characteristic thrills some and appalls others. Whatever your view, in recent years we’ve clearly crossed an intellectual threshold, says UC Irvine’s Rose: “Aging is not immutable. It’s not God’s grace. It is a genetic problem, and you can solve it.”

Mitch Leslie is a science writer in Albuquerque, New Mexico. He plans to be the first 75-year-old to win Wimbledon, which gives him 40 years to develop his backhand.

Glossary

Antagonistic pleiotropy A phenomenon in which a gene has positive and negative effects at different times of life.

Apoptosis A genetically regulated process in which a damaged or unneeded cell commits suicide; also called programmed cell death.

Ectotherms Organisms that maintain body temperature by absorbing heat from their surroundings rather than by producing heat internally; describes reptiles, amphibians, most fishes, insects, and invertebrates. Contrasts with endotherms, animals such as a birds or mammals that produce their body heat through metabolism.

Pleiotropy A phenomenon in which a gene has more than one effect.

Replicative senescence State in which a cell, after dividing a set number of times, loses the ability to replicate again and enters a semidormant state.

Senescence Synonym for aging. A decline in physiological performance accompanied by falling reproduction and a reduced probability of survival.

Telomeres Structures made of repetitive bits of DNA sequence and associated proteins that cap the ends of chromosomes.

Further Reading


References


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