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Chapter 5 What Are the Secrets of Living Cells and Organisms That Show Little or No Aging?

Aging does not appear to be universal among living things, or, at least in some organisms, it occurs at so slow a rate as to be negligible. In his encyclopedic volume on aging, Caleb Finch (1990) outlines several classes of living things that show only negligible senescence, and I will give some examples in this chapter to give an idea of the ways that have evolved for organisms to age very slowly.

Germ Cells

Cells are the units of life, and even within our own bodies there are cells that do not show normal human aging. We are made of two general kinds of cells, somal (body) cells that age, and germ-cell line cells that do not, at least not in the way that somal cells do. This is true not only of germ cells in humans but also in all organisms that have separate somal and germ cell lines--mammals, fish, reptiles, birds, insects, snails, nematodes, and plants. The germ-cell lines within each of us are involved in producing sperm and eggs (ova). As was mentioned in the last chapter, the other cells in our body, which make up organs, including brain, liver, skin, heart, and muscle, are called somal cells, and, when we talk about senescence, we are usually referring only to our somal cells. Although our reproductive organs age, the ova, sperm, and cells that generate them in our reproductive systems, do not show general signs of aging, even after many generations. This fact belies the idea that, in us, aging is inevitable. If germ cells exhibited aging the way that our somal cells do, we would deteriorate with each passing generation and certainly would not be continuing to set new world records at Olympic games.

But it would be mistaken to say that no germ cells exhibit signs of damage. If we look at female ova (unfertilized eggs), some of them show some obvious signs of damage over time, and the male reproductive system typically generates fewer viable sperm as we age. However, other ova and sperm seem to be able to contribute healthy starting material even late in our reproductive years, allowing offspring to start life anew and live as long as we do.

One explanation for the problems seen in female ova as women age is that the ova are generated early in life, and remain poised for final cell divisions just before and after fertilization. Things can go wrong in these cells as they sit and wait their turn at ovulation. Males continue to generate fresh sperm, but, of course, the stem cells that produce these sperm must continue to divide properly and maintain their genetic material. Other than the chromosomes (containing our genetic material) from sperm, it is female ova that provide most cell components to the fertilized egg. The repair and maintenance of DNA and other essential cell components in the germ cell lines that make male sperm and female ova must be at a high enough level to assure a low probability of serious damage during our reproductive life.

Of course, there are damaged cells that get destroyed in the reproductive system, and even some of the fertilized eggs do not develop properly, often resulting in miscarriages. It has been estimated that one-third to one-half of all pregnancies are aborted very early, before the woman knows she is even pregnant. Of course there can be

a number of causes of miscarriage, not just damaged starting material. Nevertheless, it is clear that not that every ovum and sperm is perfect, but enough are maintained at a level that avoids a decline in viability or rise in frailty through the generations.

Each of today's living cells can trace its ancestry directly back to the first living cell, a time span of over 3.5 billion years. Thus, senescence is not necessary in living cells, at least over a 3.5 billion year time frame, because we have a continuous line of cells that were generated, one after another, during all that time.

Ageless Beings?

Beyond germ cell lines, which are merely parts of organisms, there are known to be several kinds of whole organisms that age very slowly, if at all. Included among these are prokaryotic organisms (single cells that have no nucleus, such as bacteria), some plants that are capable of vegetative reproduction, possibly a few animals (but no known mammals), and some long-lived trees, such as the giant redwoods, Douglas firs, and bristlecone pines. In addition there are clones of some organisms that appear to have virtually unlimited existences. I'll examine each of these below.

Prokaryotic Cells

It should not be surprising to see prokaryotic cells on the list of non-aging creatures. These are simpler, single-celled creatures that reproduce by splitting, or fission. Bacteria and other prokaryotes are therefore in the direct line of reproduction—they divide, many into roughly equal parts, producing two daughter cells from a single parent cell. Some higher-order (eukaryotic), single-celled creatures, such as yeast, have more complex life cycles and divide unevenly, and these do show versions of aging. But, for the simpler prokaryotic organisms, if aging were to occur at even a low rate, they would have disappeared long before the three-plus billion years that have passed since they first evolved.

Some recent experiments (Stewart et al, 2005) suggest that, even in bacteria, there are damaged parts that need to be eliminated through the generations, and bacteria have evolved ways to assure that, at division time, one of the two daughter cells avoids getting the possibly damaged parts. This might be taken as a form of aging for the hand-me-down daughter, but it also is a way of creating a line of non-aging organisms that works for an organism that is constantly dividing. Thus, as a bacterium divides, some of its older parts can be passed selectively to one of the two daughter cells, and, if the parts are defective, that daughter cell will be at a disadvantage and divide somewhat more slowly in the future. This selective partitioning of older parts may be viewed as a sign that even bacteria show a form of aging, or generational damage, but it is quite different from what we normally call aging, and we are not sure, at this time, if the more slowly dividing cell line has a way of eventually repairing itself and dividing more quickly again. The drop in division rate is only 2.2%, so we are not talking about a large effect, at least over a couple of generations. Nevertheless, there is an indication that even bacteria may have older parts that no longer function as well.

In more complex organisms, such as humans, we do have some cells that continuously divide during our lifetimes, and these cells have the potential to renew themselves and to get rid of damaged cells by destroying them and making replacement cells. They also can dilute some kinds of toxic waste simply by continuing to grow and

divide. However, not all of our cells continue to divide. So, this is not a solution to aging that would work for all parts of our bodies.

Plants, And The Like

Some plants multiply by vegetative means—cut off a limb, put it in the ground, and a whole new plant will develop. I once brought home a large gumbo limbo tree stump, cut from the middle of a downed tree, which I placed in our yard to use as a planter. I had dug a little hole to place the stump in to keep it stable. I even had started to dig out holes in the top of the stump for holding dirt and small plants, when I noticed that a sprout had appeared from the stump itself. I let it grow and soon had a full gumbo limbo tree growing in the yard. It is a lovely tree. Being fortunate enough to live in South Florida, I also have created green dividers along fences by trimming aralias and jamming the cuttings into the ground. Each grew into a new plant, the top of which could be cut, in turn, and placed in the soil to fill in the row. This ability of a cut branch to reorganize itself into a whole plant and regrow into a full organism can be repeated indefinitely, suggesting a lack of normal aging among some of the cells in the plant, since these are able to serve as stem cells for forming all of the parts of the plant. Bananas are another example of plants that are able to grow in a vegetative way, through spreading roots, and have been doing so for centuries, without the need for seeds.

Most long-lived trees, such as the redwoods and Douglas firs that are found along the Pacific coast, grow to large sizes. Bristlecone pines are said to hold the record, at about 5,000 years. One secret to long life and low aging rates in these large trees is that they continually grow, creating new rings with a fresh production of living cells each year. Many of these trees also produce more and more potential offspring as they get larger, and their rising fecundity is a sure way to encourage the evolution of longer lifespans. Most of the interior of trees actually consists of dead cells, but there is a continuous production of living cells that occurs under the bark through the hundreds and even thousands of years that these majestic beauties live. Of course, such a fresh production of cells is no assurance of extra long life—the skin of a mouse shows signs of aging in a couple of years while constantly producing new cells. As was the case with bacteria, it should be clear that humans cannot hope to solve the aging problem just by looking at how long-lived trees do it. For us, special issues arise because of the long-lived cells that make up several important parts of us, as we will see below. More and more old-growth forests are being logged, so, if you have not already done so, it is worth the effort to see what is left of these giants. The northern coast of California, with its redwoods, is nice, but I especially enjoy the Olympic Peninsula in northwest Washington State. I get a spiritual boost just walking among the giant Douglas firs in the forests there, and think that anyone who has not had the experience ought to while they still can.

There also are plants that grow as clones and can reach tremendous sizes and ages. These include huckleberry, creosote, and quaking aspen. The older parts of the "organism," often toward the center of the clone, do appear to die over time, but the outer edges of the clone continue to survive and expand. One existing huckleberry is estimated to be older than 13,000 years, and a King's holly shrub in Tasmania has claims on being the oldest living plant at 43,000 years (Holden, 1997). However, it may be a stretch to consider this individual survival. None of the cells making up the young clone still exist, and the very structure of the organism has changed dramatically—everything about it is

new, so the major link to the past is a common cell lineage, the same link we all share with our own germ cell lines. The example of clones does point, once again, to continued growth as a potential contributor to longevity, and we will see that theme continue to be repeated.

Are There Especially Long Lived Animals?

Humans are not the longest-lived mammal, but we do appear to be the longest lived mammal of our size. Whales outlive us, as has been demonstrated by finding hundred-year-old lance tips from earlier whale hunts buried in the blubber of whales more recently caught. Maximum life expectancy is not known for whales, but they have been aged by such lance fragments at 115-130 years of age. With that number coming from such a small sample size, it is clear that some must have considerably longer life spans than humans. While whales might live to 200 years, that is not long enough to classify them as showing negligible senescence. It does not appear that there are any mammals on the list of creatures that have negligible senescence.

Looking beyond mammals, there are some other animal contenders. The problem is finding adequate data to document the age of some of these, but some appear to live longer than we do. Limited evidence supports the idea that some fish live for very long periods of time, perhaps 150 years or longer. These tend to be fish that live in cold waters and continue to grow throughout their long lives. Thus, they have lower metabolic rates, continued growth, and increased fecundity as aids to longer life. The continued growth might also allow them to dilute any toxic waste products that might be difficult to dispose of. Their lower metabolic rate allows the damages associated with oxidation and free radicals to accumulate more slowly, or have more time to be corrected before irreversible damage occurs. But, as with whales, there is no solid evidence supporting the idea of negligible senescence, merely support for the idea that they age slowly.

Some large land turtles also appear to have considerable longevity potential, perhaps for similar reasons. Tortoises appear to metabolize slowly, as reflected in their slow movements. It is difficult to say what the maximum life span is for such turtles, and records are incomplete, but there are recent reports of a Galapagos land tortoise that recently died at the Australian Zoo in Queensland at a purported age of 176 years.

Certain invertebrates, such as bivalve mollusks also appear to have long life spans, as determined by their annual growth rings. Two-hundred-twenty rings have been reported for one such species of mollusk.[1]

Other than whales, all of these animals with longer lives are ectothermic, or what we used to call “cold-blooded,” meaning they do not maintain a constant body temperature. Mammals and birds, which are endothermic (“warm-blooded”), regulate body temperature, using metabolism to help maintain a set body temperature, and this requires more fuel burning and risks more oxidative damage, which contributes to aging, as we will see. So, some ectotherms might be able to outlive humans, but they live life at a slower rate--they are not burning calories at the same rate that we do. That does not imply that we are already at a limit in terms of our lifespan, for reasons we will soon discuss, but it does place us at a higher level of risk for at least one underlying cause of aging—oxidative damage, and we require special efforts to avoid or repair the damage.

Special Risks for Human Brains

Our body (soma) can be split into three parts: extra-cellular materials, cells that turn over and can be replaced regularly, and cells that are not, or not usually, replaced. Each has its special problems when it comes to aging, and I will examine the problems and issues associated with each in Chapter 8.

For now, what is important to realize is that humans, and mammals generally, present special problems for enhanced longevity because our brains, arguably the most important part of us, since they makes us human, have cells that not only are very long lived but also exhibit high levels of metabolism. Neurons are especially active and use a disproportionate share of the body's energy as they function. As mentioned above, that puts us at risk for oxidative damage. Such damage is especially risky for neurons because most damaged or destroyed neurons in our brains are not replaced. Unlike redwoods, and other long-lived plants, we do not have the option of continuing to replace all of our cells. Especially in the case of the brain, we would no longer be ourselves if we were to create new neurons to replace the old. The old neurons have special connections with each other, and those connections are formed on the basis of our experiences and allow for our memories and give us our identity as unique individuals. This is why one might prefer to be the organ donor rather than recipient for a brain transplant! Not that I ever expect such a transplant to be possible.

The signal-transmitting cells of the brain, neurons, are, with few exceptions, as old as we are--most of the neurons in our brains were there at birth. Their connections with each other have both sprouted and been pruned during our lives, but the individual, delicate cells are not usually replaced if they are damaged or destroyed. Replacement neurons appear in only a few regions of the brain, such as the hippocampus, a region of the brain involved in allowing the brain to form new memories, but not necessary for retrieving old ones. Even were we able to develop replacement neurons, these would not be able to capture the wiring connections that developed with our lifetime of experiences. Even were we able to find a way of growing new neurons throughout the brain, and replace all of our neurons, our experiences would be lost along with the original neurons, and with that loss would go our memories and our sense of who we are. Our genes contain the blueprint only for the initial structure of the brain, not for the detailed structure that builds as a result of the experiences that mold and prune the connections during life. Those connections allow us to think, remember, and know who we are and what we have been.

Brains are very expensive in terms of energy. The brain represents only about 2% of body weight but consumes 20% of total body oxygen consumption at rest (Sokoloff, 1989). This means that there is a high risk of oxidative damage in neurons. They get their energy from oxygen and sugars in each cell's mitochondria, producing free radicals along the way. Its high-energy consumption places the brain at risk for high levels of damage from one of the molecular-level causes of aging.

There are ten-to-one-hundred-billion neurons in each of our brains, and each neuron typically makes more than a thousand connections, or synapses, with other neurons. This most complexly organized piece of matter is what allows us to think, remember, see, act, feel, and be conscious. In brief, it makes us who we are. If we cannot protect these cells, life would not be worth living. Alzheimer's disease is an example of what happens if the brain loses too many neurons. As this horrible disorder

progresses, there is less and less that is human. With advanced Alzheimer's, one no longer recognizes others, even close relatives and friends, basic body control is lost, and thoughts sputter and then die. Alzheimer's is such a devastating disorder that some have suggested that we should delay any further research on aging until we can solve the problem of Alzheimer's. That is because, with age, many people get Alzheimer's. Estimates are as high as one-third to one-half of all who live to see age 85. However, those who would have us delay the study of aging might thereby delay a solution to Alzheimer's disease, since these may well be intertwined. Alzheimer's disease is not the direct result of oxidative damage, but is thought to be caused by a protein that gets stuck in the middle of getting degraded, or broken down.

Fortunately, the breakthrough to slowing aging that I will describe in broad outline in the next couple of chapters should impact directly on brain cells, allowing them to reduce the level of oxidative damage with age, and contribute, thereby, to longevity enhancement with mind intact. But there are some special risks here when it comes to disorders such as Alzheimer's, and we will explore them after a discussion of how a partial solution to aging might soon arrive.