Mother Nature, Life, and Human Aging

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Once upon a time, there was a pretty little planet with a rocky core that orbited a stable orange-yellow sun. Through chance, the planet had collected enough gases and water from icy comets and asteroids to possess an atmosphere and oceans. Mother Nature saw that it had interesting possibilities, so She stirred in more molecules from asteroids and undersea volcanoes to transform the oceans to a warm, rich organic soup of carbon-based molecules.

Using Her tool of evolution, Mother Nature spiced the soup with four-component chains of long RNA molecules, which began to collect free components and assemble copies of themselves, making more RNA. She found that some of the long RNA strands formed themselves into very complex and useful shapes, so She evolved these into engines for generating new protein building blocks. With Her new protein building blocks, She was able to create the first cells, which had an enclosing cell wall containing rings of DNA with instructions for building more cells from proteins. *Life had come to the pretty little planet.* Cells in the new life-filled oceans flourished, fermenting needed energy by breathing in the atmospheric hydrogen. Mother Nature's tool of evolution guided the cells to compete and improve themselves as ever more efficient and successful forms of life.

Then the problems began. Some of the more innovative cells developed *photosynthesis*, allowing them to gain energy by basking in sunlight and exhaling oxygen. These tiny oxygen generators filled the oceans. Soon in the planet's atmosphere, hydrogen began to disappear, replaced by oxygen. Now Mother Nature, through Her tool of evolution, encouraged a few enterprising cells to join the oxygen bandwagon, developing the ability to breathe in free oxygen to burn sugar. Meanwhile, the bulk of the abundant life on the planet was suffocating from lack of hydrogen.

There was also another problem: the range of possibilities for single-cell life was very limited. The best cells were just too small, too lacking in available energy, and too boxed-in by their own cell walls to improve much further, despite what Mother Nature would have liked and encouraged. Her evolution had "hit the wall" in creating ever more complex life.

By good luck, Mother Nature bumbled Her way to a miraculous path around these roadblocks. *Just once* in the long history of the little planet, a very unlikely event happened. Perhaps in the intense electrical chaos of a lightening strike, a robust oxygen-breathing cell was engulfed within the outer wall of a suffocating hydrogen-breathing host cell, and the two formed a partnership. The engulfed cell would go all out in converting oxygen and sugar to a large supply of cell energy, and the host would provide housing, protection, and more fuels of oxygen and sugar. The energy-rich composite cell now had two sets of DNA, one for the host and one for the captive.

This new two-cell union prospered, and its descendants came to dominate the oceans and land masses of the little planet. The enormous new cell energy enabled Mother Nature, with her tool of evolution, to produce cells that were much larger, more complex, and more efficient, and to sequester the host's growing DNA within a protective nucleus. This powerful combination of energy and complexity then enabled Mother Nature to create *multicellular* life forms: the beginning of a profusion of complex plants and animals that now populate the little planet that we call Earth. The captive oxygen-breathing cells, dozens now residing in any host, slimmed down, shedding unneeded functions, specializing in energy production, and moving most of their vulnerable genes to the better-protected DNA of their host cell nucleus. This change made them no longer able to live independently outside their host. They became the *mitochondria* of modern cells, but they retained a small DNA ring that is coded for 13 proteins that could not be moved and were needed immediately and on the spot to keep their tiny energy-producing turbines spinning.

This final two-DNA arrangement worked very well, but it came at a high price. Mother Nature protected the large DNA of the host cell very well. It was organized into chromosomes, protectively spooled on histones, enclosed in a walled nucleus, protected by an aggressive immune system, and maintained by an elaborate and efficient repair system. On the other hand, the small DNA ring of the mitochondria was in a much more hostile and damaging environment. There was no nuclear wall or elaborate repairs, and it was located very close to the hyperactive energy production machinery. Consequently, the mitochondrial DNA accumulated damage 20 times faster than the nuclear DNA. Mother Nature did Her best to move thousands of genes from mitochondria to nucleus, but the 13 genes that could not be moved became a ticking time-bomb that ultimately would kill the host cell.

As age comes to the host cell, damage builds in the mitochondrial DNA. Copying mistakes that omit part of the DNA sequences make a smaller DNA ring, which can be copied faster. This produces *exponential growth* of the bad copies. Cells have many mitochondria, and as such damage grows, some will remain healthy for a while. But there comes a time when the bad DNA copies dominate, and the energy production for the cell shuts down. Then, the cell either dies or is "retired in place", ceasing cell division and other functions. We call this degenerative process *human aging*.

For social species like humans, Mother Nature wants individuals to live as long as possible, so that elders can protect the young and pass along their hard-won tech skills, wealth, and wisdom to following generations. She has employed epigenetic programming to selectively shut down repair, renewal, and other energy-intensive processes of youth. This is done to maintain a good energy supply to the aging heart and brain, at the expense of other organs, She has made humans the longest lived of the primates, but She has *not* found a way of avoiding the inevitable mitochondrial failure and energy collapse of old age.

But our story has a happy ending. We enterprising humans now have an emerging technology that offers the potential to vastly multiply our healthy mitochondria in a bioreactor outside the human body and then resupply our cells with healthy mitochondria, restoring the energy supply and helping Mother Nature to make us live longer. It is not clear how She will respond to this assistance, but She may choose to switch our energy-expensive repair and renewal processes back on. If not, we may need the help of the emerging technologies of epigenetic reprogramming and telomere lengthening. In any case, humans and Mother Nature, working together, can banish the diseases of old age and give birth to a new era of enhanced human longevity.

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