STRANGERS WITHIN ME

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Never had I been so cold. On the run from the chaos of war, we found ourselves stuck on an unheated train in the middle of nowhere on a February night so bitter cold that sleep was impossible. Only at daybreak did I secretly snuggle up against the man dozing beside me; the warmth of his body finally gave me the sleep I had been longing for. I will never forget that comforting warmth – but where did it come from? I could not have suspected that the heat of that man's body would one day become the focus of my research and would tell me a story from the dawn of life itself.

The cells of my body burn food to generate energy. In this 'cell respiration', they consume oxygen gas and capture part of the energy released by the combustion as useful chemical energy. The harder a cell has to work, the faster it respires. Brain cells respire faster than all other body cells and, relative to their weight, produce ten thousand times more energy per second than the sun.

I owe all this to tiny combustion machines inside my cells – the mitochondria. Under the microscope, they usually look like little worms, but they can also form a connected net running through a whole cell. They have their own DNA, which carries the blueprint for thirteen proteins, each of them an indispensable part of the combustion machine. If just one of these proteins is defective or, worse, completely missing, the result can be blindness, deafness, muscular atrophy, dementia, or early death. Why do my mitochondria have a few genes of their own, while all my other genes are stored in the chromosomes in the cells' nucleus? The explanation is a matter not of logic but of history, going back to the origins of life – and no story is as magnificent and exciting.

There have been living cells on our planet for at least 3.8 billion years. The first organisms probably drew their energy from fermentation – just like today's yeast cells, which split sugar into alcohol and carbon dioxide. Fermentation does not release much energy, but neither does it need any oxygen gas. This was crucial for early cells, as the earth's atmosphere contained no oxygen back then. As such organisms multiplied and used up the fermentable matter, they drifted into a dangerous energy crisis. Salvation came from a new kind of organism that fed on sunlight, thus tapping into an almost unlimited energy source for life on Earth – the fusion of atomic nuclei in the sun. These light-harvesting cells soon ran rampant over the globe; even today, gigantic mounds of petrified fossils bear witness to them.

However, the use of sunlight released oxygen gas from water, and oxygen causes oxidation that is harmful to cells. The resulting oxygen poisoning may well have precipitated the greatest mass extinction in the history of life. Poisonous waste, though, always stimulates the inventiveness of evolution – and so it did not take long for cells to find a way to use oxygen gas to burn the organic remains of other cells and to live on the energy of that combustion. Cell respiration entered the scene. Although these respiring cells lived as parasites on the remains and the waste of other cells, they were very successful, as they could also grow at night and in places sunlight does not reach.

About two billion years ago, then, our planet harbored three main types of organisms, all of them similar to today's bacteria. All three had only a small amount of DNA, so they did not have enough biological information to form complex, multicellular organisms. The first fed on the energy of sunlight. The second burned the remains of dead organisms. And the third did neither; like the earliest organisms, it lived as best as it could on the fermentation of organic matter. And yet it was this third kind, this throwback, that made a dazzling breakthrough: it trapped respiring organisms and used them as energy producers, in exchange for a protective environment and more efficient safekeeping of their DNA. This symbiosis apparently made both partners happy and has survived until today. It created a new kind of cell that could not only generate plenty of energy, but also combined the genetic information of two organisms. Now Nature finally had the material to build complex plants and animals. In the course of the next 1.5 billion years, the entrapped respiring bacteria adapted to their protective environment. They surrendered more and more of their DNA to their host and soon could no longer live on their own. They became their host's respiratory organs – mitochondria. I am the distant descendant of a deal made 1.5 billion years ago between two different organisms – and the DNA inside my mitochondria is the meager remnant of the DNA of those once free bacteria.

As they evolved for a sedentary life inside their host cells, the respiring bacteria took over so many important metabolic processes in their host that the latter could no longer live alone either. When the cells in my body divide, they bequeath to their daughter cells not only the DNA in the chromosomes of the cell's nucleus, but also the mitochondria – along with *their*

DNA. Fathers play no role in the passing on of mitochondria, for the mitochondria of a fertilized egg cell come only from the mother. Sperm cells have only one single mitochondrion that probably cannot penetrate the egg cell – and if it did manage to do so, it would have no chance against the hundreds of thousands of maternal mitochondria in the much larger egg cell.

Mitochondria tend their fire with great care and damp it when the cell has enough energy. If this regulation fails, catastrophe strikes. A tragic example of such failure was observed in 1959 when a 27-year-old Swedish woman sought help in a clinic because she kept sweating even on the coldest days and remained extraordinarily thin despite her voracious appetite. The doctors recognized that her mitochondrial fires were burning out of control, but could not help her. Ten years later she took her own life in despair.

Even in healthy mitochondria, combustion is not perfect and generates highly oxidizing waste products that can destroy vital cell molecules. One of these is DNA, in which almost any chemical change can cause harmful or even deadly mutations. Chemical 'sparks' from my mitochondrial fires damage my DNA hundreds – or even thousands – of times every day, but fortunately, my cells can usually quickly undo the damage. Still, a few mutations do remain, above all those in the DNA of my mitochondria, and they accumulate over the years, gradually but inexorably. As a result, my mitochondria have more and more trouble forming the thirteen proteins of their combustion machine from their own DNA, so they give my cells less and less energy. The harmful side effects of my already wheezing cell respiration are in part responsible for the aging not only of my mitochondria but of my whole body. Should I be lucky – or unlucky – enough to live to be ninety, every single one of my muscle cells will have to get by with up to ten times less energy than in my youth. But it is my brain and its outward extensions – the retinas of my eyes – that face the worst prospects. Their mitochondrial fires burn especially fast, so they feel the full force of any imperfections in my mitochondria and age more quickly than other tissues in my body. Parkinson's disease, Alzheimer's disease, degeneration of the retina – all these terrifying diseases of old age are caused in part by chemical sparks from worn-out mitochondria.

As mitochondria age, they emit more and more harmful waste that in turn accelerates the aging process even more. For a cell, the only way out of this vicious circle is often suicide. When mitochondria are so badly damaged that they can no longer meet the cell's energy needs, they emit chemical signals that order the cell to kill itself. The cell then digests itself, packs its remains into little membrane sacks and leaves these as prey for roving scavenger cells. This cellular hara-kiri produces neither messy waste nor inflammation of the surrounding tissue – the cell orchestrates its suicide as carefully as it did its growth and division. What could provide more vivid proof that life and death are inseparable parts of a greater whole? Just as Persephone, the daughter of the fertility goddess, rules beside Hades over the dead, the mitochondria that give my cells life can also herald their death. The respiring bacteria and their hosts have not yet fully come to terms with each other. They are still trying to work things out. Mitochondria may be part of me, but they are still strangers.