

Change

By Dr. Leila Kirdani

Journey to the Inside of the Cell

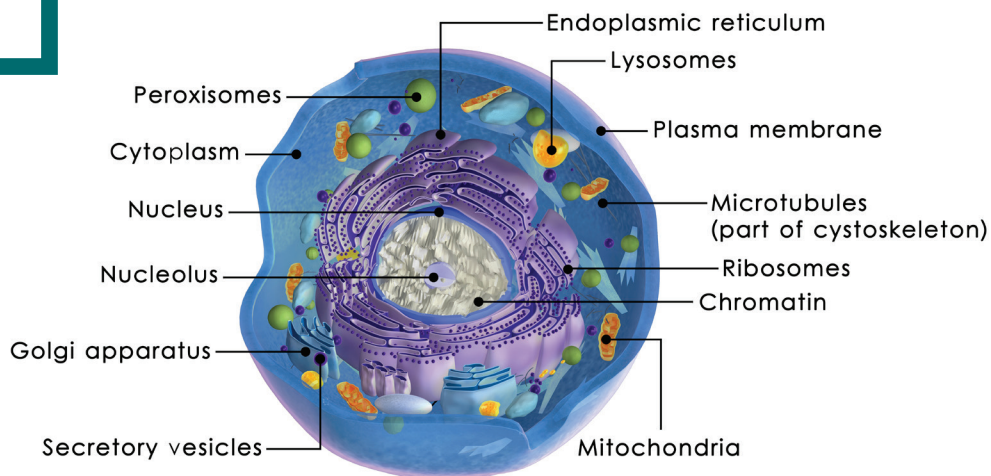
The impact of mitochondria on our health and well-being

I am absolutely fascinated – no, I am totally geeked out – by mitochondria. I often find myself telling patients that the mitochondria are “the powerhouses of our cells,” but that statement doesn’t even come close to the importance that mitochondria have in our lives and on our health. The most current research shows that it is the health of our mitochondria that determines our health and how well we age. For example, as we age, the number of mitochondria inside cells declines. Since the mitochondria are the “powerhouses of our cells” this decline results in less energy for our cells and for us! With regard to mitochondria and health, for a long time now we have known that people with fibromyalgia have a problem with dysfunctional mitochondria; however, newer research is suggesting that many diseases, including diabetes, heart disease, and even autism, are due to poor mitochondrial function. How can one little part of the cell have this much control over our health? In my effort to get as many of you as possible as geeked-out as I am by mitochondria, I thought it would be helpful to first take a journey to the “center of the cell,” so to speak.

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even walking upright on the earth. Imagine – inside of each of the cells in our body there is a command central – kind of like city hall - road ways, factories, transport systems, and even janitorial crews. All this, and an average skin cell, for example, is only 30 micrometers long. To give you some perspective, you could fit one hundred and sixty-six skin cells inside a grain of salt!

or whether the body is being attacked by bacterial invaders and more inflammatory messengers need to be sent out. All of our individual nuclei together determine and control the state of well-being of our entire body. The nucleus is also where our genetic material is stored – the very essence of us. The DNA contained in our chromosomes determines all of our physical characteristics. It is the road-map to us.



The Nucleus -- Command Central

Let's start with command central – the nucleus of the cell. This is where all of the important decisions of life are made. All kinds of messengers are constantly entering into and leaving from the nucleus. These messengers tell the nucleus information, such as if more proteins need to be made

The process by which DNA is replicated to form new proteins or enzymes is so fascinating to me. Without any conductor or director whatsoever, a perfect dance is occurring deep within our cells. Like the treasure it is, DNA is kept “locked up” deep inside of the

The Inner Workings of the Cell

It is amazing to me how much the inside of a cell is like a well-planned city. We humans think that we developed the art of civil engineering, but mother-nature had it all wrapped-up long before we were

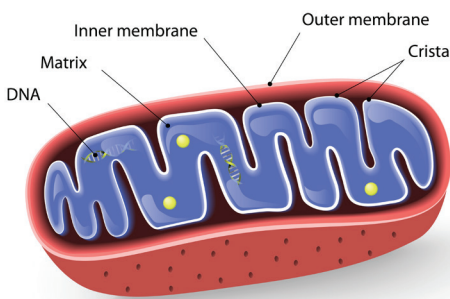
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nucleus of our cells. It is stored tightly wound into chromosomes, with the ends of the chromosomes being capped off for good measure. These caps are called telomeres, and look like the caps on shoelaces. Each time the cell needs to make a new protein or copy its DNA in order to make new cells, the telomeres must be removed

MITOCHONDRION



so that the DNA can be unwound. With each removal the telomeres become shorter and shorter. Once they are short enough, the cell gets the signal that its life is over and it dies, a process called apoptosis. There is a lot of research on how to keep telomeres long, because this lengthens the life of the cell and hence our life!

Once the DNA has been unzipped, it is copied into RNA. This is where the dance begins. Little organelles (an intra-cellular structure) called ribosomes are the factory workers of the cells, making new proteins and new copies of DNA. Ribosomes glide along the open face of the DNA, reading its nucleotide template while watching for the perfect mate to each nucleotide to float by. The ribosomes then attach the appropriate nucleotide in place along the growing chain of RNA. RNA, then, is a mirror-image of DNA – the in-between step between DNA and a new protein. It

is transported outside of the nucleus to an organelle called the endoplasmic reticulum. This is like the factory inside of the cell. It is in the endoplasmic reticulum that the ribosomes copy the RNA into the new protein. The ribosomes zip along the open face of the RNA and now attach amino acids, the building-blocks of protein, onto the growing protein strand. Once the proteins are complete, another factory worker called the golgi apparatus packages the proteins into vesicles to be transported to their final destinations. The vesicles are transported throughout the cell by the cells' internal highway system, called "the cytoskeleton." The cytoskeleton is just what it sounds like – it provides both structure and transport routes throughout the cell. Inside the city of the cell there are even storage facilities called "vacuoles," that store lipids, water, and other molecules until they are needed. These storage facilities are super-smart, though. They are also responsible for maintaining the internal pH of the cell

and storing toxic substances that might damage the cell.

The Mystery of Mitochondria

Out of all of these fascinating structures that are inside of our cells, the one that holds the most mystery and awe for me are the mitochondria. For one thing, the mitochondria, which are deep inside of us, did not even start out as part of us!

It is believe that roughly 1.5 billion years ago mitochondria actually started out as bacteria which entered into a beneficial relationship with single-celled organisms. The mitochondria/bacteria were engulfed into the cells, thus providing the cells with a more efficient way to make energy and the mitochondria/bacteria a safe environment with lots of fuel and other

items needed for survival. There are a few reasons why researchers believe this, the most incredible of which is that mitochondria have their own DNA, which is similar to bacterial DNA in that it is circular rather than helical like nuclear DNA is. When a cell replicates, copies of nuclear DNA are made to go to each of the daughter cells. The mitochondria separately replicate their DNA to go to their daughter mitochondria. Other similarities to bacteria are that mitochondria synthesize proteins in a fashion that is similar to bacterial synthesis of proteins, and finally (and quite scarily), some antibiotics used to kill bacteria also damage mitochondria. That's right – every time we take antibiotics such as doxycycline we are damaging our mitochondria! With some antibiotics, such as Cipro, that damage is permanent.

Mitochondrial DNA Comes from Mom

Let's take the mitochondrial DNA issue one step further and really blow open the mystery of mitochondria. For humans, mitochondrial DNA is passed down not from both parents, as cellular DNA is. Mitochondrial DNA is purely maternal in origin. This fact allowed Bryan Sykes, a British geneticist, to trace all of mankind back to seven origin women whom he refers to as "clan women," and those seven women back to a single "mitochondrial Eve."

Inside the mitochondria is where the body actually finally turns food into molecules of energy called Adenosine Triphosphate (ATP) – a process called oxidative phosphorylation. Oxidative phosphorylation is

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made up of a few different components including the citric acid cycle, where carbohydrates are turned into ATP, and the electron transport chain, that fuels the energy for the citric acid cycle. Every cell in the body requires ATP for energy. It truly is like the “gas” in our tank. Or perhaps a better analogy is the charge of a battery, since it is the negative charge of electrons being transported through the electron transport chain that drives food being turned into ATP.

Free Radicals

Just as factories produce pollution as a byproduct of making their product, so too do mitochondria release wastes in the form of free radicals. Just as pollution can damage the environment, free radicals damage many of the structures within the cell including proteins, lipids, cellular DNA, and mitochondrial DNA. If the cell has enough anti-oxidants on board – for example vitamins E and C, or Coenzyme Q10 – the mitochondria can continue creating energy to keep us going. If there are not enough anti-oxidants to keep up with the free-radical production of the mitochondria, or if the cell is bombarded by free radicals caused by toxins, the structures within the cells suffer overwhelming damage and the cells then die. An intermediary stage to this process is when free radicals cause damage to the mitochondrial DNA without causing as much damage to the rest of the cell. In this case the mitochondria may not be able to replicate, but the cell is still able to, however the new cells will have fewer mitochondria in them. These new cells with fewer mitochondria will not have as much energy so they will not be able to keep up quite as well on all of the things that cells do. This includes, for example, burning fat, keeping muscles active, and keeping

brains thinking. This is essentially the aging process – less energy, less muscle, more fat!

Disease Factor

It is also the crux of the process of disease. Medical research increasingly recognizes that poor mitochondrial function is a factor in the development of numerous human diseases, including diabetes, cancer, neurodegenerative diseases such as Parkinson’s disease and multiple sclerosis, and heart disease. Let’s look at diabetes, for instance. Mitochondrial dys-

Medical research increasingly recognizes that poor mitochondrial function is a factor in the development of numerous human diseases, including diabetes, cancer, neurodegenerative diseases such as Parkinson’s disease and multiple sclerosis, and heart disease.

function has been linked to both a decrease in the responsiveness of skeletal muscle to insulin, and insulin production and release by the pancreas. These are the two sides of the coin for diabetes, and both of them are linked to mitochondrial health.

With poorly functioning mitochondria, the body can’t burn fat as well and turn it into energy, so it just gets stored which means increased weight. Thankfully the reverse is also true. If we can get enough anti-oxidants on board for the mitochondria we can preserve insulin sensitivity even in the face of a high-fat diet.

What about the brain? The UCLA study that I mentioned in my newsletter on Alzheimer’s in March showed that one of the key elements in reversing dementia was optimizing mitochondrial functioning. In fact, not only Parkinson’s and Alzheimer’s diseases have been linked with poor mitochondrial function, but strokes, ADHD, depression, and schizophrenia have as well. The pathways to these illnesses in genetically susceptible people starts with free radical damage which causes damaged proteins and oxidized cell membranes. This causes poor neuronal signaling in the brain along with inflammation and over-excitation of brain cells. All of these processes not only severely interfere with the brain’s ability to function but also cause brain cells to die early – thus the declining brain function in many of these illnesses. Researchers are also very close to proving that autism is a disorder of mitochondrial function as well – that the mitochondria of children with a genetic susceptibility to autism become overwhelmed with toxic exposure, even sometimes in utero, and therefore cannot produce enough metabolic energy to keep the brains of these children functioning normally.

Mitochondria Health

When we understand that our health – our very ability to function on the planet – is all due to the health of our mitochondria, it begs the question of “what can I do to keep my mitochondria healthy?” Here



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is the simple answer: eat less, exercise more, take supplements to enhance mitochondrial function, and avoid toxins. Let's talk about each of these individually, starting with avoiding toxins.

At this point you understand that it is the balance of oxidants versus anti-oxidants that promote either health or illness. Of course toxins are huge oxidants and cause damage on many levels of our physiology, but this damage is most notable at the level of the mitochondria. I have written about toxins in past newsletters so I won't spend a lot of time on them, however I would like to point out that several commonly prescribed and used medications have been shown to cause mitochondrial damage. This not only includes antibiotics as mentioned above, but over-the-counter pain relievers such as aspirin, Tylenol, and naproxen. Some of the anti-depressant medications are toxic to mitochondria including Elavil and citalopram. The anti-anxiety medications valium and Xanax, and the anti-seizure medication Depakoate are also toxic to mitochondria. Finally, statin drugs for cholesterol are also quite bad for mitochondrial health.

Studies show that calorie restriction turns on the Sirt1 gene. This gene has been shown to promote longevity and increase the mitochondria's ability to produce energy by increasing levels of NAD (nicotinamide adenine dinucleotide). I like to think of NAD as the "push" that keeps the wheel of the citric acid cycle spinning – kind of like the wheel of

fortune game show. NAD turns the crank on the wheel and out comes more energy in the form of ATP. Therefore, it makes sense that if we can increase the amount of NAD – through calorie restriction or other means – we can make more energy. There are several ways to incorporate calorie restriction into your life. One is just to skip dinner a few nights a week. Another is to practice intermittent fasting – eating only 500 calories a day for one or two days a week. I will be quite honest that I can only "intermittently fast" once a week at best!

The next on the list for improving mitochondrial function is to exercise more. Several studies have shown that exercise improves mitochondrial function in several ways. Exercise increases the number of mitochondria per cell as well as increasing their efficiency.

As your muscles become more efficient, so do your mitochondria, meaning they are able to produce more ATP with fewer resources. It has been shown that runners burn more calories even at rest than non-runners because of the skeletal muscle mass that runners have. Studies have also shown that efficient mitochondria can use lactic acid as fuel, which is why athletes can perform for so hard and so long – muscles are actually making lactic acid from glucose to use it for fuel! In fact, a wide variety of scientific studies show that the lactate threshold of a muscle is the single best predictor of endurance performance – even better than aerobic capacity. It also turns

out that high intensity exercise (HIT) is the best way to improve both aerobic and anaerobic (ability to use lactate) fitness. Twenty-seven minutes of HIT exercise three times per week produces the same amount of aerobic and anaerobic improvement as sixty minutes of cardio five times per week!

Important Nutrients

Finally, there are several nutrients that we can take to help improve both the number of mitochondria and their health. Alpha lipoic acid (ALA) is one of my personal favorites. ALA boosts mitochondrial function in several ways. It is a powerful antioxidant on its own, but it also has the ability to regenerate two other very crucial antioxidants – vitamin C and glutathione. ALA also helps in several steps of the citric acid cycle, thus making energy production more efficient. Coenzyme Q10 is also an enzyme helper in the citric acid cycle and acts as a powerful anti-oxidant. Other nutrients that help mitochondrial function include acetyl L-carnitine, an amino acid that helps shuttle nutrients in and wastes out of the mitochondria, and resveratrol, a polyphenol compound from plants that has antioxidant properties but stimulates that all powerful Sirt1 gene, mimicking calorie restriction. Finally, fresh vegetables are chock-full of nutrients that help not only our mitochondria function, but the rest of us too!

With our "journey to the center of the cell" complete, we have unlocked many of the secrets of good health and longevity. It is still amazing to me, however, that with all of knowledge we have gained from all of the wonderful scientific research that has been done, a few basic tenants of health remain the same – eat right, don't overeat, and exercise. The only additional tenant that we should add for our lives today is just a few supplements to keep our mitochondria - and us - healthy and well.

