**THE MITOCHONDRION AND ITS FUNCTION**

**Overview**

Mitochondria are considered the “powerhouses” of the cell. Just like real powerhouses, the mitochondria supply the cell with energy, but in the form of adenosine triphosphate or **ATP** for short. ATP is the “currency” of the cell. Many processes rely on the input of ATP, such as glycolysis, muscle contraction, and active transport of molecules. Mitochondria are the main producers of ATP in the cell.

Eukaryotes are single celled or multicellular organisms that have a distinct nucleus. These can be plant or animal cells. They contain organelles such as an endoplasmic reticulum, mitochondria or chloroplasts, and a Golgi apparatus. But how did these cells obtain such complex intracellular structures? The **Endosymbiotic Theory** states that archaeons that possessed a prominent nucleus, or a nucleus with a membrane, engulfed another free-living bacterium that was capable of photosynthesis or aerobic respiration. Aerobic respiration is the process a cell uses that involves the breakdown of sugars to produce energy in the form of ATP. Thus, the mitochondria within the animal cell was once a free-living bacterium. When the archaeon cell ingested the free-living bacterium that was capable of aerobic respiration, the host cell became a eukaryotic cell. The ingested bacterium became an organelle inside the host cell, possessing its own membrane. The host cell became much more efficient in its energy production. This is believed to be the origin of the mitochondria.

Mitochondria are typically found in high concentrations within cells that use a lot of energy or ATP. These are usually cardiac muscle cells, skeletal muscle cells, and sperm cells. Cardiac cells are continually making the heart pump, skeletal muscle cells need a large amount of ATP to make the muscles contract, and sperm cells need an abundance of ATP to propel the cell forward to fuse with the egg.

**General Structure**

Mitochondria are found in the cytoplasm of eukaryotic cells. Some cell types require higher mitochondrial content that others such as cardiac muscle, skeletal muscle, and sperm. These organelles contain two separate and unique membranes. The first membrane, the **outer membrane**, surrounds the whole organelle. It comes into contact with the cellular fluids which contain ions and other small molecules. These ions and small molecules are capable of crossing the outer membrane very easily due to small holes, called porin proteins. The second membrane, the **inner membrane**, is much more selective in what can cross through it. Only certain molecules and ions can pass through the inner membrane with the help of more specialized transport proteins. The inner membrane also contains the electron transport chain machinery. The small space between the outer and inner membrane is called the **intermembrane space**. After molecules and ions pass through the semi-permeable inner membrane, they enter the **mitochondrial matrix**. The matrix is the location of few important cellular processes such as the Krebs cycle, which is important for energy production, and the production of some amino acids.

**Electron Transport Chain**

It has been established that the mitochondria are the “powerhouses” of the cell. These intracellular structures produce copious amounts of ATP that is necessary for cell growth, functioning, and proliferation. The two main mechanisms for the production of ATP is through the electron transport chain and through oxidative phosphorylation. The **electron transport chain** is found in the inner mitochondrial membrane and precedes oxidative phosphorylation. The electron transport chain consists of 5 enzyme complexes that consecutively pass along electrons between these enzyme complexes and specific molecules called electron carriers. These carriers “carry” electrons between the enzyme complexes, and in the process create small amounts of ATP. This energy is used to pump protons, or hydrogen ions, out of the inner membrane into the inter membrane space to create **a proton-motive force**, which is a gradient of protons. This process is called the **Chemiosmotic coupling** or the **Chemiosmotic Hypothesis**. These protons will later be pumped back through the inner membrane where even more ATP will be produced. As electrons are passed between the complexes, they subsequently lose energy.

Once an electron reaches the last complex, an oxygen molecule will be reduced, or bonded to two hydrogen molecules, to form water. The formation of water produces a large amount of energy that the cell can use for other processes. The complex also releases 4 protons to the inter mitochondrial space.

**Oxidative Phosphorylation**

**Oxidative phosphorylation** proceeds the electron transport chain. This process consists of a very complex structure, called ATP synthase, and involves the protons that were previously pumped into the inter mitochondrial space by the electron transport chain. The oxidative phosphorylation process creates the greatest amount of ATP in the cell. ATP synthase is a transmembrane protein, meaning that parts of the enzyme are found in the inner mitochondrial membrane and the other parts are located in the matrix. The stalk of the enzyme is situated in the inner membrane, while the rotating catalytic sites are located in the matrix. ATP synthase relies on the proton-motive force and its energy to activate and power the enzyme. The protons that were pumped into the inter membrane space by the electron transport complexes will flow through the ATP synthase, creating energy. This energy will physically “turn” the enzyme. The enzyme consists of 6 subunits, where three of them contain ATP and the other three contain ADP. **ADP** is adenosine diphosphate, which is not as energy rich as ATP. As ATP synthase is rotated, it releases one ATP molecule every 180 degree turn. Thus one rotation, 360 degrees, produces 3 ATP molecules. Because ATP synthase uses the energy produced by the electron transport chain, these processes are said to be coupled.

**Mitochondrial DNA**

**Evolutionary Origin**

It was previously stated that the mitochondrial organelle within eukaryotes was once a free-living prokaryote. Just as all living organisms require a genome, or a DNA code to survive, so too did the prokaryotes-turned mitochondria. When the free-living prokaryotes were engulfed by the host archaeon, their genome was engulfed as well. All eukaryotes now contain two genomes- a nuclear genome and a mitochondrial or chloroplast genome. In the case of mammalian cells, they contain the mitochondrial genome. Plants will contain a nuclear genome and a chloroplast genome. This theory is widely accepted due to the fact that the mitochondrial genome is very similar to bacterial genomes. The mitochondrial genomes can also differ in size between species. The human mitochondrial genome is significantly smaller compared to that of other microorganisms such as that of yeasts, amoebas, and plasmodium.

**Mitochondrial Genome vs. Nuclear Genome**

The mitochondrial genome is similar to nuclear DNA in that both are double-stranded, anti-parallel structures. Mitochondrial DNA differs, however, in that its overall structure is circular while that of nuclear DNA is linear. The mitochondrial genome is also significantly smaller in size than the nuclear genome- it codes for approximately 1% of the total human genome. The mitochondrial genome has approximately 16,569 base pairs which encodes for 37 genes in humans while the nuclear genome encodes for up to 20,000 genes and contains billions of base pairs! This reduced number is attributed to the transfer of many of the genes to the nuclear genome over time. Of those 37 genes, 13 code for proteins in the electron transport chain and oxidative phosphorylation mechanism. The rest of the information codes for rRNA and tRNA molecules also involved in the aforementioned processes. rRNA molecules make up the ribosomes, while tRNA carries amino acids to the ribosome. A tiny fraction of the mitochondrial genome contains noncoding regions- about 3%. On the other hand, the nuclear genome contains about 93% noncoding regions. Most of the replication and transcription mechanisms remain the same, however the translation mechanisms differ slightly. The mitochondrial genome contains a variant genetic code in that 4 of the 64 codons (codon = 3 nucleotides) have different “codes”. These 4 codons code for different amino acids than those of the normal 64 used in the nuclear genome. The mitochondrial tRNA also possesses a more “relaxed” mechanism. The wobble position that recognizes the third nucleotide of a codon is not as highly specific as that found in the nuclear genome. This results in fewer tRNA molecules used in the mitochondrial genome.

**Mutations**

Mitochondrial DNA is prone to significantly more mutations than nuclear DNA. This is, in part, due to the fact that the DNA polymerase that replicates the mitochondrial genome is less accurate compared to that of the nuclear DNA polymerase. Nevertheless, these mutations usually do not result in disease. In fact, in humans, it is very common and normal to contain different “versions” of the mitochondrial genome in a single cell. This cell is considered to be “heteroplasmic”, meaning that there are multiple different versions of the mitochondrial genome within the cell. Sometimes mutations within the mitochondrial genome can be detrimental. In some cases, the mitochondrial genome that a zygote inherits can be homoplasmic, meaning that if there is a mutation, then all of the mitochondria carry that mutation. Many of the mutations that occur in the mitochondrial genome affect the electron transport chain or the oxidative phosphorylation process, which causes defects in the organism’s metabolism.

**Inheritance**

The inheritance of the mitochondrial genome is different compared to that of the nuclear genome. Mitochondrial DNA is inherited strictly maternally, meaning that only mothers can pass their mitochondrial genome to her offspring. This means that if her mitochondrial genome contains a mutation, then all of her children have the possibility of inheriting the mutation. Because most humans are heteroplasmic, all versions of the mitochondrial genome will be inherited, albeit in different quantities.

**Summary**

We have seen that mitochondria are considered the “powerhouses of the cell” due to their great ability to create copious amounts of ATP in their electron transport chains and oxidative phosphorylation processes. These energy producing organelles are found in high quantities within tissues that require a great amount of energy to function, such as sperm cells, muscle tissue, and cardiac tissue.

We have also learned how mitochondria came to be an essential part of the eukaryotic cell. This process is described by the endosymbiotic hypothesis which provides an explanation on how an ancient archaeon engulfed a prokaryotic cell (mitochondria). With the ingestion of the prokaryotic cell, their genome was incorporated into the eukaryotic cell, creating a second source of genetic material.

Just as in the nuclear genome, the mitochondrial genome is subject to mutation. These mutations are usually involved in metabolic activity and are strictly maternally inherited. Because the mitochondrial genome contains many variants (heteroplasmy), the probability of a mutation causing a detrimental defect is limited.

**REFERENCES**

Friedman, R. J., Nunnari, J. (2014). Mitochondrial form and function. *Nature, 505*(7483), 335-

343.

Zimorski, V., Ku, C., Martin, F., and Gould, S. (2014). Endosymbiotic theory for organelle origins.

*Elsevier (22).* 38-48.

Green, D. E. (1983). Mitochondria- structure, function, and replication. *The New England*

*Journal of Medicine, 309*(3), 182-183.

Alberts, et al. (2015). *Molecular biology of the cell.* New York, NY: Garland Science.

Castresana, J., Lübben, M., Saraste, M., Higgins, D. G. (1994). Evolution of cytochrome oxidase,

An enzyme older than atmospheric oxygen. *The EMBO Journal, 13*(11), 2516-2515.

Song, J., Pfanner, N., Becker, T. (2018) Assembling the mitochondrial ATP synthase. *Proceedings*

*Of the National Academy of Sciences of the United States of America, 115*(12), 2850-

2852.

Althoff, et al. (2011). Arrangement of electron transport chain components in bovine

Mitochondrial supercomplex. *The EMBO Journal, 30*(22), 4652-4664.

Taanman, J. (1999). The mitochondrial genome: structure, transcription, translation, and

Replication. *Biochimica et Biophysica Acta (BBA)- Bioenergetics, 1410*(2), 103-123.

Chial, H., Craig, J. (2008). MtDNA and Mitochondrial Diseases, *Nature Education, 1(1)217.*