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Journal of Genetic Syndromes and Gene Therapy

Short Communication

Mitochondrial Eve: Its Genetic Implications

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ABSTRACT

Mitochondria are an essential cell organelle for all living cells, if they are eliminated from the cell that means the cell has undergone terminal differentiation. It works like sub-kingdom in the cell; in addition to provide energy to the cell it has its own gasket of synthetic machinery. In each individual it is contributed by mother. If there is any defect (mitochondrial DNA mutation) in this organelle whole body suffers in a variety of ways. Recent researches are contributed towards corrections of mitochondrial defects by mitochondrial replacement or by infusion of healthy mitochondria.

INTRODUCTION

Usually multiple mitochondria are found in the cytoplasm of cells. They make energy for cells from the chemical energy stored in the food we eat. .This energy is utilized in biochemical reactions and other cellular processes [1]. The theory of endosymbiosis suggests that mitochondria were once free living organisms on their own that used aerobic respiration. Larger anaerobic cells simply engulfed these aerobic mitochondria to use their energy as symbionts [2]. The DNA of the living aerobic organisms was small circular DNA which exists as Mitochondrial DNA .Thus mitochondria have their own genome consist of 37 genes that rarely change, they contain a "hypervariable" region, which changes fast enough to provide a molecular clock calibrated to times comparable to the age of modern humanity. Because each person's mitochondrial genome is inherited from his or her mother, all mitochondrial lineages are maternal [3].

MITOCHONDRIAL EVE

The maternal ancestor of all living humans "mitochondrial Eve" the maternal ancestor of all living humans ~ confirms that she lived about 200,000 years ago. . According to mythological in scripts, Kali Mata [4] contributed mitochondria to all of us. Mitochondrial DNA (mtDNA) is subject to mutations just like regular DNA. Due to this, and the pattern of human migrations, there are actually quite a few different groups of mtDNA (Human Mitochondrial Haplogroups). Thus, they are the most recent common female/male ancestor of all humans. Study about Mitochondrial eve provide a genetic past to learn more about mutation, selection and other genetic processes that play key roles in disease[5].

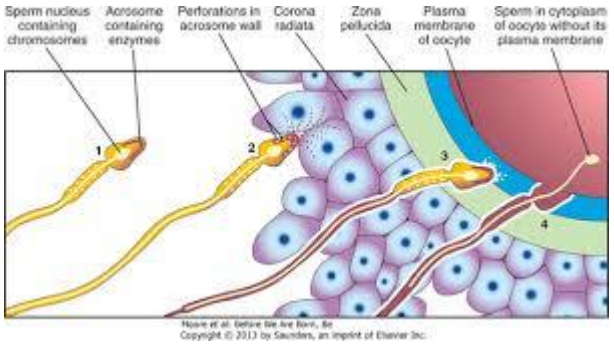

Figure 1: During fertilisation sperm mitochondria will not enter in the Ooplasm

Using histochemical techniques for the first time Ward [6] presented evidence for the origin of crystals within a single crista of mitochondria in some chondrocytes, several crystals were found, sometimes combined in a single mitochondrion. Crystals were preferentially aligned along the long axis of the cells, thus appearing in the same orientation as the chondrocytes in the tissue [7]. Later, we have shown DNA in mitochondria [8] and hence protein synthesis can take place within the mitochondria. Out of 37 genes thirteen provide instructions for making enzymes involved in oxidative phosphorylation. However for the first time we have shown that succinic dehydrogenase, the marker enzyme, is synthesized under nuclear as well mitochondrial genome [9].

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Received: November 11, 2019; **Accepted:** November 23, 2020; **Published:** November 30, 2020

Citation: Gupta P D (2020) Mitochondrial Eve: Its Genetic Implications. J Genet Syndr Gene Ther. 11: 334. DOI: 10.4172/2157-7412.20.11.334

MITOCHONDRIAL DNA AFFECTS HEALTH AND DEVELOPMENT

The first case of suspected mitochondrial disease occurred in1962 where a woman has an extremely fast and efficient metabolism, and mitochondria that were larger in size and number in her muscle tissue. Mitochondrial myopathies a group of neuromuscular diseases caused by damage to the mitochondria with some examples including Kearns-Sayre syndrome (KSS), Leigh's syndrome, Mitochondrial Depletion syndrome (MDS), Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS) [10,11].

Inherited changes in mitochondrial DNA can cause problems with growth, development, and function of the body's systems. These mutations disrupt the mitochondria's ability to generate energy efficiently for the cell. Conditions caused by mutations in mitochondrial DNA often involve multiple organ systems. The effects of these conditions are most pronounced in organs and tissues that require a lot of energy (such as the heart, brain, and muscles) [12]. Recently it was shown that mitochondrial dysfunction in placental trophoblast cells can be the cause of gestational diabetes mellitus [13]. From that time onwards, mitochondrial dysfunction, including that associated with mtDNA mutations, has been identified in human diseases, including seizure, ataxia, cortical blandness, dystonia, exercise intolerance, ophthalmoplegia, optic atrophy, cataracts, diabetes mellitus, short stature, cardiomyopathy, sensorineural hearing loss and kidney failure [14-16]. Interestingly, disruption of mitochondrial function in mouse zygotes led to telomere attrition, telomere loss, and chromosome fusion and breakage, mediated by alterations in ROS production [17] Accumulation of mtDNA mutations has also been suggested to play a major role in aging and the development of various age-related degenerative diseases. It is also possible that mutation may occur in the mitochondrial genes of sperm but not in the blood cells [18].

Mitochondrial DNA is also prone to somatic mutations, which are not inherited. Somatic mutations occur in the DNA of certain cells during a person's lifetime and typically are not passed to future generations. Because mitochondrial DNA has a limited ability to repair itself when it is damaged, these mutations tend to build up over time. Interestingly, high levels of mtDNA mutations have been found in many tumors and cancer cells [19,20] A build-up of somatic mutations in mitochondrial DNA has been associated with some forms of cancer and an increased risk of certain age-related disorders such as heart disease, Alzheimer disease, and Parkinson disease. Additionally, research suggests that the progressive accumulation of these mutations over a person's lifetime may play a role in the normal process of aging.

It is conceivable that mitochondrial deficiency could lead to mutagenesis in the nuclear genome also. In yeast, it was reported that mitochondrial dysfunction caused by respiration inhibition, mtDNA depletion or mtDNA deletion resulted in a twofold to threefold increase in the nuclear DNA mutation frequency [21].

MITOCHONDRIAL REPLACEMENT THERAPY (MRT) TRENDS MOLMED

MRT or Mitochondrial Gene Therapy (MGTis a medical technique in which defective mitochondria carried by a woman is replaced with the healthy mitochondria of a donor Through in vitro fertilization technique (IVF), the egg is then fertilised with the partner's sperm. Thus the embryo remains free from any such defects. The two most common techniques in mitochondrial donation are maternal spindle transfer and pronuclear transfer [22-24].

Thus this medical technique prevents the transmission of mitochondrial (genetic) disease from one generation to the next. MRT proposes to give parents chance of having a child that is over 99% genetically matched to them and most importantly free of the mitochondrial disease.

It will prevent transmission of mitochondrial (genetic) disease from one generation to the next. It will give parents chance of having a child that is over 99% genetically matched to them and most importantly free of the mitochondrial disease. It has no impact on personality or looks of the offspring from third DNA set, as surrogate mitochondrial DNA is separate from core DNA in cells.

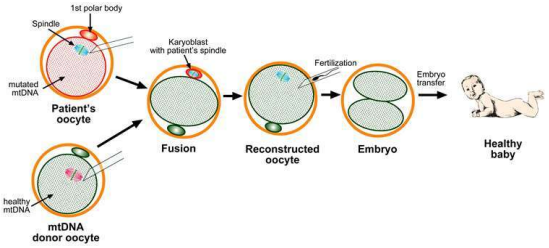

Figure2: Process of eliminating the defective mitochondria

MITOCHONDRIAL INFUSION

Like cell infusion technique, more recently 2018, Dr. Sitaram Emani and his colleagues have restored dying organs to Life by infusing mitochondria into a blood vessel feeding the heart, instead of directly into the damaged muscle. Somehow the organelles will gravitate almost magically to the injured cells that need them and take up residence, as we did in liver.

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