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HUMAN HEALTH
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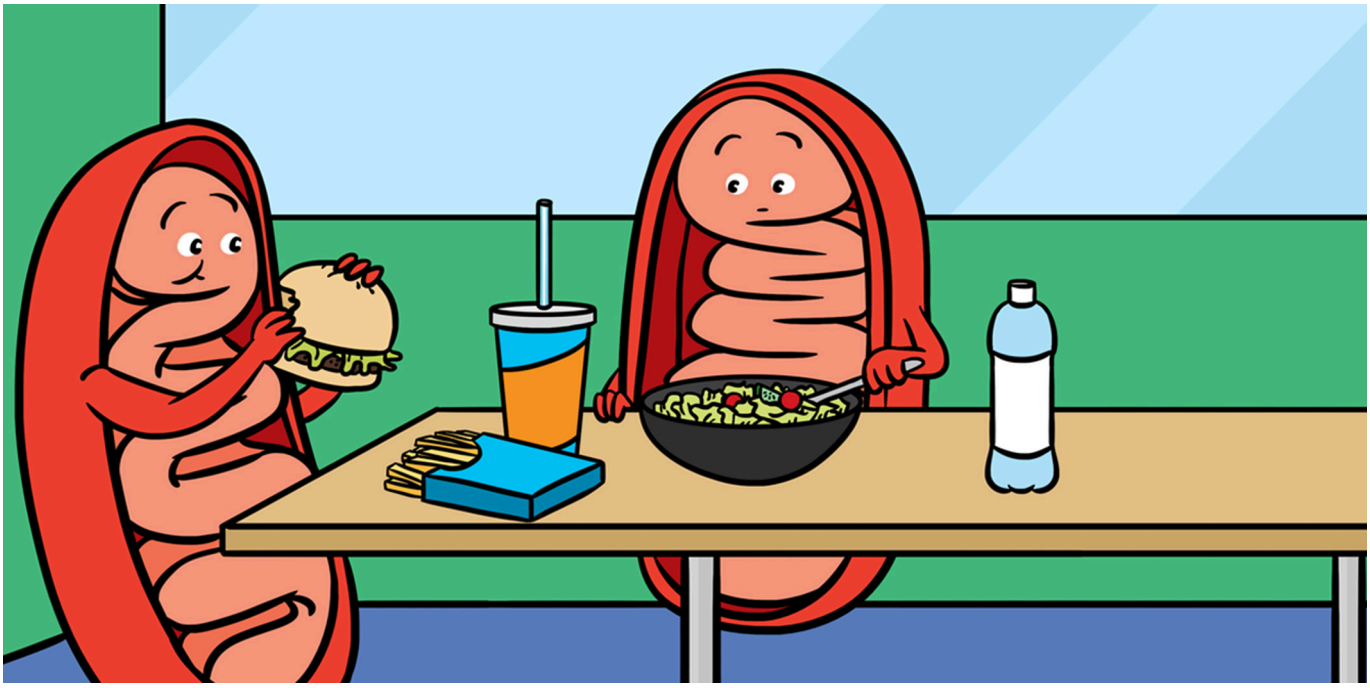

FEED YOUR MITOCHONDRIA AND SHAPE YOUR BODY!

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YOUNG REVIEWERS:

ANASTASIA
AGE: 13

KAÏKE
AGE: 11

KENZO
AGE: 9

If your body were a train, what would give it the power to move? The food you eat, which is burned by the train's engine. Do you know how many engines your body has? Thousands of millions! They are called mitochondria. Mitochondria are tiny structures contained within the cells of your body that burn food, providing energy. The power of each mitochondrion is due to its own gearwheel: the circular mitochondrial DNA. There are many gears in each mitochondrion. Together, they regulate the mitochondrion's ability to produce energy. Obesity modifies both the abundance and the function of the mitochondrial DNA, altering the ability of the body to efficiently produce energy, with some differences between males and females. Eating healthy foods not only makes you slim, but also boosts your mitochondria and makes you powerful!

BODY COMPOSITION: NOT JUST A MATTER OF WEIGHT!

Do you know what makes up your body? The human body can be viewed as a combination of several "packages"—muscle, fat, bones, fluids, organs, ligaments, and tendons. Body weight is a combination of all of these "packages." While everyone's body contains these packages, each body is different in regard to the size of each package (especially fat and muscles). Two people could look similar on the outside and even weigh the same, but be very different on the inside! Determining **body composition** is extremely important: your health is not defined by your body weight, but by your body composition. But how can we see a person's body composition from the outside?

One of the easiest ways to measure body composition includes a combination of body weight, height, and waist circumference. The ratio between weight and height is called body mass index (BMI), and it is commonly used to study obesity in human populations. There are also scientific technologies that can be used to study body composition. Bioimpedance analysis (BIA) measures the ability of the body to resist a weak, painless flow of electric current. Since electric current cannot pass through fat, BIA can estimate the amount of fat and muscles in a person's body. But what if we want to know about how well the body's cells are functioning? There are also methods to collect information about how well the body is working. They rely on sampling body cells or fluids (such as blood or a cheek cells) and measuring some **biomarkers**, which are molecular signals of the body's health or disease status.

MITOCHONDRIA: TURNING FOOD INTO ENERGY

Mitochondria are the powerhouses of the cell. They break down nutrients and, through a sort of "assembly-line," produce energy in the form of substance called **adenosine triphosphate (ATP)**. ATP can then be used by the cell whenever energy is required. This process is also called **cellular respiration**. Mitochondria are small structures **(organelles)** that float freely throughout the cell. Some cells have only a few mitochondria while others have several thousand. If a cell needs more energy to survive, more mitochondria can be created.

Mitochondria are unique organelles because they contain their own DNA (The only other organelle that contains DNA is the nucleus, the commander-in-chief of the cell). The mitochondrial DNA is double stranded (like nuclear DNA), but it is circular, and is present in multiple copies. Mitochondrial DNA can be thought of as a sort of gearwheel that regulates both the number and functions of mitochondria.

BODY COMPOSITION

The content of the body—not only the weight, but also the relative abundance of each body component (fat and muscles in particular).

BIOMARKER

Any measurable parameter or molecule that can give us some hints about the health status of the subject, or could be used to predict the risk of a disease.

MITOCHONDRIA

Small organelles that produce energy (in the form of ATP) by burning food.

ADENOSINE TRIPHOSPHATE (ATP)

A small molecule used by the cell as a type of energy storage. ATP is used for most cellular functions that require energy.

CELLULAR RESPIRATION

A biochemical process, occurring in mitochondria, used by the cell to produce ATP from food.

ORGANELLES

Is a subcellular structure that has one or more specific jobs to perform in the cell.

EPIGENETIC MECHANISMS

A series of biochemical modifications that regulate which proteins are produced from a certain DNA molecule, without modifying its sequence.

DNA METHYLATION

A chemical modification of the DNA that regulates how DNA should be read and, consequentially, whether proteins can be made from it.

Figure 1

Epigenetic mechanisms, such as DNA methylation (flags), affect the activity of DNA molecules by regulating whether the DNA is "open" (functional/active) or "closed" (inactive). "Open" sections of DNA are accessible to activating factors that lead to protein production. Whether methylation works the same way in mitochondrial DNA is currently under investigation.

Specifically, the higher the number of mitochondrial DNA copies, the higher the mitochondrial abundance and functionality.

Epigenetic mechanisms are one way to regulate the function of DNA, meaning whether the DNA can be used to make proteins with various jobs within the cell. Epigenetic mechanisms modify the 3D structure of the DNA molecule, making it either more "open" (functional/active) or more "closed" (inactive) (Figure 1). One of the most important epigenetic mechanisms is called **DNA methylation**, which is the addition of a chemical structure called a methyl group (CH_3) to the DNA. We can imagine methyl groups as "flags" that can be added to or removed from specific DNA sequences to regulate them [1, 2].

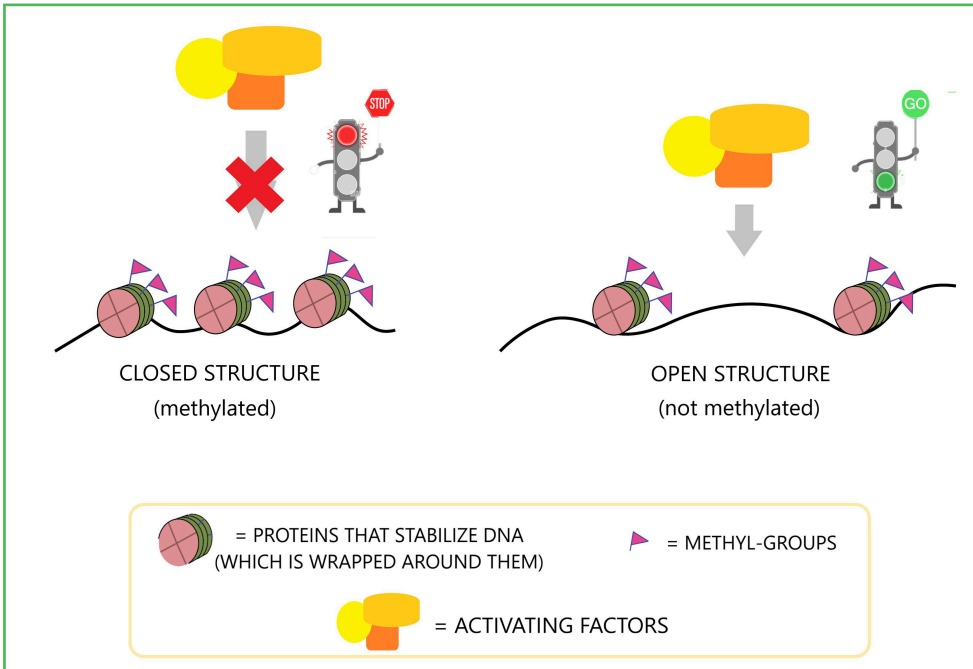

Figure 1

It has recently been suggested that, like nuclear DNA, the function of mitochondrial DNA might also be regulated methylation (Figure 2), especially in a regulatory area called the D-loop. Our cells obtain methyl groups from the foods we eat. Food provides us with both methyl groups and the B vitamins that help methyl groups move around inside cells. Since methyl groups regulate the functions of DNA, they are very important! Incorrect DNA "flagging" is associated with disease, and improper methylation of mitochondrial DNA might cause poor mitochondrial function!

OVERWEIGHT GIRLS HAVE REDUCED MITOCHONDRIAL POWER

A group of adolescents from central Italy was recruited to study the association between body composition and mitochondrial DNA status.

Figure 2

Mitochondria burn food to produce energy, so they are the powerhouses of the cell. The circular molecules of mitochondrial DNA (mtDNA) contained in the mitochondrion help to regulate its functions.

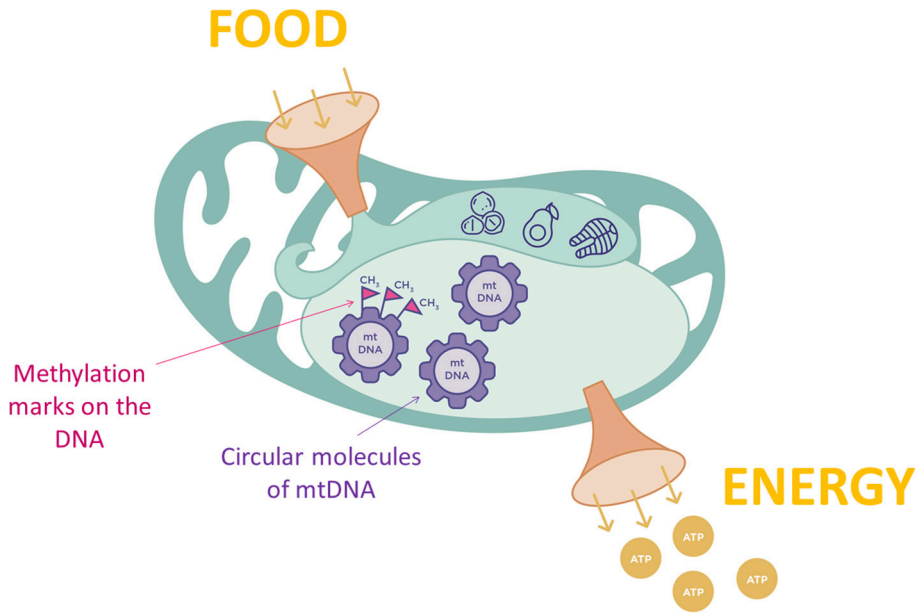

Figure 2

Mitochondrial DNA was extracted from cheek swabs (collecting cells from the inner part of the cheek, inside the mouth) and the abundance of mitochondrial DNA copies and D-loop methylation were measured. Results showed that there were fewer copies of mitochondrial DNA in overweight subjects (Figure 3A).

Moreover, overweight subjects showed higher levels of methyl groups in the D-loops of their mitochondrial DNA (Figure 3B). This suggests that problems with mitochondrial function might occur in individuals with an unfavorable body composition, even when they are young. In boys, we saw only small differences in mitochondrial biomarkers so, to know for sure whether obesity is correlated with mitochondrial DNA methylation in boys, more samples must be studied.

MITOCHONDRIAL EPIGENETICS AS A BIOMARKER?

A reduced number of mitochondrial DNA copies and increased methylation levels might be associated with reduced functioning of mitochondria. It looks like the condition of being overweight might favor these mitochondrial changes. The exact mechanisms through which mitochondria DNA methylation and copy number affect the functions of mitochondria are still being studied. Despite many missing details, it appears that the state of the mitochondria may be an interesting biomarker of cellular health. Mitochondrial biomarkers seem to vary as a consequence of exposures to pollution or tobacco smoke [3] and in diseases like cardiovascular disease [4]. Since diet is also an environmental exposure, mitochondrial biomarkers might represent a sort of "alarm signal" that could be easily measured

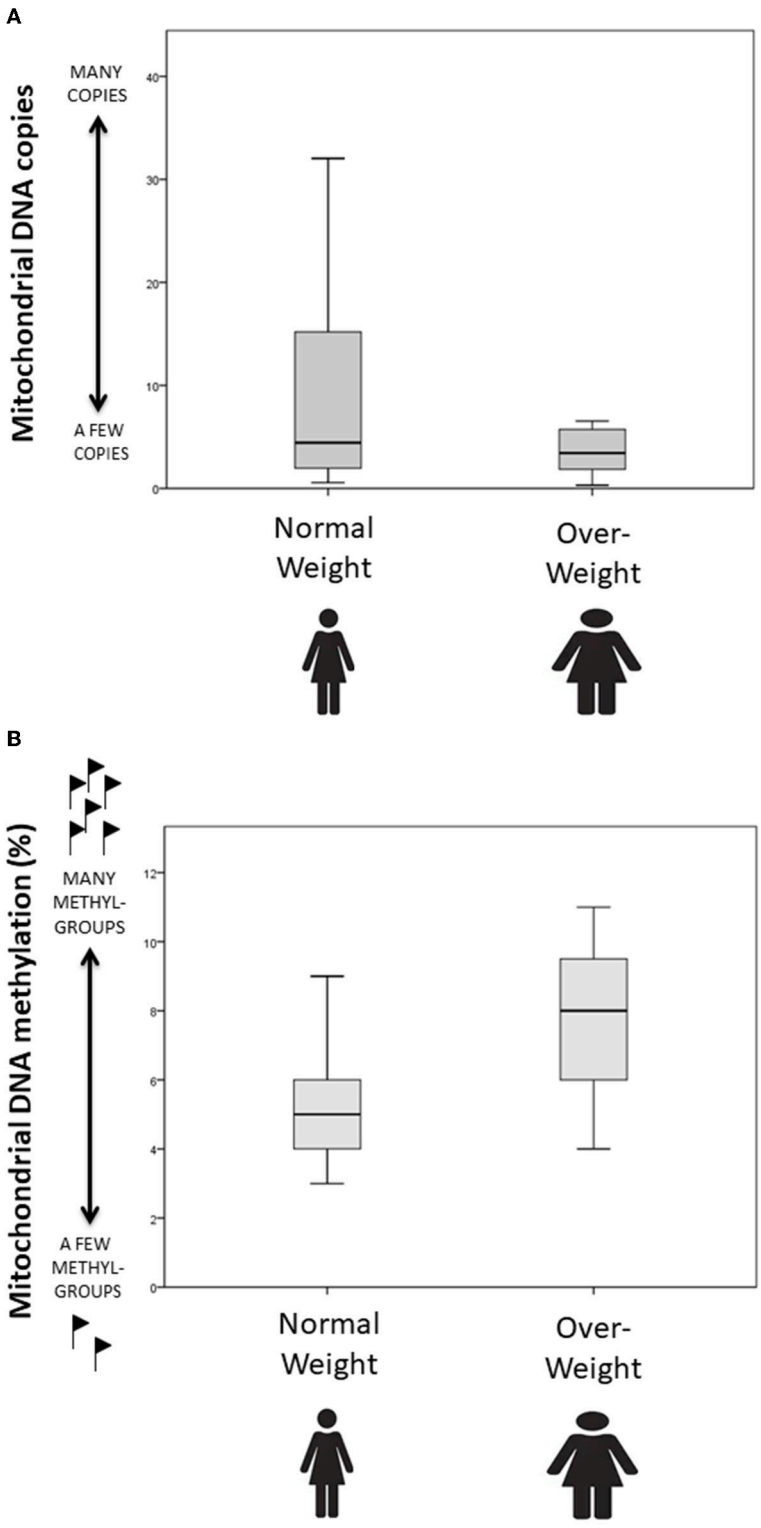

Figure 3

(A) The number of copies of mitochondrial DNA is reduced in obese and overweight girls compared with lean girls. **(B)** Mitochondrial DNA methylation is higher in obese and overweight girls compared with lean girls[1].

[1] The box and the "whiskers" represent all the measured values. The box includes half of the measured values. The "whiskers" include the remaining half of the measurements (25% for each whisker). If most of the measurements are close the mean (the central line), the box will be small; if there is a lot of variability in the values, the box will be larger.

at an early stage, before unbalanced diets and unhealthy lifestyles cause serious problems [5]. Hopefully, future studies will confirm that measures of mitochondrial DNA copy number and methylation status can be used as a biomarker of health.

LOOKING TO THE FUTURE

Nutrition and physical activity, along with genetics and age, determine how much fat and muscle each person has inside their body. If we have unhealthy eating habits and are not active, our bodies store extra fat that they do not need. Unhealthy body composition and poor diet have consequences not only on body shape but, more importantly, on body functions. Specifically, an unhealthy body composition might impair the activity of mitochondria and their ability to produce energy efficiently, while eating healthy foods keeps the body lean and powerful. This is not only because healthy foods are good fuel for our cells, but also because healthy foods keep the engine of our cellular powerhouses—the mitochondrial DNA—properly functioning. This is why balanced nutrition, together with moderate physical activity, makes us feel healthy and energetic.

This study suggests that poorly regulated epigenetic mechanisms, specifically DNA methylation, might happen in obese girls, highlighting a way that mitochondrial functions might be regulated. However, always remember that scientific evidence can be confirmed only after many repetitions! Further experiments using more samples are necessary to confirm these findings. Replication of experiments might also help to clarify the inconclusive findings that we saw in boys in our study. We hope that the new findings emerging from this work will encourage the scientific community to keep investigating mitochondrial DNA methylation, because such studies might provide new insights on the effects of diet on human health.

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ORIGINAL SOURCE ARTICLE

Bordoni, L., Smerilli, V., Nasuti, C., and Gabbianelli, R. 2019. Mitochondrial DNA methylation and copy number predict body composition in a young female population. *J. Transl. Med*. 17:399. doi: 10.1186/s12967-019-02150-9

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YOUNG REVIEWERS

ANASTASIA, AGE: 13
I am Anastasia, a year 9 student captivated by science! I am very passionate about learning and discovering new opportunities. My dream is to study medicine, as I am very interested in how our body works and how it can be affected. Outside of my studies, I love painting, drawing, and crafting, as well as many other extracurricular clubs. But most of all, I love cooking deserts (I have a sweet tooth)!

KAÏKE, AGE: 11
My name is Kaïke. I love football, gaming, and eating. I am from Brazil, France, Egypt, America, Lebanon, Italy, and Syria. I have many friends and I love seeing them. I also love anime. My favorite Animés are Naruto, Dragon ball Z, and Demon slayer. I am a very good baker and I cook lot of cakes and cookies. My favorite football player is Cristiano Ronaldo and my favorite team is Manchester United and Real Madrid.

KENZO, AGE: 9

Hi, I am 9 years old, always exited and super friendly. I have a lot of friends and make new friends easily. I like listening to songs and playing video games. I also really like fighting and self defense. My favorite hobby is parkour. At school, I enjoy sports, arts, math, and the breaks. I often express my thoughts and talk while the teacher explains so time goes faster ☺. I love reading comics.

AUTHORS

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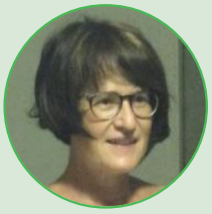

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