



# MEA Summary Review: The role of Mitochondria in ME/CFS

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## Introduction

For many years, a leading theory of causation in ME/CFS has been problems with the mitochondria (the part of the cell responsible for generating energy).

However, [researchers are now suggesting](#) that this is less likely and that we should be looking for something that is impacting the mitochondria's ability to function properly – rather than at the mitochondria themselves.

In light of this, we have created an overview of mitochondrial research to date; explaining what mitochondria are, exploring the possibility of mitochondrial dysfunction as the cause of ME/CFS and offering other possible explanations if the mitochondria are not to blame.

## Key Points

- Mitochondria are the part of the cell responsible for producing most of the body's energy.
- Problems with energy production have been found in ME/CFS and have been primarily linked to mitochondrial dysfunction.
- No 'faulty genes' or mutations have been discovered in the mitochondria of people with ME/CFS, suggesting it is not a form of classic mitochondrial disease.
- There is conflicting research on the role of mitochondrial function in ME/CFS; some studies have found increased mitochondrial activity, some have found reduced activity, and some have found no differences between ME/CFS and healthy controls.
- Recent research is now indicating that there is a problem with something 'upstream' of the mitochondria that is impacting their ability to function i.e. it is not a problem with the mitochondria themselves.
- More research is needed on larger cohorts to identify this upstream factor, but there are already a few theories (see below).

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## What are Mitochondria?

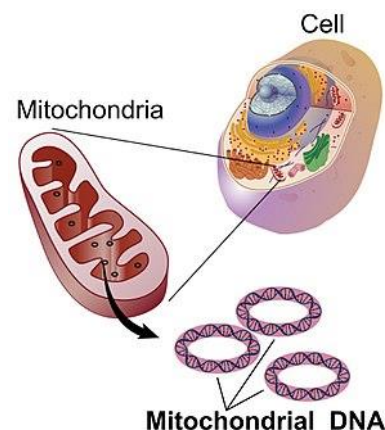
Mitochondria are small structures inside our cells that generate energy and are often referred to as ‘the powerhouse of the cell’.

They are responsible for converting chemical energy from food into a form that’s readily available for use by the cell, called ATP (adenosine triphosphate).

These energy-rich ATP molecules are the fuel for all of the different functions of the body. Mitochondria allow the cell to produce up to 15x more ATP than they would without them (Davidson, 2015).

Mitochondria are found in every cell in the body, except red blood cells, and there can be up to 2000 mitochondria per cell! There are more of them in parts of the body that use a lot of energy, such as the brain, the heart, the muscles and the liver.

But producing energy is not all these ‘powerhouses’ do; they are also involved in a range of other processes, such as cellular defence mechanisms, immune response signalling, cell signalling, cell growth and cell death (McBride *et al.*, 2006).



Source: Wikipedia.com

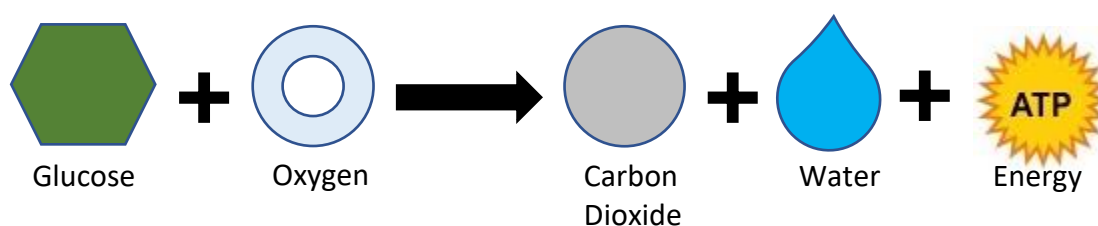


Mitochondria in a cell. Source: parkinsonsnewstoday.com

## Production of ATP

ATP (fuel for the cell) is made through the process of ‘cellular respiration’. This is a series of chemical reactions that combines glucose from food with oxygen to make energy.

Water and carbon dioxide are also produced as waste products of this reaction. Special proteins called enzymes are needed to carry out the chemical reactions involved.



*Simplified diagram of the reaction that takes place during cellular respiration.*

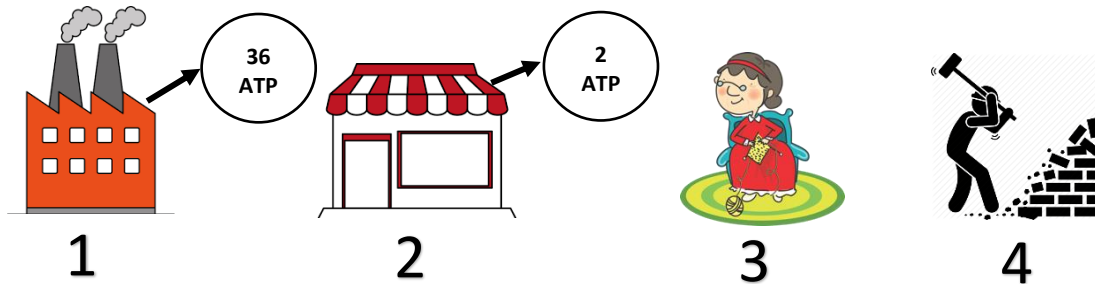
## Types of energy production

Although mitochondria are responsible for around 90% of the cell's energy production, there are other methods of energy production that the cell can use that don't require mitochondria.

However, these are a lot less efficient processes that either use a limited fuel supply, produce harmful by-products or are a lot slower.

There are 4 main types of energy production. The first two use glucose as the 'fuel' source, whereas the second two use fat and protein:

1. **Aerobic** (requires oxygen). The classic form of respiration that the mitochondria adopt, as described above. It is the main form of energy production the body uses to carry out basic functions and low-intensity activities. On average, 36 molecules of ATP (energy molecules) are produced from 1 molecule of glucose.
2. **Anaerobic** (doesn't require oxygen). This is what the body switches to during vigorous activity, where your oxygen supply can't keep up with the energy demand. This reaction produces lactic acid as a by-product, which is harmful and causes muscle fatigue and aching. Only 2 molecules of ATP are produced from 1 molecule of glucose.
3. **Gluconeogenesis** (or fat burning!). This is the slowest form of energy production and can't be used to supply energy for exercise. The body uses this when glucose is not available and fatty acids become the source of fuel. 1 small fatty acid chain can be used to produce 48 ATP molecules!
4. **ATP Phosphocreatine** (Protein breakdown). This is the quickest, most immediate source of energy, used for short quick bursts, such as sprinting. Lots of ATP are produced from a component of muscle called 'Creatine phosphate', until the stores of it run out. This is not a good form of energy to be using often as it breaks down muscle.



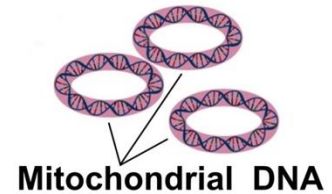
*Cartoon representing the 4 main types of energy production. Source: Clipart.*

## ROS and mitochondria

During the reactions that produce energy, mitochondria also produce other ‘waste products’, that include small molecules called reactive oxygen species (ROS) and ‘free radicals’, which are known to damage DNA and lead to inflammation and disease.

## Mitochondrial DNA (mtDNA)

Mitochondria are unique as they have their own DNA, separate from the DNA of the cells in your body, called mitochondrial DNA (or mtDNA for short). Mitochondrial DNA is inherited solely from the mother, not from the father.



Mitochondrial DNA mutates up to 10x faster than ‘normal’ cellular DNA. This means it is much more likely to have a mutation that may lead to a dysfunction or a disease (Xu *et al.* 2018).

**Note:** A mutation is a change in DNA sequence and is not necessarily bad. However, when a mutation occurs in an important gene and alters the production of a protein, it can contribute to disease.

These mutations can occur spontaneously, due to errors in DNA replication and repair, or as a result of exposure to chemicals or reactive oxygen species (ROS).

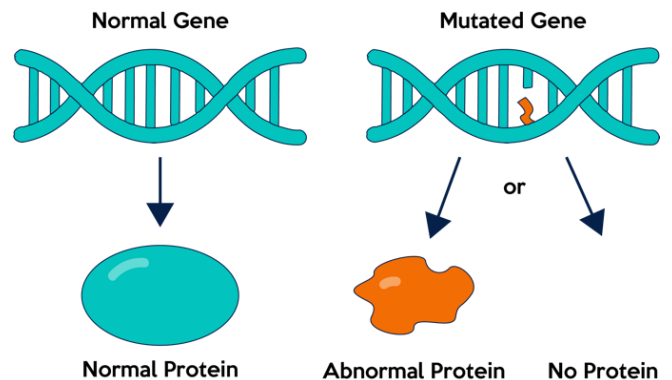


Diagram showing a mutated gene. Source: Kintalk.org

## Mitochondrial disease

Classic mitochondrial disease is where someone inherits a mutation in their mitochondria (they are born with it), which causes changes in their genes and results in disease, that may present itself at birth or later on in life.

Around 1 in 5,000 people have a form of mitochondrial disease. Some examples of these include Kearns-Sayre syndrome, Pearson syndrome and MELAS syndrome.

## Inhibition of Mitochondria

Mitochondrial function can be impaired in two main ways:

### 1. Substrate or co-factor deficiency:

- This would be a lack of supply of any of the components needed to carry out respiration (the process that creates energy), such as glucose or oxygen. Or a lack of or problem with any of the enzymes involved in respiration.
- Or there can be a lack of minerals or nutrients that are important for mitochondrial function, such as magnesium, selenium, zinc, B vitamins and CoQ10.



Source: Helpguide.org

### 2. Inhibition by chemicals (from the environment or produced by the body):

- Examples of environmental chemicals include pesticides or heavy metals, like mercury. Examples of chemicals produced by the body include ROS or cytokines.

## Role of Mitochondria in other diseases

Faulty mitochondria have been implicated in various diseases, including dementia, Alzheimer's disease, Parkinson's disease, epilepsy, stroke, cardiovascular disease, cancer, arthritis and diabetes mellitus (Duchen and Szabadkai, 2010).

## Mitochondria and ME/CFS

Mitochondrial dysfunction ('faulty' mitochondria that aren't working properly) is an attractive explanation for the cause and disease pathology of ME/CFS, as it can be used to explain many of the symptoms experienced.



Given that ME/CFS is primarily an energy disorder, it would make sense that the main source of energy in the body would be faulty – so it's the 'best fit' and easiest explanation. However, this by no means makes it the right one!

ME/CFS is a complex condition, with several organs and systems throughout the body affected. As mitochondria are located in cells all over the body, a defect in them could explain the wide-spread nature of the disease.

Also, given that infection is often a trigger for the onset of ME/CFS, the fact that viruses, bacteria and parasites can all induce changes in mitochondrial function gives more support for mitochondrial dysfunction being involved in ME/CFS pathology.

Fatigue is a common symptom in patients with mitochondrial disease and there was even a reported case of a patient with mitochondrial disease who was misdiagnosed with ME/CFS, suggesting that the two illnesses are similar in presentation (Gorman *et al.*, 2015). This further points towards the involvement of mitochondria in ME/CFS.

## Mitochondrial Activity

Previous studies have shown energy production, including mitochondrial activity, to be significantly impaired in ME/CFS compared to controls (Fluge *et al.*, 2016; Tomas *et al.*, 2017).

Dr Cara Tomas recently showed that mitochondrial functioning is impaired in ME/CFS immune cells, both at rest and when stimulated to their maximum capacity.

The lower maximal respiration in ME/CFS immune cells suggests that when the cells experience stress, they are less able to increase their energy production to keep up with demand. This implied that mitochondrial dysfunction might contribute to ME/CFS, at least in regard to immune cells.

- The ME Association Ramsay Research Fund helped finance Dr Tomas's work on bioenergetics and [she kindly provided a lay explanation](#) of the 2017 study

However, Dr Tomas and her research team went on to publish another study in April 2019 that examined the activity of individual complexes within the mitochondria (they looked 'under the hood' at the mitochondrial engine) and found there to be *no differences* in activity between ME/CFS patients and healthy controls.

The researchers concluded that the differences in mitochondrial function they observed in their previous study were "due to causes upstream of the mitochondrial respiratory chain".

"Given the results here, the future of bioenergetic studies in CFS should concentrate on mechanisms upstream of the mitochondrial respiratory chain." Tomas *et al.*, 2019

- Dr Tomas also [helped to explain the results from the 2019 study](#), which was also supported by the ME Association Ramsay Research Fund.

So, what they originally found was that mitochondria aren't keeping up with energy demands in ME/CFS but then, on further investigation into the inner workings of the mitochondria, found there to be nothing wrong with the mitochondria themselves.

This is in accord with results reported by other groups, that suggest the differences seen in mitochondrial ATP production should be attributed to other causes, such as impaired transport of oxygen into the cell (Lawson *et al.*, 2016; Vermeulen *et al.*, 2010).

## The Acumen ATP Test

Dr Sarah Myhill and Norman Booth created an 'ATP profile' test, looking at various aspects of mitochondrial respiration in order to assess function. They concluded that ATP production was significantly impaired in people with ME/CFS and that the mitochondrial dysfunction also correlated with the severity of the illness.

The researchers said that there is “measurable mitochondrial dysfunction in ME/CFS” and concluded that “The ATP Profile is a valuable diagnostic tool for the clinical management of ME/CFS” (Myhill *et al.*, 2009; Booth *et al.*, 2012).

Furthermore, Dr Myhill has developed a treatment programme that she has found to be affective in improving mitochondrial function, as measured by the ATP profile test (Myhill *et al.*, 2013).

However, Dr Karl Morten’s team from Oxford, working with a team from Newcastle, recently attempted to test the efficacy of this approach compared to the ‘gold standard’ method of determining mitochondrial function.

The results of the study, which was funded by the ME Association Ramsey Research fund, are still pending publication, but Dr. Morten gave a presentation in December 2018 that suggested the Acumen test could not be replicated or validated.

- Read [about the research we are funding at Oxford University](#), and the recent [update from Dr. Morten](#)

## ATP production

Other research groups looking at mitochondrial ATP production in ME/CFS found that it was either no different to controls, or that it was actually increased.

Lawson *et al.* (2016) reported that the number, size, shape and enzyme function of the mitochondria in ME/CFS patients is the same as controls. They also showed that the amount of ATP being produced by mitochondria was the same between ME/CFS patients and healthy controls.

However, they found *increased* ATP production from *non-mitochondrial* sources, suggesting that abnormalities in other ATP-producing pathways may contribute to the disease. They concluded, “Our results indicate that the fatigue symptom in this cohort of patients is unlikely caused by lack of ATP and severe mitochondrial malfunction.”

Smits *et al.* (2011) found a *higher rate of ATP production* and mitochondrial activity in people with ME/CFS compared to patients with known mitochondrial disorders, demonstrating that the pathology of ME/CFS does not reflect that of a mitochondrial disorder.



## mtDNA variation

Although mitochondrial DNA analysis is not yet comprehensive, from looking at the variants that can be studied, it doesn't appear that mutations in mitochondrial DNA are involved in the pathogenesis of ME/CFS. Therefore, it is unlikely that ME/CFS is a form of mitochondrial disease.

Schoeman *et al.* (2017) looked for evidence of clinically proven mtDNA mutations and found none, indicating that ME/CFS does not fall within the spectrum of mitochondrial disease originating from mtDNA mutations. Billing-Ross *et al.* (2016) also found no association between mtDNA variants and ME/CFS.

## Exercise and Muscle Studies

Differences in recovery from exercise have been observed in ME/CFS, with muscle studies showing excess lactate build-up in patients after exercise (Jones *et al.*, 2012; Fluge *et al.* 2016; Lien *et al.* 2019).

This suggests that during exercise, ME/CFS patient's cells are shifting to anaerobic energy production (see blue box below) to fulfil energy demands. This could mean that mitochondrial energy production is insufficient and is having to be compensated for by non-mitochondrial sources of ATP production.

2-day Cardiopulmonary exercise testing (CPET) has repeatedly demonstrated that ME/CFS patients reach their anaerobic threshold\* and maximal exercise capacity a lot quicker than controls, which implies a possible decrease in mitochondrial ATP production.

Vermeulen *et al.* (2010) found that CPET results are *not* due to a defect in mitochondrial enzyme complexes (the 'inner workings' of the mitochondria), which catalyse respiration.

More research is needed in order to find out what is causing this early switch away from mitochondrial respiration during exercise, as it does not appear to be caused by faulty mitochondria.

Some possible explanations could be a lack of available oxygen or a problem with key processes needed to produce components required for respiration (more on this later).



2-day CPET testing shows that people with ME/CFS are switching to non-mitochondrial sources of energy production much sooner than healthy controls.

Source: 123RF

**\*Anaerobic Threshold** = the point at which cells switch from aerobic to anaerobic respiration. This is assessed by the levels of lactate that build up in the blood.

Aerobic respiration is how mitochondria make energy and it uses oxygen to do it. This is the most efficient form of energy production, so we want to be mainly using this method.

Anaerobic respiration is not carried out by mitochondria, it happens elsewhere in the cell and it does not require oxygen. However, it is a lot less efficient and lactate is produced as a waste product.

Lactate causes muscle cramps, muscle fatigue and inflammation, as well as brain-fog. The body has to use a lot of energy in order to get rid of the excess lactate.

In healthy people, during strenuous exercise such as running or riding a bike, they switch from aerobic to anaerobic respiration for a short time to keep a steady supply of energy to their muscles.

However, it would seem that people with ME/CFS may be switching to this less-efficient form of energy production much sooner, after often quite minimal activity, leading to an unnecessary build-up of lactate.

## If Mitochondria were cars...

We have a car that is slow and not running as it should be, not doing as many miles to the gallon as it should, maybe a clunking noise somewhere... we might take it to the garage.

The mechanics find that the car is indeed running slower and when the accelerator is pressed, the car does not respond in the normal manner.

The mechanics look under the hood to make sure the engine is working correctly and find that it is (The mitochondrial enzyme complex).



They also check to see if any modifications have been made that may be affecting its function, but they don't find any (mutations).

So, then they start to think, maybe the fuel is not being utilised properly, or the engine is not taking in enough oxygen, which is needed for the engine to run. Or perhaps there is an electrical fault which is signalling the car to run slower...

## Are mitochondrial/metabolic dysfunctions a cause or consequence of ME/CFS?

Another thing to consider is that even if mitochondrial dysfunction is present in ME/CFS, is it the primary driving force behind symptoms, or is it simply the result of a bigger process going on?

Could treating the mitochondrial defect, if found, actually be just a band-aid-solution to a bigger, unknown problem?

Mitochondrial dysfunction may actually be a consequence of cellular hypoxia, increased oxidative stress, immune system abnormalities, increased inflammation or muscle degeneration; all of which have been hypothesised to be involved in ME/CFS.

## Latest Research on Mitochondria in ME/CFS

The February, 2019 review from Dr Elson and Dr Tomas at Newcastle University [covered the possibility of mitochondrial dysfunction](#) in ME/CFS, providing an overview of all the evidence for it and all the evidence against it.

They confirmed that patients with ME/CFS do not appear to have significant mtDNA mutations. There appears to be no definitive consensus on the role of mitochondria in ME/CFS, and there are many conflicting findings.

This may be due to the lack of large, longitudinal (long-term) studies, along with different methodologies being used and a lack of studies in general being replicated.

“Taken together, these studies show some suggestive evidence for abnormalities in the bioenergetics in ME/CFS. Nonetheless, caution should be used when trying to determine the exact role of mitochondrial abnormalities in this disease as many of these studies are small, single-site studies, using different techniques and are yet to be repeated by other research groups.”

“There is suggestive evidence that mitochondrial function may be impaired in at least a sub-set of ME/CFS patients.”

“Future studies need to include larger cohorts from multiple centres, with standardized sample handling taking a multi-disciplinary approach.”

(Tomas et al. 2019)

## If not the Mitochondria then what?

If faulty mitochondria are looking less likely to be the cause, then what are the possible contenders for the factor 'upstream' of the mitochondria that could be affecting mitochondrial function or having an overall effect on energy production?

There are multiple contenders including reduced oxygen supply to cells, problems with oxygen uptake into the cell, problems with glucose transport into the cell, oxidative stress, signalling factors or even some unknown mystery factor in the blood! I will be covering some of these possibilities below.

"...abnormalities found in whole cells shown previously is not due to abnormalities in the mitochondrial respiratory chain complexes but rather at different points of the respiration pathway, such as movement of glucose into cells, AMPK abnormalities, or altered functioning of other mitochondrial enzymes" (Tomas et al., 2019).

### Lack of Oxygen

Several researchers have suggested that there may be a problem with oxygen in ME/CFS. Either that there is a lack of oxygen supply to tissues, due to reduced blood flow, or that cells are not taking up enough oxygen, perhaps because of some sort of block.

- [You might like to read this 2013 blog from Cort Johnson on Health Rising forums](#)

As oxygen is needed for mitochondria to produce energy, a lack of oxygen in the cell would lead to impaired energy production. Evidence in support of low oxygenation being a problem in ME/CFS would include:

- Reduced cerebral blood flow, that could result in inadequate brain oxygenation, as well as reduced blood volume, factors that have both been found in ME/CFS (Streeton and Bell, 2011; He et al. 2013).

"Disturbances in circulation and provision of oxygen to tissues could underlie many symptoms of ME/CFS."

(Germain et al. 2018)

Reuter and Evans (2011), established that a key amino acid, L-carnitine, which is highly important in oxygen metabolism, is deficient in ME/CFS patients.

- Calcium ions are needed to ensure sufficient uptake of oxygen into the cell. There have been reported problems with calcium ion channels in ME/CFS cells (Cabanas *et al.* 2018), which suggests ME/CFS cells may have a problem with taking in enough oxygen.
- Ron Davis found that red blood cells in people with ME/CFS are not very good at changing shape, meaning they are less able to flow through capillaries, which may lead to a shortage of oxygen supply to tissues.  
[MEA Summary Review: Red blood cells in ME/CFS demonstrate reduced ability to change shape](#)
- Hyperbaric (high pressure) oxygen therapy has been found to improve symptoms and quality of life in some people with ME/CFS (Akarsu *et al.* 2013; Efrati *et al.* 2015).

## Problems with Glucose Uptake

As glucose is the ‘fuel source’ which mitochondria convert into energy, problems with taking enough glucose into the cell could result in reduced energy production.

One study found impaired stimulation of glucose uptake in skeletal muscle cells taken from ME/CFS patients (Brown *et al.* 2015). Usually, when cellular energy is low, a special protein called ‘AMPK’ is activated, which triggers the cell to take up more glucose, which is needed for mitochondrial respiration.

However, the study found that activation of AMPK is impaired in ME/CFS patients, meaning that the mitochondria may not be receiving enough glucose in order to carry out respiration and produce energy in the most efficient and normal manner.

## Cytokines

Increased levels of pro-inflammatory cytokines (which have been demonstrated in ME/CFS) can inhibit mitochondrial respiration, interfere with ATP production and cause mitochondrial shutdown (Morris and Maes, 2014).

So increased levels of cytokines, which may be a result of a problem with the immune system or due to neuroinflammation, could be causing the mitochondria to misbehave.

## Oxidative Stress

Oxidative stress relates to an imbalance between the generation of reactive oxygen species (ROS), which can be toxic to cells, and the ability of the body to counteract or detoxify their harmful effects via antioxidants.

Increased levels of reactive oxygen species (ROS) and/or a lack of antioxidants may be causing oxidative stress in ME/CFS, which may be inhibiting mitochondrial function.

Oxidative stress has been previously associated with ME/CFS in a number of studies (Morris *et al.*, 2018; Germain *et al.*, 2018).

“Increased ROS in CFS and FM, resulting in impaired mitochondrial function and reduced ATP in muscle and neural cells, might lead to chronic widespread pain in these patients.”  
(Meeus *et al.* 2013)

In his latest research, Dr. Ron Davis demonstrated Higher levels of ROS in ME/CFS red blood cells compared to controls.

- [MEA Summary Review: Red blood cells in ME/CFS demonstrate reduced ability to change shape](#)

Interestingly, oxidative stress can also lead to oxygen deprivation in the cell. So, lack of oxygen and oxidative stress could be two factors that are perpetuating each other – causing a vicious cycle.

## Enzymes

Pyruvate Dehydrogenase (PDH) is an enzyme (a special type of protein) that is important for the first step of respiration (energy production).

It regulates the production of a molecule which feeds into the mitochondria and is the starting point for mitochondrial respiration. Therefore, abnormalities in the function of PDH are likely to have consequences for mitochondrial function.

Fluge *et al.* (2016) reported functional impairment of PDH in ME/CFS (it's not working as it should be). A study investigating the use of sodium dichloroacetate as a treatment for ME/CFS found some benefit in a subgroup of patients (Comhaire 2018).

Sodium dichloroacetate works by stimulating PDH activity, which boosts mitochondrial function and increases the production of ATP. This suggests that some ME/CFS patients may indeed have a problem with their PDH enzymes.

“These preliminary findings sustain the hypothetical role of mitochondrial hypo-metabolism due to inhibition of the activity of the pyruvate dehydrogenase in the pathogenesis of primary ME/CFS and suggest a possible benefit of nutraceutical treatment by sodium dichloroacetate.”

(Comhaire F 2018)

In a recent study of a mice model of ME/CFS by Obha *et al.* (2019), they concluded that their findings indicate that a decrease in mitochondrial PDH activity is involved in the symptoms of ME/CFS.

### ‘Mystery Factor’ in the Blood/Plasma

Recently, several researchers have noted an effect on healthy control cells when plasma from ME/CFS patients is applied- it affects the energy production of the cell. This has led them to believe that there is a factor in the plasma/serum of ME/CFS patients that is having an effect on their cells.

This factor could be anything from a virus, to a protein or a signalling factor or something else. Further studies are needed in order to identify this factor, but the research so far is very intriguing!

- [ME Research Summary: Something In The Blood by Simon McGrath](#)

The first researchers to find this affect were Drs. Fluge and Mella, who added serum (a component of blood) from ME/CFS patients to healthy muscle cells grown in a lab. They found that adding the serum made the muscle cells produce more lactate and use up more oxygen (a measure of mitochondrial activity).

In addition, this effect was even stronger when the cells were put under ‘stress’ (made to work harder). This demonstrates that some factor in the serum of ME/CFS patients is affecting healthy cells, somehow making them work harder.

“Based on these observations, ME/CFS patient serum appears to carry substance(s) that induce a cellular response to support mitochondrial energy production. In accordance, optimization of mitochondrial respiration could be regarded as a protective response to avoid energy depletion caused by PDH dysfunction.”

“Additional studies are required to identify the substance(s) in ME/CFS serum that mediate the effects on cultured muscle cells, which could act directly on the metabolic apparatus or indirectly via signalling factors.”

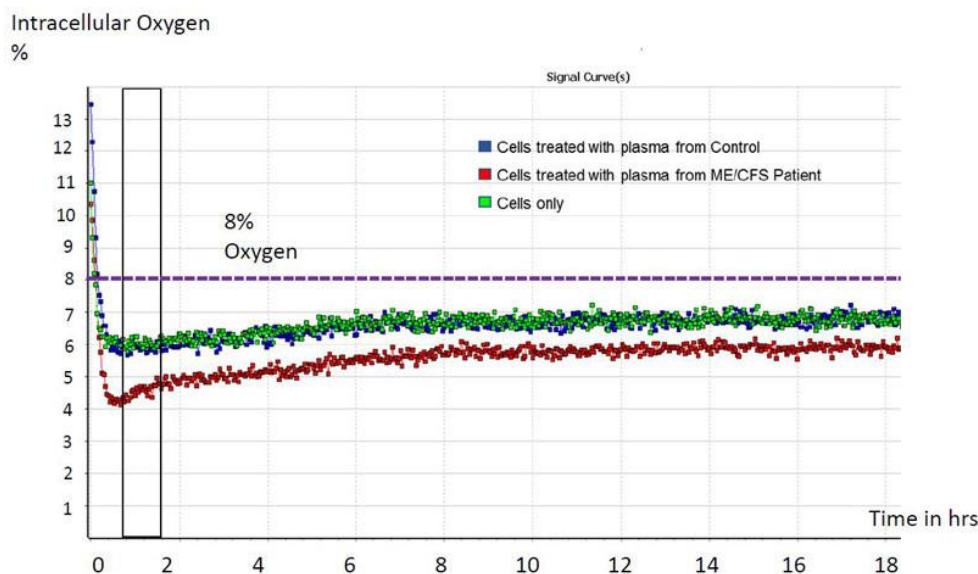
(Fluge et al. 2016)

Dr Karl Morten’s team from Oxford university also looked at energy metabolism in lab grown muscle cells.

They used a probe to measure oxygen concentration in the cells to assess mitochondrial activity and found that adding plasma from ME/CFS patients caused oxygen levels to fall.

Similarly, to Fluge and Mella’s results, this indicated that the mitochondria are working harder.

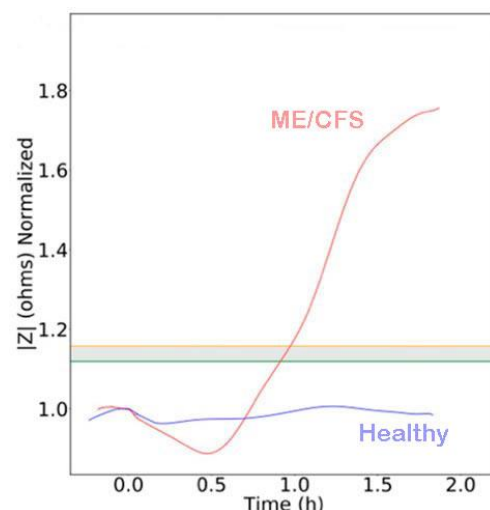
- [Dr Karl Morten announces £1.6million grant application to study disease pathology in ME/CFS](#)



*Plasma from ME/CFS patients leads to lower oxygen levels in cells*

Dr Ron Davis team from Stanford University also demonstrated this effect in a plasma swap experiment using his ‘nanoneedle’ test. The test involves applying patients’ blood to a ‘nano-electronic’ device, which is like a tiny needle that measures how easily an electrical current can pass through a cell.

The cells were first put under stress using salt, to force them to use more energy, then the nanoneedle measures the response to that stress. They found that the response was much greater in ME/CFS blood than in healthy controls (see graph). This means the cells were much less able to deal with the stress put on them and cope with the increased energy demand.





Next, the team put blood cells from healthy donors into plasma from ME/CFS patients and found that the healthy cells then gave the same results as the ME/CFS cells. And when they put ME/CFS cells into healthy plasma, the ME/CFS cells gave the same response as healthy cells.

This is really interesting as it clearly demonstrates that something in the plasma of ME/CFS patients is affecting the cells ability to cope with stress.

- [Stanford: Biomarker for Chronic Fatigue Syndrome Identified?](#)

## Conclusion

The exact involvement of mitochondria in the pathology of ME/CFS is unclear, with lots of conflicting evidence. Although it seems pretty unlikely to be a form of mitochondrial disease involving a mutation. This is good news in a way, as it helps narrow the possibilities and means that whatever is causing the mitochondria to miss-behave should (in theory) be reversible!

The mitochondria may well be affected and not working optimally and there are certainly lots of demonstrated metabolic disturbances. However, there doesn't seem to be a physical problem with the mitochondria themselves and so studying them doesn't get to the root of the problem – we are likely just seeing the aftereffects of a problem elsewhere.

What is clear is that there are energy production problems present in ME/CFS, in terms of an inability to keep up with demand and switching to non-mitochondrial sources of production. However, it is not yet clear what is driving this. While there are many theories about what might be causing this, we need more and larger studies to pinpoint this 'mystery factor' and discover why energy production is so inefficient in ME/CFS.

We are now starting to move away from the idea of mitochondrial dysfunction being the central theory of causation for ME/CFS and exploring lots of other avenues, such as oxidative stress and neuroinflammation.

Research in ME/CFS requires a multi-factorial approach from many different angles, with lots of collaboration. More importantly, much larger studies over a longer period of time are needed, as well as better-defined patient study groups and the identification and differentiation of the many subgroups within the patient population. Only then are we going to start seeing clearer results that point toward answers.

# The ME Association

Real People. Real Disease. Real M.E.

We are a national charity working hard to make the UK a better place for people whose lives have been devastated by an often-misunderstood neurological disease.



If you would like to support our efforts and ensure we are able to inform, support, advocate and invest in biomedical research, then please donate today.

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