

## What are mitochondria?

Mitochondria are often called the ‘cell’s powerhouse.’ They are specialized compartments within almost every cell. They are responsible for producing 90% of the energy needed by our body to sustain life. Mitochondria combine oxygen from the air we breathe with calories from food to produce energy.

## What is mitochondrial disease?

Mitochondrial diseases result when there is a defect that reduces the ability of the mitochondria to produce energy. As the mitochondria fails to produce enough energy, the cell will not function properly and if this continues, cell death will eventually follow. Organ systems will begin to fail and the life of the individual is compromised, changed or ended.

Imagine a major city with half its power plants shut down. At least, such conditions would produce a “brown out” with large sections of the city working far below optimum efficiency. Now imagine your body working with one-half of its energy-producing facilities shut down. The brain may be impaired, vision may be dim, muscles may twitch or may be too weak to allow your body to walk or write, your heart may be weakened, and you may not be able to eat and digest your food. This is precisely the situation people with mitochondrial disease find themselves.

Mitochondrial disease can affect any organ of the body and at any age. Symptoms are extremely diverse and often progressive. They include: strokes and seizures, muscle weakness, gastrointestinal disorders, swallowing difficulties, cardiac disease, liver disease, diabetes, blindness and deafness and susceptibility to infections.

## What causes mitochondrial disease?

For most patients, there is a genetic mutation in either the mitochondrial DNA or the nuclear DNA. The mutation may have been inherited from the mother or from both parents, or it may represent a spontaneous mutation. For most patients with mitochondrial disease, the genetic mutation has not yet been identified.

There are environmental factors, even certain medicines that may interfere with the mitochondria and result in symptoms.

## How common are mitochondrial diseases?

Every 30 minutes a child is born who will develop a mitochondrial disease by age 10.

At least 1 in 200 individuals in the general public have a mitochondrial DNA mutation that may lead to disease.

Mitochondrial disease is a relatively newly diagnosed disease – first recognized in an adult in the 1960s and in the 1980s for pediatric onset cases. It is greatly under diagnosed and the true prevalence is difficult to determine.

Research has consistently shown that mitochondrial dysfunction is at the core of many very common illnesses and chronic conditions of adulthood. These include: Alzheimer's Dementia, Parkinson's disease, diabetes, hypertension, heart disease, osteoporosis, cancer and even the aging process itself. Furthermore, autoimmune disease such as multiple sclerosis, lupus and rheumatoid arthritis appear to have a mitochondria basis to illness.

### **Why is research so critical?**

There are no known treatments or cures for mitochondrial disease.

Mitochondria may play a far greater role in human health than scientists and doctors have realized. Any health concern that is an energy problem could be related to the mitochondria.

Further research into the mitochondrion and primary mitochondrial diseases (those due to genetic defect) would benefit millions of people. It would offer hope to the thousands suffering from this debilitating and often fatal disease and provide a broad range of new therapeutic approaches for attempting to treat these other very common and incapacitating illnesses and conditions.

### **Mitochondrial Defects are a central factor in human health and disease.**

Mitochondrial dysfunction is at the core of a surprising range of very common illnesses and conditions, and represents a promising new avenue for their treatment. As the mitochondria are responsible for producing energy, any illness that has an energy problem could be related to the mitochondria. Diseases in which mitochondrial dysfunction have been implicated include:

- Alzheimer's Dementia, Parkinson's disease, Huntington disease, Amyotrophic Lateral Sclerosis (ALS), mental retardation, deafness and blindness, diabetes, obesity, cardiovascular disease and stroke. Over 50 million people in the US suffer from these chronic degenerative disorders. While it cannot yet be said that mitochondrial defects cause these problems, it is clear that mitochondria are involved because their function is measurably disturbed.
- Even autoimmune diseases such as multiple sclerosis, Sjogrens syndrome, lupus and rheumatoid arthritis appear to have a mitochondrial basis to illness.
- Mitochondrial dysfunction has been associated with a wide range of solid tumors, proposed to be central to the aging process, and found to be a common factor in the toxicity of a variety of physical and chemical agents.

### **Success to date**

The National Institutes of Health (NIH) recently established a cross-cutting research initiative on the mitochondria that cuts across all the NIH institutes (an ROI Project.) In one of his last official actions, former NIH Director Dr. Zerhouni, recently testified before the House Energy & Commerce Committee about the importance of cross-cutting research initiatives as being the key to future advances in science and medicine.

Congress has also expressed its intent to further explore the far-reaching role that mitochondria play in a wide range of diseases. Report language included within the 2008 Labor, HHS Appropriations legislation "...encourages the NIH to intensify its research efforts into primary

mitochondrial disease, which is also implicated in numerous other diseases such as Parkinson's, Alzheimer's, heart disease, diabetes and cancer. The Committee understands that intensified research into primary mitochondrial disease will help to further understand these other conditions."

While some steps are being taken, there is a lot more opportunity and promise that could be realized with greater financial resources. Interestingly, research in Europe and Asia is proceeding in a much more intensive manner. Recently for example, China established a mitochondrial university.

### Highlights in research

Until recently, the broad range of diseases that may be caused by mitochondrial dysfunction was not well understood or appreciated. A relationship between mitochondrial dysfunction and a wide range of disease states was known to exist, but whether mitochondrial dysfunction was responsible for the particular disease was still in question. This changed with the discovery that mutations of the mitochondrial DNA could cause certain diseases. For the first time, scientists showed that a single nucleotide change in mitochondrial DNA of a mouse led to the development of muscle weakness and progressive heart disease.

Research supporting the link between mitochondrial dysfunction and some of these other common illnesses includes:

- Mitochondrial coenzyme Q10 levels are reduced in patients with Parkinson's disease and mitochondrial function in these patients is impaired.
- Results of the first placebo-controlled clinical trial of the compound coenzyme Q10 suggest that it can slow disease progression in patients with early-stage Parkinson's disease.
- These findings are consistent with another recent study involving patients with early onset Huntington's disease. These patients showed slightly less functional decline in groups receiving coQ10.
- Investigators believe coQ10 works by improving the function of the mitochondria.
- A drug once approved as an antihistamine in Russia improved thinking processes and the ability to function in Alzheimer's disease patients. The drug works by stabilizing mitochondria.
- Cancers are also associated with defects in the mitochondria. Within the cell, signaling must occur between the mitochondria and the nucleus. When the signaling malfunctions, the defect can cause cancer.
- Researchers discovered that mutations in the mitochondrial DNA may play a role in tumor metastasis and suggests a possible new avenue for the development of a treatment to suppress metastasis.
- Researchers have found a very consistent decline in mitochondrial function that is found in diabetes and pre-diabetes.
- There is increasing interest in the possibility that mitochondrial dysfunction might play an important role in the etiology of autism. A subset of autistic children have already been shown to manifest biochemical alterations that are commonly associated with mitochondrial disorders, and a few have been linked to specific alterations in the mitochondrial genes.

It is clear that research into mitochondrial disease offers hope to the millions who are afflicted with these other common conditions and diseases.