

# Mitochondrial disease, dysfunction and preserving mitochondrial health

The term mitochondrial disease covers a multitude of heterogeneous diseases that are linked clinically and biochemically. There is primary genetic disease and also secondary mitochondrial disease where there is evidence of mitochondrial dysfunction. These include but are not limited to neurodegenerative, later-onset diseases such as ALS, Alzheimer's and Parkinson's disease and Type 2 diabetes. There is growing evidence that virtually any disease may have some mitochondrial dysfunction component because mitochondria are so critical to metabolism.

## **1 in 5000 Canadians have primary mitochondrial disease.**

According to Mark Tarnopolsky MD, PhD, FABEM, FRCPC, Professor and Division Head of Neuromuscular & Neurometabolic Disorders at McMaster University,

*"although some people may feel that mitochondrial disorders are rare, it is now clear that they affect at least 1 in 5000 individuals and as we learn more about mitochondrial disease this number will undoubtedly increase. To put this into perspective, there is a huge amount of support for Duchenne muscular dystrophy which affects 1 in 3500 and ALS which affects 1 in 50,000 adults. By relative comparison, mitochondrial diseases are vastly under supported and under recognized and yet they touch the lives of far more people in Canada than many other disorders. Support for mitochondrial disorders is very important not just to enhance the quality of life but also to improve overall survival" (Tarnopolsky, 2012).*

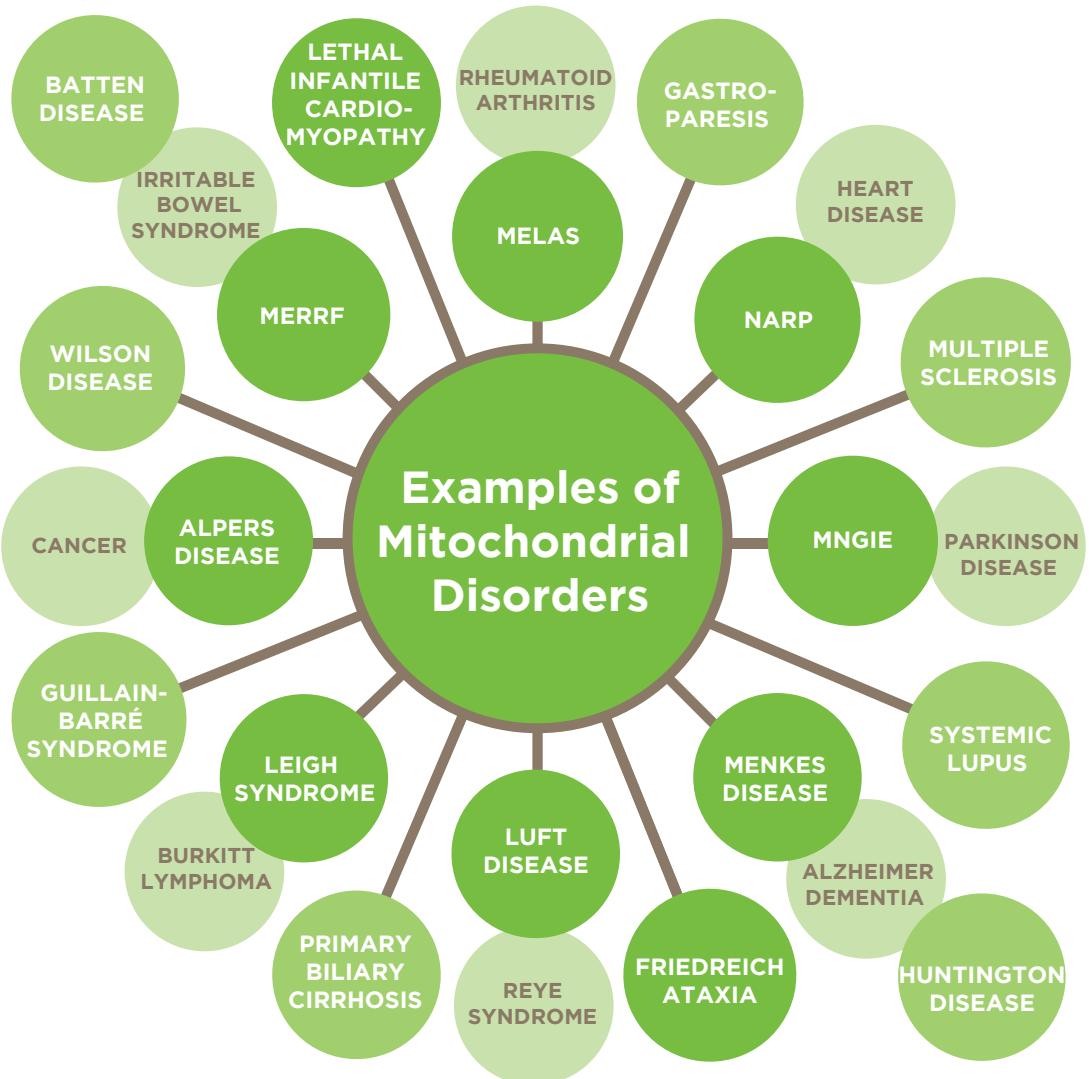
Currently there is no cure and diagnosis can sometimes take months or years because symptoms often mimic other diseases.

## **The spectrum of mitochondrial disease**

There is growing interest in understanding disturbances in mitochondrial metabolism and the connection between mitochondrial dysfunction and more common diseases of aging. According to F.D. Kendall author of Mitochondrial disorder diagnostic trends published in Mitochondrial disorders: Overview of diagnostic tools and new diagnostic trends, Journal of Pediatric Biochemistry 2 (2012) 193-203

*"Mitochondrial disorders have a far larger footprint and impact than was previously noted with an incidence of at least 1 in 5,000 individuals [1,3-6]. Recent studies have also shown that 1 in 200 newborns carry one of the ten common mtDNA mutations, perhaps contributing to the onset or development of many common place diseases ..."*

The illustration below shows some examples of diseases along the mitochondrial dysfunction spectrum. Disorders in dark circles are examples of primary mitochondrial disease while those in light circles are examples of other diseases associated with mitochondrial dysfunction.



## Mitochondrial health

Because evidence suggests that mitochondrial dysfunction is implicated in neurodegeneration, antioxidants including beta carotene and vitamins C and E have been identified for their oxidative protection in neurodegenerative diseases. Other therapies believed to improve mitochondrial function include creatine, coenzyme Q10, idebenone, and calorie-restricted diets. Beside nutrient support, there is exciting early evidence that exercise may have a role in repairing malfunctioning mitochondria.

The potential to restore or preserve mitochondrial health holds great promise for treating mitochondrial disease in the future.

# Mitochondrial disease research update 2015

Since 2011, the MitoCanada Foundation has proudly supported mitochondrial disease research in Canada, administering more than a half million dollars in research grants, awards, and partnerships. Scientists we support are dedicated to making discoveries and advancing knowledge about diagnostics, treatment and a cure for this complex disease. While the research we fund is diverse in its scope, the key aspects of every study remain the same: to improve the quality of life of people living with mitochondrial disease and to find a cure.

In 2015 researchers we support will see their work showcased nationally and internationally at several prestigious scientific meetings.

## **Investigating all aspects of mitochondrial disease**

MitoCanada funded researchers continue to set a standard that offers hope to Canadians currently living with the disease and their families. Although research progress may seem to move slowly, we know that with each new discovery made we are that much closer to solving the mystery of mitochondria disease.

The following are the 2015 recipients of the MitoCanada Foundation's Research Grants.

*Using a novel and unique assay to screen small compound libraries for drug candidates to enhance mitochondrial function by improving ubiquinone-dependent respiratory chain function*

Siegfried Hekimi Department of Biology, McGill University, Montreal, Canada

*Exome & RNA sequencing as a molecular diagnostic tool for Infantile Mitochondrial Diseases; integration of effective computational strategy and functional analysis to characterize pathogenicity of variants in both mitochondrial DNA and nuclear genes encoding mitochondrial proteins*

Eric A. Shoubridge (Montreal Neurological Institute, McGill University, Montreal, Canada), Isabelle Thiffault (Children's Mercy Hospital, Kansas City Missouri, USA), Geneviève Bernard (Montreal Children's Hospital Research Institute, McGill University, Montreal, Canada)

Previously Mito-Canada funded researchers who have demonstrated recent successes are:

MacNeil, L.G., Gillen, J.B., Gibala, M.J., Potter, M.A., Tarnopolsky, M.A. (2015) *Short-term storage of intact skeletal muscle for measurement of mitochondrial function by HRR identifies varied alteration to the complexes of the electrontransport chain.*

MacNeil, L.G., Potter, M.A., Tarnopolsky, M.A. (2015) *Rotenone-elevated mitochondrial respiration with inflammatory myopathies indicates a secondary impairment to NADH: ubiquinone oxidoreductase that attenuates succinate dehydrogenase activity. Frozen versus fresh: What type of muscle sample works the best for the diagnosis of mitochondrial disease in a clinical laboratory?*

# About the MitoCanada Foundation

MitoCanada is Canada's only patient advocacy organization for mitochondrial disease, dysfunction and mito-health in general. Active in communities across country, MitoCanada offers patient support and programs, research funding, public education and awareness campaigns, and advocacy. We rely on individual and corporate support, communities and health-care partners to help us carry out our work.

## **In pursuit of a cure**

Since 2011, the MitoCanada Foundation has proudly supported mitochondrial disease research in Canada, administering more than a half million dollars in research grants, awards, and partnerships.

## **We are Canada's resource for support, information and education**

For people with mitochondrial disease, their caregivers and family, we provide support, information and education programs. For health-care providers, we provide information and resources to encourage early diagnosis and support individuals and their families throughout the continuum of the disease.

## **The MitoCanada Foundation advocates for change nationally and internationally**

Our goal is to collaborate with industry, health system decision-makers, the research community and governments in order to improve the quality of life for people living with mitochondrial disease. We work collectively with the international community to make mitochondrial disease a global health priority, raise awareness and increase investments in research.

## MitoCanada Foundation

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