CENTOGENE

THE RARE DISEASE COMPANY

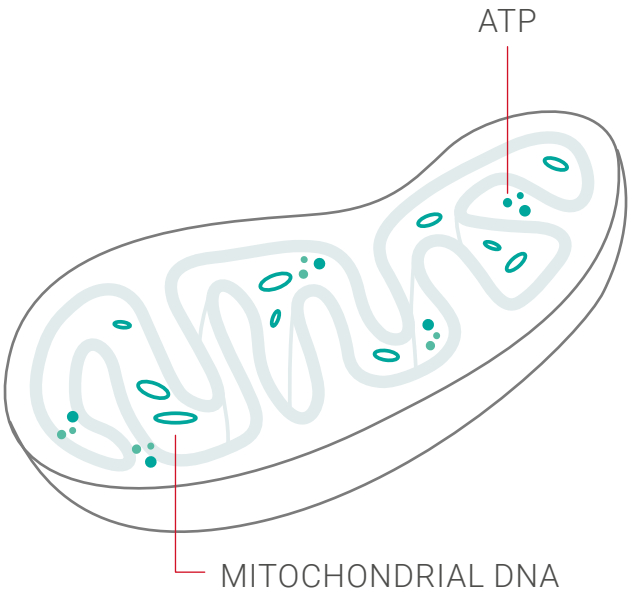
CentoMito

Mitochondrial Disease Testing

Working together…

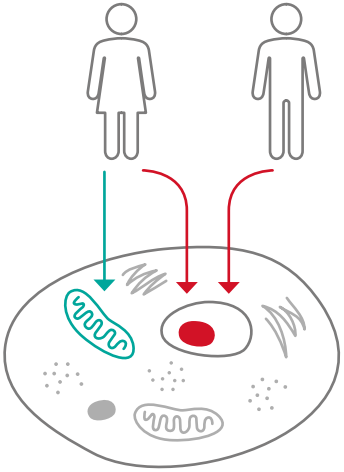
What are Mitochondria?

Every cell in the body has small structures called mitochondria that act as “powerhouses”. Mitochondria are responsible for producing almost 90 % of the energy (in the form of ATP molecules) needed by cells via respiration and also regulate cellular metabolism. Cells contain hundreds of mitochondria, and each mitochondrion contains several copies of mitochondrial DNA, which contains the information for making mitochondrial proteins. Cells that require more energy tend to have more mitochondria (eg. brain, muscles, heart).



Mitochondrial Disease and Inheritance

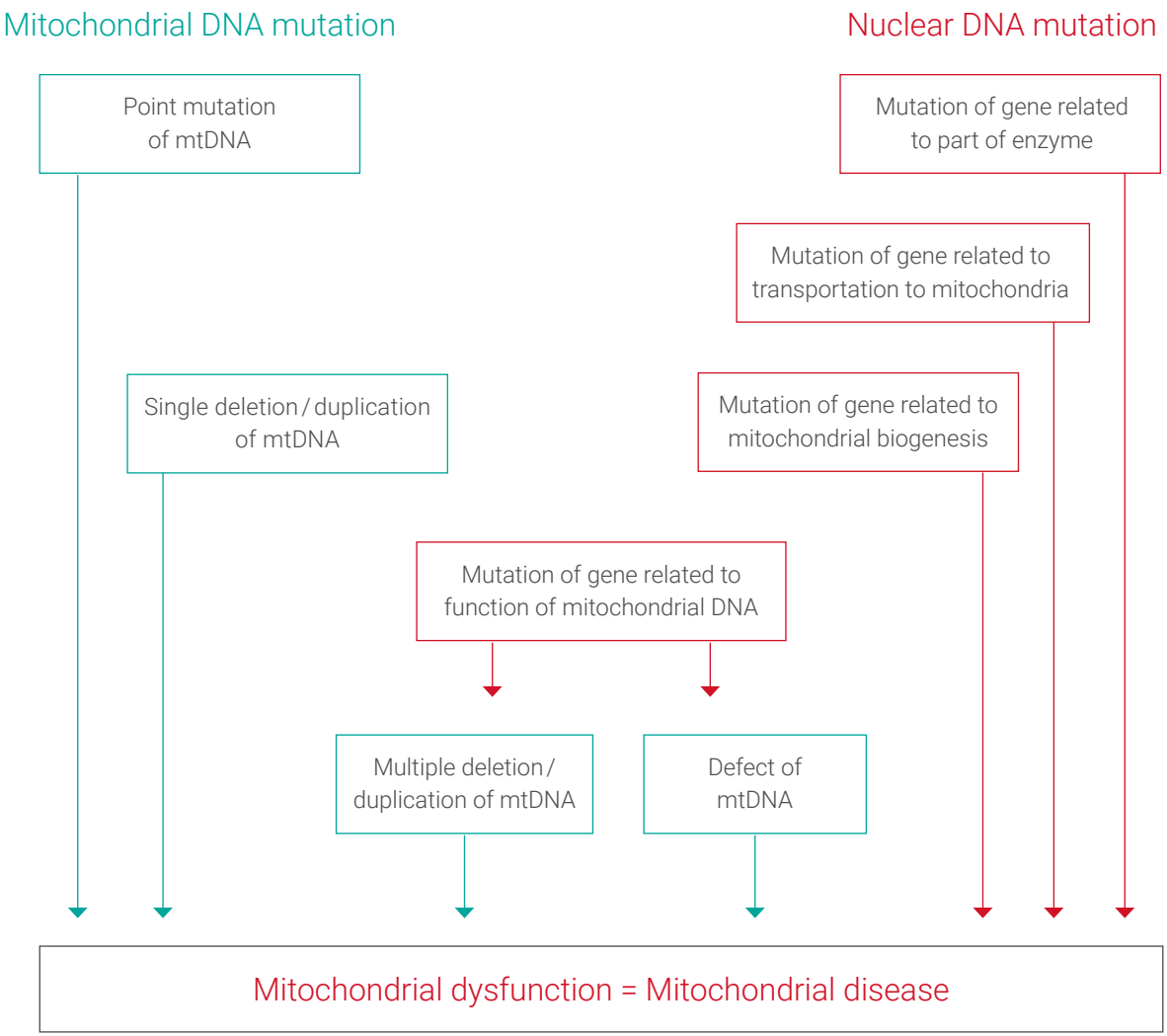
Mitochondrial disorders affect 1 in 4,000 people and occur when mitochondria fail to produce enough energy for the cell's requirements. Mitochondrial failure causes cell death and can turn in organ failure if many of the cells in any organ die. They can be caused by genetic mutations in the mitochondrial genome or in nuclear genes encoding proteins that function inside mitochondria.



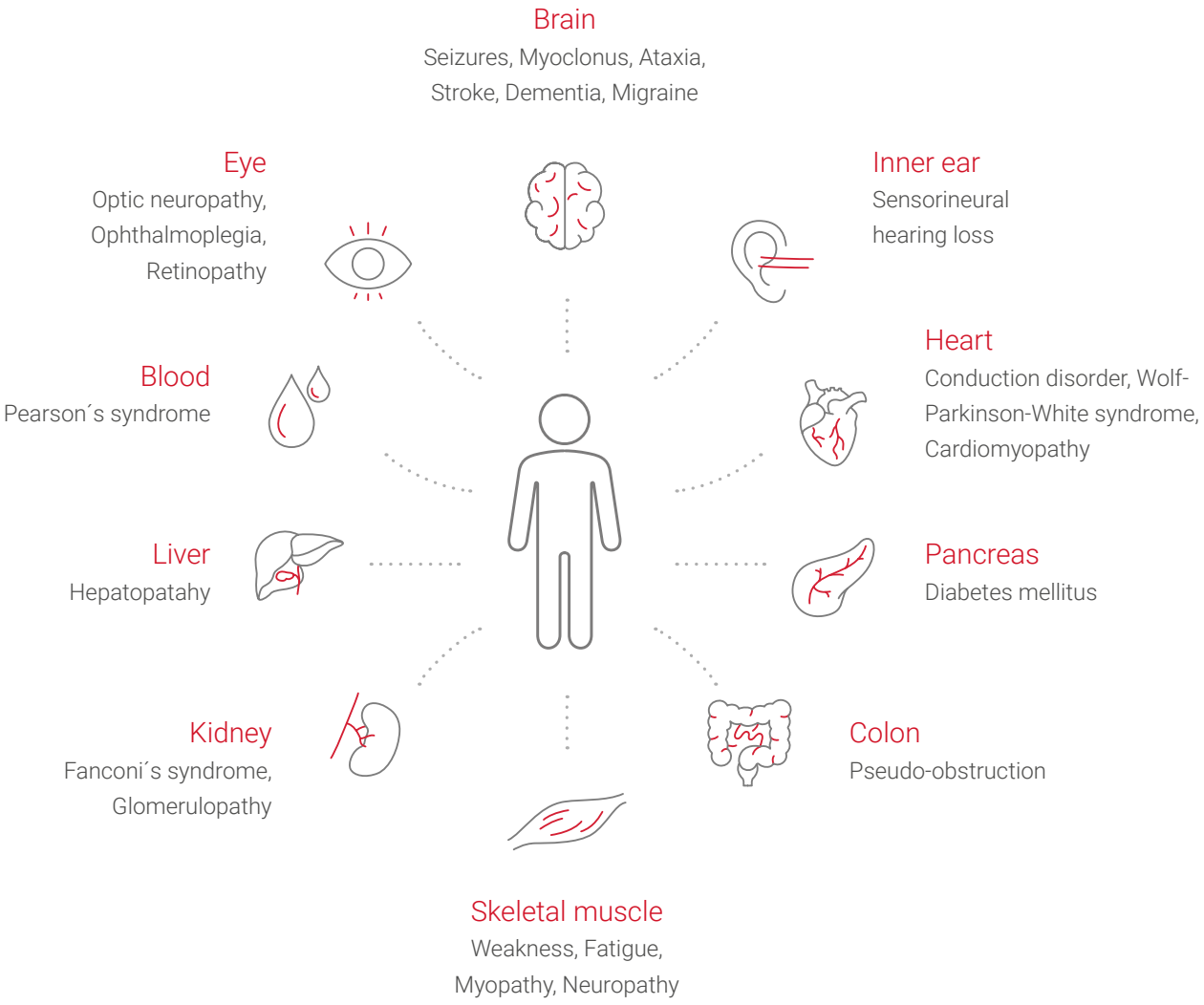
When different mutations are present in all mitochondria in the same organism, this state is called 'homoplasmy' and when it is present in some mitochondria but not others, it's called 'heteroplasmy'. We use complex new techniques able to identify levels of heteroplasmy in the patients affected with mitochondrial disorders.

Mitochondrial mutations are only transmitted through the mother while nuclear gene mutations are inherited from either parent or both parents. Changes in either the mitochondrial or nuclear DNA instructions for making proteins can lead to very similar disease symptoms. Diseases caused by nuclear genes are predominantly inherited from both parents in an autosomal recessive way, whereas diseases caused by mitochondrial genes can only be inherited from the mother.

Causes of Mitochondrial Disorders



mtDNA = Mitochondrial DNA


Brain
Seizures, Myoclonus, Ataxia,
Stroke, Dementia, Migraine
Eye
Optic neuropathy,
Ophthalmoplegia,
Retinopathy
Inner ear
Sensorineural
hearing loss
Blood
Pearson´s syndrome
Heart
Conduction disorder, Wolf-
Parkinson-White syndrome,
Cardiomyopathy
Liver
Hepatopatahy
Pancreas
Diabetes mellitus
Kidney
Fanconi´s syndrome,
Glomerulopathy
Colon
Pseudo-obstruction
Skeletal muscle
Weakness, Fatigue,
Myopathy, Neuropathy

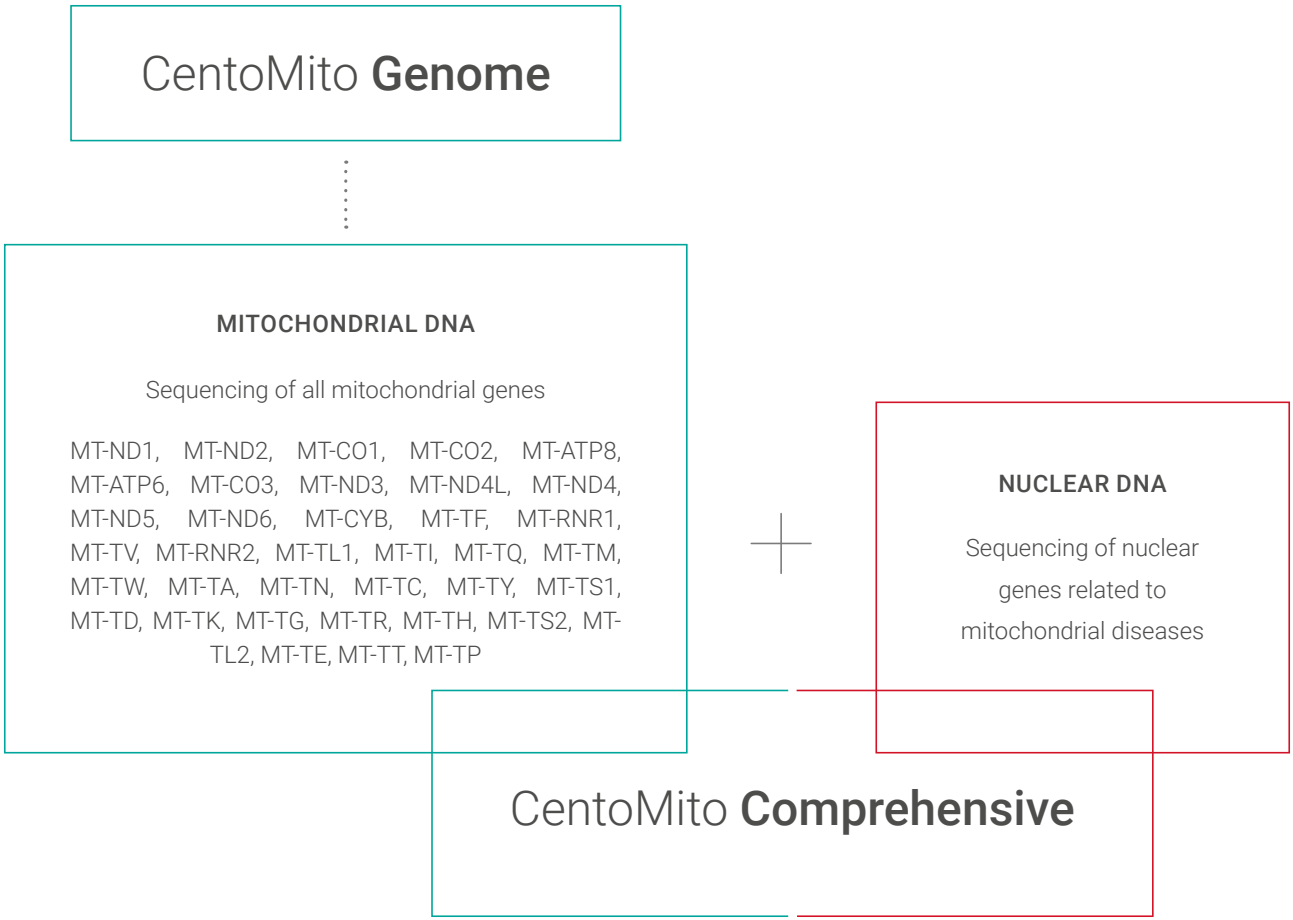
Symptoms of Mitochondrial Disorders

Mitochondrial disorders occur when mitochondria do not function properly, resulting in low or no energy production in cells. As all cells require energy for growth, maintenance and performing their respective functions, this dysfunction leads to multisystemic disease and various organs in the body are affected. The major symptoms caused by mitochondrial dysfunction are described below.

Who Should be Tested for Mitochondrial Diseases?

- Individuals with clinical symptoms characteristic of a specific mitochondrial disorder
- Individuals with any progressive multisystem disorder of unknown etiology
- Individuals with multiple complex neurologic features or a single neurological symptom with other system involvement
- Children presenting with lactic acidosis

Testing at CENTOGENE for Mitochondrial Disorders



CentoMito Comprehensive

COMMON SYNDROMES AND DISORDERS COVERED	Chronic progressive external ophthalmoplegia, Kearns-Sayre syndrome, Leigh's syndrome and maternally inherited, Leigh's syndrome, Mitochondrial disorders, Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes, Myoclonus epilepsy with ragged red fibers, Myogastrointestinal encephalomyopathy, NARP, Neonatal mitochondrial hepatopathies, Pearson syndrome
COVERAGE	• Nuclear genes: ≥ 99.0 % covered ≥ 20 x • Detection of heteroplasmy ≥ 15 %
TAT	25 business days
SAMPLE REQUIREMENTS	CentoCard®, EDTA-blood, ready to use DNA and buccal swab

CentoMito Genome

COMMON SYNDROMES AND DISORDERS COVERED	Chronic progressive external ophthalmoplegia, Kearns-Sayre syndrome, Leber hereditary optic neuropathy, Leighlike syndrome, Leigh syndrome, Mitochondrial disorders, NARP
COVERAGE	• Nuclear genes: ≥ 97.0 % covered ≥ 200 x • Detection of heteroplasmy ≥ 5 %
TAT	25 business days
SAMPLE REQUIREMENTS	CentoCard®, EDTA-blood, ready to use DNA and buccal swab

The CENTOGENE Advantage

OUR DIAGNOSTIC SERVICES ARE MORE THAN LABORATORY AND BIOINFORMATICS.

CentoCard®

Our quick, cost-effective, and hassle-free solution for shipment of clinical blood samples for genetic testing. CentoCard provides a single sample for complete patient diagnostics: enzyme assay, biomarker analysis, and genetic testing.

Extended Phenotyping

Structuring your patient's symptoms into Human Phenotype Ontology (HPO) terms ensures the best quality of clinical information for data interpretation.

Data Safety and Research Use

With transparent and easy-to-understand consent forms, your patients can make educated decisions without worrying about data protection. By consenting to the research and storage option, you and your patients will advance research, the understanding of rare diseases, and the quality of future diagnoses and therapies.

Multiomics Testing

We have pioneered a multiomic testing strategy – combining panel technology with biochemical testing. By starting out with a complete clinical picture, you can now direct patients to the most precise diagnosis and potential treatment options.

CentoPortal®

Our user-friendly and fully-secure online service www.centoportal.com is designed to assist in ordering tests, transferring patient data, administering patient's samples, and accessing your diagnostic reports 24/7.

The CENTOGENE Biodatabank

The world's largest real-world data repository for rare and neurodegenerative diseases.

Clinical Studies and Pharma Partnerships

By participating in clinical studies, your patients benefit as they foster the development of new therapies and improved monitoring. Through pharmaceutical partnerships, we also leverage our expertise to speed up drug development in rare diseases.

World-Class Expertise

At CENTOGENE, we connect patients around the world to empower innovative solutions for the global rare disease community. With our unique expertise in rare disease diagnostics and insights from over half a million patients, we provide answers today so that your patients can have a better tomorrow.

... for a patients' better tomorrow.

FOR ORDERING

www.centoportal.com

FOR MORE INFORMATION

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