Assess the mtDNA mutation load in mesoangioblasts of mtDNA mutation carriers

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON42480

Source
ToetsingOnline

Brief title
mtDNA mutation load analysis MABs

Condition

- Metabolic and nutritional disorders congenital
- Muscle disorders
- Neuromuscular disorders

Synonym
mitochondrial myopathy; mitochondrial muscle disease

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: ZonMW,Prinses Beatrixfonds;Metakids;Ride4Kids

Intervention

Keyword: mesoangioblasts, mitochondrial myopathy, mtDNA

Outcome measures

Primary outcome

mtDNA mutation load in single MABs and skeletal muscle

Secondary outcome

mtDNA copy number in MABs

OXPHOS capacity in MABs

Proliferation capacity MABs

Myogenic differentiation capacity of MABs

Study description

Background summary

Mitochondrial diseases caused by defects in oxidative phosphorylation (OXPHOS) due to heteroplasmic mitochondrial DNA (mtDNA) mutations are rare (frequency 1/5,000), but severe multisystem disorders. Clinical manifestations are highly variable, but predominantly affect energy demanding tissues, like brain and muscle. Myopathy is a common feature of mtDNA disorders, being present in more than 50% of the mtDNA mutation carriers, and seriously affects patients* general well-being and quality of life. Currently, no treatment is available for these patients, although the induction of muscle regeneration by exercise treatment has been shown to alleviate the myopathy in patients. This implies that the patients can produce muscle fibres, which perform better, most likely because the mutation load is lower. This is based on the activation of myogenic precursor cells, called satellite cells, with a very low or absent mtDNA mutation load in these patients. In recent years, other myogenic precursors termed mesoangioblasts have been recognized as a source for development of a systemic myogenic stem-cell therapy and allogeneic transplantation has been successfully applied to mice and dogs with Duchene muscular dystrophy, followed by an ongoing trial in affected boys. For mtDNA diseases autologous stem-cell

therapy could be feasible to treat myopathy, if mtDNA disease patients would produce mesoangioblasts without the mtDNA mutation or with a very low mutation load. Therefore, the aim of this project is to determine the mtDNA mutation load in myogenic stem cells (mesoangioblasts) of mtDNA disease patients and identify the patients or mutations for which this is a feasible approach.

Study objective

The primary objectives of this project are to assess the mtDNA mutation load in carriers of a mtDNA mutation and identify patients and/or mutations with with no/low mtDNA mutation load in mesoangioblasts. Secondary objectives aim at determining the proliferation, myogenic differentiation and OXPHOS capacity of mesoangioblasts.

Study design

Monocenter observation study

Study burden and risks

Participation is not result in direct benefit for the participant. The primary benefit of this study will be about a better knowledge on the mtDNA mutation load in mesoangioblasts, which could potentially serve as therapeutic option to ameliorate myopathy in mtDNA mutation carriers for which currently no therapy is available. The risk of complications associated with the muscle biopsy. In some cases, the muscle biopsy can be painful. Infections and bleeding afterwards are possible, but rare

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Adult carriers of a mtDNA mutation in blood >10%

Exclusion criteria

Significant concurrent illness
Pregnant or lactating women
Psychiatric or other disorders likely to impact on informed consent
Patients unable and/or unwilling to comply with treatment and study instructions
Any other factor that in the opinion of the investigator excludes the patient from the study

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped

Start date (anticipated):	01-02-2016
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	14-01-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL55092.078.15