Similar but not the same: Why are specific muscles less susceptible to damage than others in muscular dystrophies?

Published: 15-07-2016
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1. Compare molecular signatures in six leg muscles using RNA-sequencing;2. Correlate these signatures to the muscle involvement pattern in three muscular dystrophies and identify regulators for muscle strength preservation

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON50296

Source
ToetsingOnline

Brief title
MD biopt

Condition

- Musculoskeletal and connective tissue disorders congenital

Synonym
Duchennes disease, Muscular Dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: molecular signature, Muscular dystrophy, Skeletal muscle

Outcome measures

Primary outcome

Correlation of the molecular and cellular profile to the order of muscle

involvement in muscular dystrophies

Secondary outcome

na

Study description

Background summary

Muscular dystrophies (MDs) are characterized by muscle degeneration which starts in specific muscles and spreads to others as the disease progresses. Virtually all MDs lack an effective therapy. The order in which muscles degenerate differs between MDs. The reason for the disease-specific involvement pattern is unknown and the pathophysiology of the muscle degeneration process is incompletely understood. Elucidation of this phenomenon could hold the key for the development of new therapies, by stimulating protective characteristics in early involved muscles to resemble those in preserved muscles.
We hypothesize that differences in the molecular constitution of muscles significantly explain differential involvement of skeletal muscles in MDs. This constitution can be identified using molecular approaches by generating reference profiles in healthy subjects. Assessment in healthy muscle is essential as in diseased muscle, tissue changes due to the disease will mask the constitutive differences between muscles.

Study objective

1. Compare molecular signatures in six leg muscles using RNA-sequencing;
2. Correlate these signatures to the muscle involvement pattern in three muscular dystrophies and identify regulators for muscle strength preservation

Study design

Proof of concept
Three percutaneous muscle biopsies, two muscles sampled directly from the graft and one using a incision needed for ACL surgery, all performed during the surgery procedure and in the surgical area

Study burden and risks

In this study, biopsies will be taken from six muscles during surgery of the knee. As the material from two of these muscles, the Gracilis and Semitendinosus, is directly from the graft they will pose no extra burden. The other five muscles, the Gastrocnemius Medialis and Lateralis, and Biceps Femoris Short Head, Vastus Lateralis and Rectus Femoris, are in the direct vicinity of the operational area. As biopsies will be performed using a percutaneous biopsy with a minimally invasive biopsy needle, will pose a minimal extra burden on the participants. A short questionnaire about athletic activity and the presence of exclusion criteria will be filled out prior to participation, which will cost extra time for the patients.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
LEIDEN 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
LEIDEN 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients undergoing reconstructive surgery of the ACL using hamstrings autografts who are:
- Between 18-30 years old
- Of average athletic fitness (exercise up to three times a week)

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Age < 18 and > 30 years
- No informed consent
- Comorbidity: any muscle disease, neurological disorders (stroke, M. Parkinson, dementia), rheumatoid arthritis, polymyalgia rheumatica, heart failure, COPD
(Gold III-IV), chronic pain syndrome (fibromyalgia, complex regional pain syndrome etc)
- Metabolic diseases (e.g. insuline dependent DM)
- Cancer
- Medication: immunosuppressive drugs (e.g. prednisone, methotrexat, biologicals (TNF-alpha antagonists etc))
- Severe muscle atrophy as judged by standard pre-operation MRI
- pregnancy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-01-2017
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	15-07-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	23-09-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	17-02-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	08-11-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	06-02-2019

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	26-10-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	04-07-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL54081.098.16

Study results

Date completed:	01-05-2021
Actual enrolment:	27

Summary results

Trial is onging in other countries