Exome sequencing of consanguineous couples 1: Proof of principle

Published: 29-08-2012
Last updated: 26-04-2024

The objective of the study is to show that it is in principle possible to diagnose carriership of both partners of a couple by means of exome sequencing (proof of principle)

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational invasive

Summary

ID

NL-OMON37790

Source
ToetsingOnline

Brief title
ExSeqCons

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
carriers of autosomal recessive disease alleles

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Consanguinity, Exome sequencing, Proof of principle

Outcome measures

Primary outcome

The primary study parameter will be the diagnosis, by the 'blinded' laboratory,

of carriership of both parents for the disorder of thier child.

Secondary outcome

Potentially we will find carriership of another recessive disorder, but the

chance to do so is low

Study description

Background summary

Children of conanguineoud parents are, in comparison to children of non-consanguineous parents, at increased risk to have an autosomal recessive condition. This occurs only when both parents are carriers of a mutation in the concerning responsible gene. When both parents are carriers of a mutation is such a gene, each of their children will have 25% chance to develop the concerning disorder; in case they are both carriers of mutations in 2 such genes the risk becomes 44%, and so on. The probability that both parent are carriers is, however, much lower than the chance that they are not both carriers. For first cousin marriages the probability that both partners are carriers is less than 8%. It would be a great relief for consanguineous parents to learn that they are not both carriers, while at the same time finding carriership in both partners of the other couples would increase their possibilities for an informed reproductive choice substantially.

Study objective

The objective of the study is to show that it is in principle possible to diagnose carriership of both partners of a couple by means of exome sequencing (proof of principle)

Study design

Blood samples of both parents of children with an autosomal recessive condition, which is already characterized at DNA level, will be presented for exome sequencing, without information about the disorder in the child, to a

laboratory that was not involved already in the diagnosis in this family. Exome sequancing therefore is performed blindly. If te laboratory succeeds in diagnosing carriership for the concerning disorder in the child, the method can be tried out in future in a prospective study of consanguineous parents who have not (yet) an affected child.

Study burden and risks

Parents are invited to come to the hospital or visited at home. We wil take just one blood sample of each parent. There is a very very small chance of un unsollicited finding.

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

Consanguineous and non-consanguineous couples who have or had a child with an autosomal recessive disorder, whose DNA's (of couple and child) have not been tested before in the laboratory involved in the exome sequencing (in order to guarantee that the testing is performed blindly)

Exclusion criteria

When information on the responsible mutations in the child is lacking

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):	03-12-2012
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	29-08-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL39242.029.12