Gene expression during ciliagenesis: Towards a novel candidate gene list for Primary Ciliary Dyskinesia

Published: 29-07-2013
Last updated: 24-04-2024

We aim to assess gene expression patterns in cilia-producing cells from healthy controls to develop a candidate gene list for PCD.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON40308

Source
ToetsingOnline

Brief title
Gene expression during ciliagenesis.

Condition

- Respiratory disorders congenital
- Respiratory tract infections

Synonym
immotile cilia syndrome, primary ciliary dyskinesia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cell culture, DNA, Gene expression, Primary ciliary dyskinesia

Outcome measures

Primary outcome

Primary endpoints: gene expression levels and pattern.

Secondary outcome

Secondary endpoint: cell culture success rate with brush biopsies.

Study description

Background summary

Primary Ciliary Dyskinesia (PCD) is a hereditary disorder occurring in 1:15.000-30.000 live births, with increased frequency in genetically isolated populations. PCD is characterised by dyskinesia of epithelial cilia causing chronic respiratory disease. Diagnosing patients can be challenging, as there is no gold standard test. Due to the many unknown disease causing gene defects, genetic testing is still not possible in most cases. To this date, our understanding of the molecular composition of cilia is far from complete. Investigating which genes are important in cilia genesis will contribute to a more complete candidate gene list and development of a diagnostic test for Primary Ciliary Dyskinesia.

Study objective

We aim to assess gene expression patterns in cilia-producing cells from healthy controls to develop a candidate gene list for PCD.

Study design

This observational study will be conducted at the VU University Medical Center. Nasal curette and brush biopsies will be performed on healthy volunteers to obtain respiratory epithelial cells. Cells will be cultured and RNA will be isolated at three different time points during cilia genesis. Subsequently, RNA will be enriched for mRNA, fragmented and copied into cDNA. Next generation sequencing of these fragments will show the number of fragments per transcript to obtain an estimate for gene expression levels. Differential gene expression for different time points will be tested and we will asess whether all known

PCD genes show a similar gene expression pattern.

Study burden and risks

Healthy volunteers participating in this study will undergo a nasal curette and brush biopsy to obtain normal functioning respiratory epithelial cells. There are no risks associated with this procedure. The procedure may cause temporary discomfort during the scraping or brushing of the nasal mucous membrane. This resides immediately after the curette or brush is removed. In rare cases, slight and temporary bleeding of the nasal mucosa may occur. This usually only happens when the mucosa is irritated or infected. To minimize this risk, subjects with any respiratory symptoms will be excluded from the study. PCD patients will benefit from the results of this study as a more complete gene candidate list can be developed which will enable genetic testing in the future. In addition, comparing the cell culture success rate of the less invasive brush biopsy, with the rate of the curette biopsy, will indicate its clinical utility.

Contacts

Public
Vrije Universiteit Medisch Centrum

Van der Boechorstraat 7
Amsterdam 1081BT
NL
Scientific
Vrije Universiteit Medisch Centrum

Van der Boechorstraat 7
Amsterdam 1081BT
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* * 18 years of age

Exclusion criteria

* Any signs of upper or lower airway infection
* Coagulation disorders (or any symptoms of easy bruising, heavy bleedings)
* Use of anti-coagulants

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-10-2013
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO

Date:	29-07-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2014
Application type:	Amendment
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	NL43604.029.13
Other	NTR candidate nr 14462