Center for Translational Pediatric Pulmonology
Modelling the bronchial epithelium in children

Published: 19-12-2019
Last updated: 09-04-2024

The main objective of our Center for Translational Pediatric Pulmonology (CTPP) is to establish models of bronchial epithelial function in children, by (1) epithelial organoid cultures derived from bronchial epithelial cells; (2) bronchial brushings...

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

Summary

ID

NL-OMON48628

Source
ToetsingOnline

Brief title
CTPP

Condition

- Respiratory disorders congenital
- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
asthma, cystic fibrosis, wheeze javascript:saveABR('C')

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,TEVA Pharma

Intervention

Keyword: bronchial, epithelium, organoids, single-cell-sequencing

Outcome measures

Primary outcome

• To establish a model of the bronchial epithelium by epithelial organoid cultures derived from the bronchial and nasal brush, as well as bronchial and nasal brushes of the pediatric airways. We will validate these models using comparative RNA seq with matched single cell RNA seq of airway wall biopsies.

Secondary outcome

• Comparative genomics of nasal and bronchial epithelial cells in children. Using gene expression and epigenetic DNA markers of epithelial cells of the upper and lower airways, we will describe which markers of the upper airway (nose) can be used as a valid reflection of the lower airways by validating them against matched single cell RNA seq of airway wall biopsies. We will publish a catalogue of gene expression signatures in children that reflect the bronchial epithelium that can be used by researchers all across the world.

• Establishment of an Epithelial Organoid Repository for mechanistic and interventional pediatric respiratory research.

• To describe the single cell composition of the airway wall in pediatric respiratory disease, including asthma, severe wheeze, and cystic fibrosis (CF). As airway wall biopsies contain 50 - 70 % epithelial cells, this may serve as

an excellent validation of our epithelial organoids and provide more insight

into the cell types and states of pediatric respiratory disease.

Study description

Background summary

Many respiratory diseases, such as asthma, severe preschool wheeze, cystic fibrosis and even low lung function predisposing to COPD, arise in the first years of life. These diseases are the outcome of the interaction of a genetically susceptible host with a permissive environment. Most lung diseases can therefore be conceived as a developmental disease, as these arise in a child with a developing lung and immune system. The bronchial epithelium is a key cell orchestrating the response of the airways and the immune system, and bronchial epithelial cells express many respiratory disease genes.
We hypothesize that curative, early life treatment for lung disease needs to be based on detailed, mechanistic insights into the inception of disease in the bronchial epithelium rather than established disease in adults. To identify these *early mechanisms*, we will need to study children, investigate cells from the bronchial airways, and develop models that reflect bronchial epithelial cell function. However, performing invasive research in children is limited by ethical constraints, so we will need to develop and validate models that do not pose a burden on the child. In contrast to the bronchial epithelium, the nasal epithelium is accessible in young children. However, it is not known how well the upper airway reflects the lower airways in children with different disease conditions.

Study objective

The main objective of our Center for Translational Pediatric Pulmonology (CTPP) is to establish models of bronchial epithelial function in children, by (1) epithelial organoid cultures derived from bronchial epithelial cells; (2) bronchial brushings; and (3) nasal brushings. These models will be validated by comparison of gene expression from epithelial cells of these three models to the gold standard: bronchial (single cell) gene expression in bronchial airway biopsies. Furthermore, this will enable future mechanistic and intervention studies, as it will be known which aspects of the bronchial epithelium will be reflected in nasal cells, and which are retained in epithelial organoid cell culture.

Study design

Observational, cross-sectional cohort study

Study burden and risks

Ethical concerns are highly relevant when performing invasive research in children. We propose to perform research in (young) children, who already undergo bronchoscopy for clinical indications. During bronchoscopy the major risk is that of anesthetics. It has been well documented that risks related to a bronchoscopy (biopsy and brushings) itself are limited to the incidental need for bronchodilators, minor bleeding that always stopped spontaneously, and fever. The main ethical aspect of our project therefore is obtaining (extra) primary bronchial epithelial and nasal cells for research purposes, which will prolong the planned bronchoscopy with 5 - 10 minutes. The benefits of this research will relate to the validation of less or non-invasive methods to study primary and cultured airway epithelial cells in children, which may reduce the need for future invasive studies.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)

Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

children requiring brochoscopy for clinical indications
bronchoscopy will take place during offica hours

Exclusion criteria

children with malignancies requiring bronchoscopy

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-11-2020
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	19-12-2019
Application type:	First submission

Review commission: METC Universitair Medisch Centrum Groningen (Groningen)

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	NL66928.042.19