Investigating immune-epithelial cells in patients with cystic fibrosis

Published: 25-06-2021
Last updated: 04-04-2024

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Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON52014

Source
ToetsingOnline

Brief title
Terrific start up

Condition

- Autoimmune disorders
- Bronchial disorders (excl neoplasms)

Synonym
Cystic fibrosi, Mucoviscidosis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,TAAI

Intervention

Keyword: Cystic fibrosis, Epithelial cells, Immune response

Outcome measures

Primary outcome

Detailed characterization of immune and epithelial cells composition as well as

functional properties in peripheral blood, sputum/BAL and tissue biopsy

samples.

Secondary outcome

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Study description

Background summary

The major focus of cystic fibrosis (CF) research has been on CF transmembrane conductance regulator (CFTR) ion channel dysfunction and how it deregulates epithelial cell biology. The broader role of the immune system in this context has received less attention, despite the importance of cellular crosstalk between epithelial cells and immune cells to regulate each other's function. CF patients suffer from recurring immune cell activation and chronic inflammation, which can have a major impact on epithelial dysfunction and vice versa. We hypothesize that a better understanding of the nature of the chronic inflammation and the epithelial-immune cell dialogue in CF will yield new insights into disease pathophysiology - including leads for new therapeutic interventions.

Study objective

The primary objective of this study is to characterize the immune cell composition and epithelial-immune cell crosstalks in patients with CF. The endpoint will be constituted from several read-outs on peripheral blood mononuclear cells (PBMC's), sputum, bronchoalveolar lavage (BAL) and endobronchial biopsies.

Study design

This is a observational study in patients with CF. During regular out-patient clinic visits, in addition to regular blood and sputum samples as part of standard care, additional blood, sputum and nose brush samples will be collected from included patients once. Additionally, patients will be asked to undergo a bronchoscopy to collect BAL and endobronchial tissue samples. The additional blood, sputum, BAL and endobronchial biopsies will be analyzed by flowcytometry (BD Symphony system with up to 30 protein markers per cell), imaging mass cytometry (Hyperion system with up to 37 protein markers on histological samples) and single cell transcriptomics (10x Genomics 3* v.3.1 mRNA-seq with on average ~5000 genes detected per cell). These multi-dimensional read-outs of the lung tissue microenvironment in CF patients will allow us to construct a cellular atlas of the epithelial and immune cell biology in the CF lung. Patients will be enrolled from the 1st of April 2021 until 1st of April 2025.

Study burden and risks

After informed consent, peripheral blood and sputum will be collected once during routine outpatient visit. Peripheral blood will be collected by means of vena puncture. Vena puncture can cause mild discomfort; the puncture could be experienced as being painful, and a hematoma could result from this procedure. There are no further risks associated with participation.

No risks are associated with sputum collection.

Nose brush collection could cause mild discomfort, which disappears very quickly. No risks are associated with nose brush collection.

Bronchoalveolar lavage (BAL) and endobronchial biopsies will be obtained through bronchoscopy during an additional outpatient visit. Bronchoscopy with lavage and collecting endobronchial biopsies is a well tolerated routine procedure that can be safely performed on a outpatient basis. Adverse events related to bronchoscopy are rare and the lethality is below 0.01%. common adverse events are pneumonia, bleeding, heart arrhythemias and pneumothorax. Although subjects will not have direct benefit from findings in this study, their contribution will be of great value for improving our understanding of the role of the immune system in CF disease pathophysiology. In the future, these insights could lead to the development of new therapies that will benefit CF patients.

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

Patients (18-70 years) diagnosed wit cystic fibrosis
Non-smoking for a minimum of 3 months, including cigarettes, marijuana, cigars, and e-cigarettes/vaping.

Exclusion criteria

Patients with an active or treated malignancy
Patients who underwent a lung transplant

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2021
Enrollment:	45
Type:	Anticipated

Ethics review

Approved WMO Date:	25-06-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-05-2022
Application type:	Amendment
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	NL76489.078.21