Epithelial Ion Transport Defects in Pancreatitis: establishment of an organoid model

Published: 11-02-2022
Last updated: 04-04-2024

Primary: To evaluate the ability to culture PDEC organoids from pancreatic duct biopsies.
Secondary: (i) To evaluate ion transport in PDEC organoids derived from pancreatitis patients. (ii) To evaluate the ability of duodenal organoids to mimic ion...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Exocrine pancreas conditions
Study type	Observational invasive

Summary

ID

NL-OMON52348

Source
ToetsingOnline

Brief title
C-PIE

Condition

- Exocrine pancreas conditions

Synonym
chronic pancreatitis, inflammation of the pancreas

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,Cystic Fibrosis Foundation (CFF)

Intervention

Keyword: Ion Transport, Organoid, Pancreatitis

Outcome measures

Primary outcome

Assess the ability to culture PDEC organoids from pancreatic duct microbiopsies, to study the pathophysiology and pharmacotherapy of pancreatitis in vitro.

Secondary outcome

• Asses the phenotype of PDEC organoids derived from pancreatitis patients, as compared to those derived from non-pancreatitis patients, by investigation of:

o Genetic makeup

o Gene and protein expression

o Ion transport

o Response to known pancreatitis-inducers and/or ion transport modulators, to further elucidate the molecular mechanisms involved in the disruption of CFTR function in PDECs in pancreatitis and potentially to advance the development of pharmacotherapy for pancreatitis.

• Assess the ability of duodenal organoids to mimic key features of ion transport in PDEC organoids, to explore a more readily accessible surrogate model to study the pathophysiology and pharmacotherapy of pancreatitis in vitro.

Study description

Background summary

Pancreatitis is a common cause of hospitalization, with no specific therapy available currently. Dysfunction of the cystic fibrosis transmembrane conductance regulator (CFTR) and/or insufficiency of electrolyte and fluid secretion by pancreatic ductal epithelial cells (PDECs) is associated with pancreatitis. CFTR modulators might increase CFTR levels and/or function in PDECs and may ameliorate pancreatitis. However, current human PDEC model systems have limited success in establishment and expansion and require an invasive sample collection. A human model system to study electrolyte and fluid secretion in pancreatitis patients is missing. We hypothesize that pancreatic duct biopsies can be grown into organoids and expanded long enough to perform short circuit current measurements, and that duodenal organoids can be used as a surrogate model to study CFTR in pancreatitis patients.

Study objective

Primary: To evaluate the ability to culture PDEC organoids from pancreatic duct biopsies. Secondary: (i) To evaluate ion transport in PDEC organoids derived from pancreatitis patients. (ii) To evaluate the ability of duodenal organoids to mimic ion transport in PDEC organoids derived from pancreatitis patients.

Study design

Pancreatic duct and duodenal biopsies will be obtained from pancreatitis patients and grown into organoids, which will be phenotyped and stored in a biobank for further investigation.

Study burden and risks

Patients undergoing pancreatoscopy will receive a single blood collection prior to the procedure. In addition, 2 microbiopsies from the pancreatic duct and 2 biopsies from the duodenum will be taken during the procedure. There is no extra burden, as these patients are undergoing the pancreatoscopy within the framework of regular diagnostics and treatment. The risk of participation is negligible, constituting marginal bleeding of the mucosa.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL
Scientific

Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

A subject must meet all of the following criteria:
- Must be an adult (>18 years old)
- Must be undergoing pancreatoscopy within the framework of regular diagnostics or treatment in the Erasmus MC
- Must sign informed written consent

Exclusion criteria

None

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-06-2022
Enrollment:	9
Type:	Actual

Ethics review

Approved WMO

Date:	11-02-2022
Application type:	First submission
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	NL75856.078.21
Other	NL9772