SINGLE-CELL RNA SEQUENCING OF LYMPHOCYTE SUBSETS AND CHOLANGIOCYTES IN NON-ENDSTAGE PSC PATIENTS

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hepatic and hepatobiliary disorders
Study type	Observational invasive

Summary

ID

NL-OMON51642

Source
ToetsingOnline

Brief title
Single cell RNAseq in PSC (SCRIPT)

Condition

- Hepatic and hepatobiliary disorders

Synonym
Primairy sclerosing cholangitis, PSC

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC

Source(s) of monetary or material Support: PSC partners

Intervention

Keyword: Primary sclerosing cholangitis, Single cell RNA sequencing

Outcome measures

Primary outcome

To characterize the disease specific composition and activity of immune cell subsets and cholangiocytes in active inflammation in the central/extrahepatic bile ducts of PSC patients and *normal* bileduct tissue using surface markers and in-depth transcriptomic analysis.

Secondary outcome

1. To characterize immune cell subsets between peripheral blood of PSC patients and compare these to the bile duct derived subsets in relation to samples taken from *healthy* bileduct epithelium.

2. To align the outcome of this transcriptomic analysis with known drug target genes.

3. To align the outcome of this transcriptome analysis with previously identified inflammatory patterns in the colon of IBD patients with and without PSC

Study description

Background summary

Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease, for which there is currently no therapy that can halt disease progression. PSC is generally regarded as an immune-mediated disease, but disease etiology and pathogenesis is still largely unknown. This is mainly due to the rarity of the

disease and the fact that the diseased tissue is hidden deep in the body. In order to deep-dive into the immune dysregulation that characterizes the chronic inflammation in and the progressive fibrosis around the bile ducts, it is imperative to study the two cell types that presumably play a central role in disease initiation and perpetuation of inflammation: the cholangiocyte as antigen presenting cell, and lymphocyte subsets such as T-lymphocytes and natural killer cells as effector cells. The novel technique of single cell RNA sequencing combined with advanced bioinformatic analysis can yield a myriad of information about development, function, behavior, and interaction of cells in their relevant microenvironment. To this end, tissue must be harvested not from explanted livers, in which the original inflammation has evolved to fibrosis, but from early stage disease patients, in whom the inflammatory process is still ongoing. Using what is known as the *last frontier of endoscopy*, i.e. cholangioscopy, it is possible to gain access to the bile ducts and sample the tissue of interest: the mucosa of the bile duct. Single cell RNA sequencing technology provides a unique opportunity to do comprehensive analysis from the minute amounts of tissue that are obtained through cholangioscopy.

Study objective

The aim of this project is to characterize the composition and activity of lymphocytes immune cell subsets and cholangiocytes in active inflammation in the central/extrahepatic bile ducts through surface markers and an in-depth transcriptomic analysis. Furthermore In addition, immune cell composition lymphocyte subsets in the colon and peripheral blood will be studied and compared to the liver bile duct derived subsets.

Study design

Multi-center, cross-sectional case-control study

Study burden and risks

The is a very limited risk of complications as the biopsies for this study will be taken only when there is also a clinical/diangostic indication for biopsies with the same low-risk technique (spy-bite or transpapillary biopsy) as will be done to exclude malignancy and perform.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

Cases:
- established diagnosis of large duct PSC and concurrent inflammatory bowel disease.
- Patients should be able to give written informed consent
- age >=18 year
- Child-Pugh-Turcott score <7
- Clinical indication for ERC, i.e. progressive complaints together with increase in biochemical cholestasis or suspicion of malignancy.
- Thickened bile duct wall at the location of interest as evidenced by dedicated ultrasound or MRC.

Controls:
- A suspected diagnosis of (peri)hilar cholangiocarcinoma
- Clinical indication for ERC, i.e. cholestatic itch, pre-operative drainage
- Patients should be able to give written informed consent

- Age >=18 year

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

Cases:
- signs of bacterial cholangitis
- mandatory anticoagulation

Controls:
- signs of bacterial cholangitis
- mandatory anticoagulation

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):	07-02-2023
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	09-01-2023
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-10-2024
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	NL80240.018.22