In depth characterization of the mucosal microbiota in patients with IBD using novel, potent high-throughput approaches and their interaction with the immune system

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON36766

Source
ToetsingOnline

Brief title
Microbiota and immune cells in IBD

Condition

- Gastrointestinal inflammatory conditions
- Autoimmune disorders

Synonym
Crohn's disease, Inflammatory Bowel Disease, Ulcerative Colitis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Broad Foundation

Intervention

Keyword: Crohn's disease, HITChip, Intestinal mucosa, Microbiota

Outcome measures

Primary outcome

- Nature and transmural spatial distribution of the enteric microbiota in IBD

patients.

- Changes in mucosal microbiota of the sigmoid in IBD after diverting ostomy.

- Phenotype and characterise the immune cells involved in IBD.

Secondary outcome

- Presence of microbial DNA in granuloma*s of CD patients.

- Assessment of co-localisation and signalling between invading microbes,

lamina propria macrophages dendritic cells and adaptive and innate immune cells.

- Alterations of phagosome maturation and autophagy, as well as apoptosis of

mucosal macrophages and dendritic cells in IBD.

Study description

Background summary

Inflammatory bowel disease (IBD) consists of Crohn*s disease (CD) and ulcerative colitis (UC). Patients suffer from chronic intestinal inflammation leading to bloody diarrhea, weight loss and fatigue. The current prevailing hypothesis states that the pathogenesis involves an inappropriate and ongoing activation of the mucosal immune system driven by the intestinal microbiota in a genetically predisposed individual. However, it is not known which constituents of the microbiota and which components of the innate and adaptive

immune response are involved. The human microbiota forms a highly complex ecosystem with its host and may comprise more than 1800 phylotypes. We hypothesize that the perturbed interplay between certain constituents of the microbiota and the host is caused by invading organisms, which after crossing the epithelial barrier, are capable of initiating and/or persisting an activated immune response. The clearing of certain microbiota might be impaired by dysfunctioning of the intestinal housekeeping cells. This dysfunction may be due to either interaction of invading microorganisms with these housekeeping cells, or, alternatively, by inhibitory signalling of these cells by other immune cells The delicate balance between pro- and anti-inflammatory cells in the intestinal lamina propria is therefore disturbed and this may result in IBD. Different types of immune cells produce cytokines involved in inflammation in the intestine, including both adaptive and innate immune cells. When the role and interaction of microbiota and immune cells is elucidated, new therapeutic strategies can be investigated for improvement of the care for IBD patients.

Study objective

The aim of our project is in-depth characterization of the microbiota components both adjacent to and within the mucosa in patients with IBD, by applying novel high-throughput analysis technology in a global description strategy approach. Furthermore, we aim to assess the interaction between invading microorganisms, local housekeeping cells and the adaptive and innate immune system in the intestine.

Study design

This is an exploratory global description approach with a subsequent hypothesis-driven part.

Study burden and risks

Since this is an exploratory global description study there is no risk of participation in this study for most of the patients. Blood is obtained during routine laboratory control, with a negligible risk of haematoma.
In patients who are scheduled for ostomy a minimal risk of perforation or bleeding exists due to endoscopy.
Only resection material which is not used for routine histology of the specimen is investigated, thus no diagnostic procedures are hampered by this study.
There is no direct potential benefit for patients participating in this protocol. However, this project may generate important data regarding the disturbed interplay of the microbiota with the innate immunity in IBD, which will increase our understanding of this chronic debilitating conditions and may lead to designing new therapeutic strategies.

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

*18 year old male or female, able to give informed consent
Established Crohn*s disease or ulcerative colitis (according to the Lennard-Jones criteria), or patients scheduled for diverting ostomy due to IBD.
control patients: patients who undergo intestinal resection due to a gastrointestinal malignancy

Exclusion criteria

Ischemia of the bowel
Positive stool cultures or parasite tests for common enteric pathogens (with exeption of non pathogenic parasites such as Blastocystis hominis or Endolimax nana)

Use of Antiobiotics in preceding 4 weeks
use of probiotics in preceding 8 weeks

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:	Recruitment stopped
Start date (anticipated):	11-11-2011
Enrollment:	88
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
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	NL34133.018.10