Inflammatory bowel disease associated genotypes and their immunological phenotype in periheral blood leukocytes of patients

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The aim of this project is to assess differential responses in immune cells derived from peripheral bloodof IBD patients concerning:Immunological phenotype in CD patients:1. defining the genotype in CD patient cohort2. production of interleukin-8...

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

Summary

ID

NL-OMON33711

Source
ToetsingOnline

Brief title
NVT

Condition

- Gastrointestinal inflammatory conditions

Synonym
Chronic Intestinal Inflammation, Crohn's Disease and Ulcerative Colitis), IBD

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Zonmw

Intervention

Keyword: Crohn's Disease, Genetic Susceptibility, Immunology, Pathogenesis

Outcome measures

Primary outcome

nvt

Secondary outcome

nvt

Study description

Background summary

Inflammatory bowel disease (IBD) is comprised of two major disorders: ulcerative colitis (UC) and Crohn's disease (CD). UC affects the colon, whereas CD can involve any component of the gastrointestinal tract from the oral cavity to the anus. It is commonly recognized that the disease that we currently mark as IBD is rather a group of diseases with 5 or more marked pathogenetic pathways, each requiring different therapeutic approaches.
In normal healthy individuals the immune response to commensals in the intestine is kept under strict regulation. When these regulatory mechanisms fail, an inflammatory response in the intestines can result in IBD. What has become clear from research in the last years is that it is a complex genetic as well as immunological disease. Antigens in the lumen of the gut initiate an inadequate immune response in a genetic susceptible host. In the last few years enormous progress has been made on the genetic field by identifying new susceptibility loci in genome wide association studies. The current grant proposal is based on the recently identified Crohn*s associated genes NOD2, IL23R and ATG16L1 and their function within several yet unidentified cellular pathways. As there is still little

known about these pathways questions regarding these functions rise and will be addressed in this
project. As such, the objectives of this project are (1) to link CD immunological phenotypes to cellular
pathways and thereby create insight in the pathogenesis of CD and (2) to associate the immunological
phenotype to the clinical phenotype and associated genotypes known from our data stored in our
extensive IBD database consisting of 1400 IBD patients and 1500 healthy controls.
In this translational study we will use an immunological approach to determine the different pathways. By
means of inventarisation of immunological phenotype and correlation of this phenotype to the genotype,
patients and healthy controls will be included. All subjects included will be subjected to various ex vivo
assays that assess: (1)genotyping of newly identified associated genes,(2) production of cytokines and
chemokines,(3) phagocytosis and oxidative burst,(4)sensitivity to apoptosis and (5) killing of microbes.
The proposed studies may provide more knowledge on the variety of functional pathways in the different
IBD phenotypes and thereby maybe create a new insight in the pathogenesis of IBD.

Study objective

The aim of this project is to assess differential responses in immune cells derived from peripheral blood
of IBD patients concerning:
Immunological phenotype in CD patients:
1. defining the genotype in CD patient cohort
2. production of interleukin-8 after c5a stimulation
3. production of key cytokines after CD3/CD28 stimulation
4. phagocytosis and oxidative burst by granulocytes
Correlation of genotype to immunological phenotype:
5. sensitivity to apoptosis of monocytes and DC's
6. killing of microbes by monocytes and macrophages
Next, the differential responses, that we call the immunological phenotype will be correlated with the
known CD associated genotypes. We expect that we can group several associated genotypes in distinct
pathways that give rise to the specific immunological phenotype. In addition the immunological
phenotype can be correlated with the clinical phenotype by means of the data gathered during clinical

care in our IBD database.

Study design

objective study

Study burden and risks

minimal

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

objectively diagnosed IBD patients

Exclusion criteria

no IBD patient/ <18 years

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):	01-01-2009
Enrollment:	500
Type:	Anticipated

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	NL25781.018.08