IBD geassocieerde genotypes en hun immunologische fenotype in perifere bloed leukocyten

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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...

Ethische beoordeling	Goedgekeurd WMO
Status	Werving nog niet gestart
Type aandoening	Maagdarmstelselontstekingsaandoeningen
Onderzoekstype	Observationeel onderzoek, met invasieve metingen

Samenvatting

ID

NL-OMON33711

Bron
ToetsingOnline

Verkorte titel
IBD en immunologisch fenotype

Aandoening

- Maagdarmstelselontstekingsaandoeningen

Synoniemen aandoening
(ziekte van Crohn en Colitis Ulcerosa), chronische darmaandoeningen, IBD

Betreft onderzoek met
Mensen

Ondersteuning

Primaire sponsor: Academisch Medisch Centrum
Overige ondersteuning: Zonmw

Onderzoeksproduct en/of interventie

Trefwoord: Genetische aanleg, Immunologie, Pathogenese, Ziekte van Crohn

Uitkomstmaten

Primaire uitkomstmaten

niet van toepassing

Secundaire uitkomstmaten

niet van toepassing

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

observationeel onderzoek

Inschatting van belasting en risico

minimaal

Contactpersonen

Publiek

Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL

Wetenschappelijk

Academisch Medisch Centrum

Meibergdreef 9
1105 AZ Amsterdam
NL

Locaties

Landen waar het onderzoek wordt uitgevoerd

Netherlands

Deelname eisen

Leeftijd
Volwassenen (18-64 jaar)
65 jaar en ouder

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

het hebben van een objectief gediagnosticeerde vorm van IBD

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

geen IBD patient/ jonger dan 18 jaar

Onderzoeksopzet

Opzet

Type: Observationeel onderzoek, met invasieve metingen

Blindering:	Open / niet geblindeerd
Controle:	Geen controle groep
Doel:	Algemeen wetenschappelijk

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-01-2009
Aantal proefpersonen:	500
Type:	Verwachte startdatum

Ethische beoordeling

Goedgekeurd WMO

Soort:	Eerste indiening
Toetsingscommissie:	METC Amsterdam UMC

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
CCMO	NL25781.018.08