Impaired regulation of Toll-like receptor-2 mediated T helper type 1 responses in NOD2/CARD15 deficient Crohn*s disease patients

Published: 28-04-2006
Last updated: 14-05-2024

Aim:With this study we would like to prove that also in humans, NOD2 signaling inhibits the TLR2-mediated immune response.

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

Summary

ID

NL-OMON30051

Source
ToetsingOnline

Brief title
Regulation of TLR-responses

Condition

- Gastrointestinal inflammatory conditions

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Inflammatory Bowel Disease, monocytes, NOD2, Toll-like receptors

Outcome measures

Primary outcome

Levels of cytokine production, mRNA expression and NFkB activation as a

response to stimulation with the different stimuli.

Secondary outcome

N/A

Study description

Background summary

NOD2 is an intracellular receptor for the bacterial product MDP. Mutations in the CARD15 gene, coding for NOD2, lead to in increased risk for developing Crohn's disease, however, the mechanism responsible for this is not fully understood yet. Recently, it has been shown in mice, that simultaneous activation of NOD2 and Toll-like Receptor (TLR) 2 lead to a less strong immune response that TLR2 activation alone.

Hypothesis: In Crohn's disease patients with CARD15/NOD2 deficiencies, NOD2 signaling is altered, leading to a loss of the inhibition of TLR2-mediated immune responses.

Study objective

Aim:
With this study we would like to prove that also in humans, NOD2 signaling inhibits the TLR2-mediated immune response.

Study design

Procedure:
-Drawing of 50 ml venous blood in heparinized tubes
-Isolation of monocytes with densit gradients
-Culture and stimualtion of the cells
-Harvesting of supernatants, isolation of nuclear extracts

-Measuring cytokine production, NF-kB activation with ELISAs, measuring mRNA levels with qPCR

Study burden and risks

Drawing of blood can lead to a bruise and in some cases some tenderness. No other risks are involved in this study. For the study, blood is only drawn once, therefore, the burden for the patients can be scaled as *minimal*.

Contacts

Public
Vrije Universiteit Medisch Centrum

Van der Boechorststraat 7
1081BT Amsterdam
Nederland
Scientific
Vrije Universiteit Medisch Centrum

Van der Boechorststraat 7
1081BT Amsterdam
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patient with Crohn's disease

at least 18 years of age
known NOD2/CARD15 genotype

Exclusion criteria

severe anaemia

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:	Pending
Start date (anticipated):	15-03-2006
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	28-04-2006
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	NL11534.029.06