De rol van de slijmvliezen bij het ontstaan van auto-antistoffen in reumatoïde artritis

No registrations found.

Ethical review	Positive opinion
Status	Suspended
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON23860

Source
NTR

Brief title
MUCOSA

Health condition

Rheumatoid arthritis

Sponsors and support

Primary sponsor: No direct sponsoring of this trail
Source(s) of monetary or material Support: Study clinician is funded by a MD/PhD grant of the directory board of the LUMC, the principal investigator is supported by the Target to B-consortium, directed by topsector Health Holland

Intervention

Outcome measures

Primary outcome

The main study parameter investigated will be the detection of several RA associated anti-

modified protein antibodies (AMPA) and their specific characteristics in feces, saliva and sputum of patients and healthy controls. This will be compared to the autoantibody profile in serum for each subject. Among the distinct antibody features that will be explored are isotype usage, fine-specificity, glycosylation of Fc-and Fab-region, avidity and affinity.

Secondary outcome

The presence and characteristics of other biomarkers reflecting the mucosal immune response in feces, saliva and sputum of patients with RA and healthy controls will be assessed. These biomarkers include the presence of (anti-) inflammatory cytokines and chemokines and the structure and origin of post-translationally modified antigens as determined by mass spectrometry. In the future we also might investigate microbiome composition in collaboration with other centres.

Study description

Background summary

Rationale: A subset of rheumatoid arthritis (RA) patients harbour antibodies against several post-translational modifications and are frequently positive for rheumatoid factor. The exact pathophysiology of the development of the autoantibody response and of RA remains unknown. Investigations into genetic and environmental risk factors and systemic immune dysregulation have led to the hypothesis that the mucosal surfaces might be involved in the pathogenesis of seropositive RA. It is proposed that tolerance against post-translational modifications is broken at the mucosa, inducing an cascade leading to a systemic inflammatory response and clinical disease.

Objective: We aim to perform an in-depth investigation into the role of the mucosal immune response in the pathogenesis of rheumatoid arthritis. Our objectives are to study the presence of RA-specific autoantibodies and several other biomarkers (cytokines, antigens and microbiome) in mucosal fluids of RA-patients.

Study design: At the rheumatology department of the LUMC a cross-sectional study will be performed in which peripheral blood, feces, saliva and sputum (optional) from patients with rheumatoid arthritis and healthy controls are collected and several clinical (patient) characteristics will be recorded. (Due to the covid-19 pandemic no sputum will be collected at the moment)

Study population: Patients older than 18 years with a definite diagnosis of rheumatoid arthritis according to the ACR/EULAR 2010 criteria, and healthy controls without inflammatory arthritis, are eligible provided that they meet the inclusion criteria and no exclusion criteria.

Main study parameters: The detection of several RA associated antibodies and their distinct antibody features in feces, saliva and sputum of patients. This will be compared to the

autoantibody profile in serum. Among the distinct antibody features that will be explored are isotype usage, fine-specificity, glycosylation of Fc- and Fab-region, avidity and affinity.

Nature and extent of the burden and risks associated with participation and benefit: Participant will need to self-collect feces. Saliva is collected by the passive drooling method. Blood sampling will be performed at the central blood draw facility of the LUMC and a questionnaire will be used to collect clinical parameters. If participants give additional consent for sputum donation, sputum induction will take place using a disposable device, the LungFlute®, through which they have to breath out several times. The risks of this study are limited to the collection of peripheral venous blood and sputum. Any symptoms caused by blood sampling or sputum induction are usually mild and symptoms will recover fully and spontaneously. The participants do not benefit from this study, but their participation could lead to improved future therapeutic care for RA patients.

Study objective

A subset of rheumatoid arthritis (RA) patients harbour antibodies against several post-translational modifications and are frequently positive for rheumatoid factor. The exact pathophysiology of the development of the autoantibody response and of RA remains unknown. Investigations into genetic and environmental risk factors and systemic immune dysregulation have led to the hypothesis that the mucosal surfaces might be involved in the pathogenesis of seropositive RA. It is proposed that tolerance against post-translational modifications is broken at the mucosa, inducing an cascade leading to a systemic inflammatory response and clinical disease. We aim to perform an in-depth investigation into the role of the mucosal immune response in the pathogenesis of rheumatoid arthritis.

Study design

1 time point

Intervention

Participants will donate blood, saliva, sputum (optional) and feces once and will have to fill out an online questionnaire

Contacts

Public
LUMC, department rheumatology
Veerle Derksen

0715298035
Scientific
LUMC, department rheumatology

Veerle Derksen

0715298035

Eligibility criteria

Inclusion criteria

- Age 18 years or older
- Ability to understand the patient information form and ability to provide written informed consent
- Written informed consent

For patients:
- a definite diagnosis of rheumatoid arthritis based on the ACR/EULAR 2010 criteria for RA

For healthy controls:
- No previous prolonged and/or current symptoms of inflammatory arthritis

Exclusion criteria

- Individuals who fail to meet the inclusion criteria
- Individuals for whom relevant safety issues apply (for example, dyspnoea or severe anaemia) that preclude the
provision of sputum, saliva, peripheral blood or feces
- Individuals who are currently suffering from upper airway infections, influenza or other contagious (lung)diseases
- Dental treatment within the previous month
- The presence of oral ulcers
- Individuals with known inflammatory bowel disease

Additional exclusion criteria for sputum donation:
- Eye surgery within the past 6 weeks
- Chest trauma within the past 6 weeks
- Exacerbation of chronic obstructive lung disease

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Suspended
Start date (anticipated):	01-02-2020
Enrollment:	260
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion

Date:	16-01-2020
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 48311
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8306
CCMO	NL71319.058.19
OMON	NL-OMON48311

Study results