Synoviomics II: Advanced genomics intitiative in different phases of arthritis

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- To investigate different pathogenetic mechanisms underlying the clinical syndrome termed RA - To investigate changes in the synovial tissue in relationship to the duration of disease- To identify new therapeutic targets in the synovial tissue in...

Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON31664

Source
ToetsingOnline

Brief title
Synoviomics II

Condition

- Autoimmune disorders
- Joint disorders

Synonym
inflammatory joint diseases

Research involving
Human

Sponsors and support

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

Intervention

Keyword: genomics, inflammatory joint disease, synovial tissue

Outcome measures

Primary outcome

none, observational study

Secondary outcome

not applicable

Study description

Background summary

Heterogeneity
Although RA is thought of as an autoimmune disease, its etiology is unknown. Different stimuli, including exogenous infectious agents and endogenous connective tissue proteins like cartilage components have been suggested as possible primary causes that activate the immune response. There is growing evidence that patients with RA, as defined by the American College of Rheumatology Classification Criteria, represent a highly heterogeneous group. This heterogeneity of RA is indicated by notable variability in clinical presentation, the existence of erosive versus non-erosive disease, and the presence of distinct autoantibody specificities, such as rheumatoid factor and anticyclic citrullinated peptide antibodies in the serum.
Window of opportunity
Disease heterogeneity is also apparent in histological features of the synovium and in a marked variation in gene expression profiles, allowing identification of molecularly distinct forms of RA synovium. Consistent with this finding is the wide variation in responsiveness to treatment in RA. The relative contribution of these probable different disease mechanisms in RA may vary between patients and in different stages of the disease. This has been posted as the reason for the existence of a so-called therapeutic *window of opportunity phase* of the disease, which means that applying the right therapeutic intervention during the right phase of the disease will lead to a better control of the disease activity and consequently to less radiographic damage. The pathogenetic mechanisms underlying these differences found in patient characteristics and reactions to treatment are subject of extensive research.
One hypothesis is that the features of the inflamed synovial tissue change over

time. Transformation of resident fibroblasts into invasive cells, intruding into the cartilage and bone, could be one of the explanations that patients with longer disease duration are more likely to fail on therapy. Other factors include the release of crystals from degraded bone and cartilage with secondary pro-inflammatory effects. It is likely that these phenomena are not limited to RA and they may occur in other chronic arthritides as well
Disease activity and new therapeutic targets
As a consequence of the above mentioned hypothesis, different stages of the disease could require different therapeutic regimens. Identification of new therapeutic targets in relationship to the phase of the disease and disease activity might lead to novel strategies to improve treatment of RA.
Pathogenesis of inflammatory joint diseases other than RA
Furthermore, the pathogenesis of other inflammatory joint diseases, such as different forms of seronegative spondyloarthritis like psoraitic arthirits, ankylosing spondylitis and reactive arthritis, as well as crystal deposition disease, and inflammatory osteoarthritis, has not been elucidated. Since the synovial tissue is the target tissue of all inflammatory joint diseases, studying the specific features of this tissue in different stages of the disease process, using different innovative techniques, will contribute to an understanding of the processes underlying these diseases. This could lead to the identification of novel therapeutic targets for these diseases. Comparison with RA synovial tissue will allow identification of variables associated with persistence and destruction.

Study objective

- To investigate different pathogenetic mechanisms underlying the clinical syndrome termed RA
- To investigate changes in the synovial tissue in relationship to the duration of disease
- To identify new therapeutic targets in the synovial tissue in different stages of the disease
- To study the different pathogenetic pathways in the synovial tissue leading to the various inflammatory joint diseases
- To investigate new diagnostic markers in synovial tissue using molecular signatures of different inflammatory joint diseases

Study design

Inclusion criteria:
Patients with inflammatory joint disease and active inflammation of at least a knee or ankle joint

Clinical evaluation and demographics:
Recording of:
- Demographic data - date of birth, sex, and race.

- Disease duration.
- Disease activity parameters (Visual analog scale of disease activity and pain, 68 joint score, ESR, CRP)
- Present use of NSAIDs, corticosteroids, DMARDs, biologicals or other experimental drugs.
Joint destruction will be evaluated by conventional X-ray of the joint.

Collection of material:
During mini-arthroscopy synovial tissue will be collected through a biopsy technique.
Synovial biopsies will be collected and processed using a standard protocol for formalin fixation, to allow standard histological evaluation, and samples will be frozen en bloc for immunohistochemistry, PCR, micro-array and protein expression analysis. Samples will be collected for fibroblast like synoviocyte cell culture using a standard protocol.

Bloodsampling: blood (14 ml) will be collected to classify the patients. Rheumatoid factor, anti-CCP antibodies, CRP, and ESR will be determined. If informed consent is given for genetic studies, an extra blood sample of 7 ml will be drawn from the patient.

Study burden and risks

A mini-(or needle) arthroscopy perfomed under local aneasthesia at the outpatient clinic. Afterwards the patients are capable of walking. 24 hours of relative rest will be advised.

There is a small change of a joint inflammation (less then 3 percent).

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9 F4-218
1105 AZ Amsterdam ZO
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9 F4-218
1105 AZ Amsterdam ZO
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

active inflammation of at least one joint

Exclusion criteria

When in the opinion of the responsible investigator it is not in the interest of the patient to be enrolled (eg for safety reasons or severe co-morbidity).

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2007
Enrollment:	1500

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	NL19576.018.07