Detection and function of IL-17 producing CD4+CD25+Foxp3+ regulatory Tcells in peripheral blood and skin of patients with atopic dermatitis versus patients with psoriasis

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Epidermal and dermal conditions
Study type	Observational invasive

Summary

ID

NL-OMON35217

Source
ToetsingOnline

Brief title
Treg/Th17 in

Condition

- Epidermal and dermal conditions

Synonym
psoriasis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: atoptic dermatitis, psoriasis, regulatory T cells (Treg), Thelper-17 (Th17) cells

Outcome measures

Primary outcome

Skin biopsies are processed and tissue sections will be analyzed for the presence of IL-17-producing Treg using multicolour immunohistochemestry and multicolour immunofluorescence. Tissues will be visualized using microscopy, photographed and analysed using computer software. From the peripheral blood we will isolate CD4+CD25+Treg cells and look whether they have the propensity to differentiate and to produce cytokines upon ex vitro stimulation.

Secondary outcome

We will also look for several other surface differentiation markers, T lineage-specific transcription factors and cytokines.

Study description

Background summary

Atopic dermatitis (AD) and psoriasis are both chronic inflammatory skin diseases which result from a complex interaction between genetic components and environmental influences. In both skin diseases, deregulation of the immune system plays an important role in the pathogenesis. In this project we will focus on several T-cell subsets that we already saw in psoriasis. We would like to address whether these T cell subsets are also present in AD and compare the results to psoriatic patients and healthy controls. More specific we will focus on regulatory T-cells (Tregs) and Thelper-17 cells (Th17). Tregs are important in the *off-switch* of inflammation, and are characterised by the expression of

CD25 and transcription factor Foxp3. Impaired functioning of these cells is considered in the context of several auto-immune inflammatory diseases. In contrast, Th-17 cells are important in the *on-switch* of inflammation, and are characterised by the expression of transcription factor RORγt and the production of IL-17. Recent findings demonstrate that under pro-inflammatory conditions Tregs can differentiate in vitro into inflammation associated IL-17-producing cells. This conversion is also seen skin and peripheral blood derived-Tregs from severe psoriasis patients. Moreover, there are indications that Th17 cells also play an important role in the pathogenesis of atopic dermatitis.

Study objective

In the present project we would like to find out whether we can observe Treg into Th17 conversion in lesional skin and in the peripheral blood of patients with AD and compare the results to our findings in psoriatic patients and healthy controls. Furthermore, we are interested in several other lymphocyte subsets, T lineage-specific transcription factors and cytokines that might contribute to the process of inflammation in these skin conditions.

Study design

This is an explorative observational study in order to assess Treg into Th17 conversion in AD versus psoriasis. We will demonstrate this by analysing peripheral blood (100 ml) and a 4 mm skin biopsiy from each volunteer.

Study burden and risks

All volunteers have to sign an informed consent paper before entering the study. On their first and only visit we will obtain a punch biopsy of the skin and peripheral blood. Punch biopsies and venapunctures are taken according to standard procedure and may be slightly tender. Scar formation after biopsies does not occur or is barely visible. Venapunctures can lead to the formation of a small and self-limiting haematoma. The study-visit is extra. After the interventions, the volunteers are released from follow-up. Participating in this study does not lead to direct benefit for the volunteers. Participation will not interfere with the preferred medical care that is given to the patient.

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

Patients with atopic dermatitis must meet the following criteria:
• Adults older than 18 years of age
• Patients with moderate to severe atopic dermatitis (TIS score >=3)
• Patients must be willing to give a written informed consent
• Patients must be able to adhere to the visit schedule ;Patients with psoriatis must meet the following criteria:
• Adults older than 18 years of age
• Patients with severe psoriasis (PASI >=15)
• Patients must be willing to give a written informed consent
• Patients must be able to adhere to the visit schedule ;Healthy volunteers must meet the following criteria:
• Adults older than 18 years of age
• Volunteers must be willing to give a written informed consent
• Volunteers must be able to adhere to the visit schedule

Exclusion criteria

Patients with atopic dermatitis will be excluded from this study when any of the following criteria listed below are met:
• Children or adolescents younger than 18 years of age
• Patients with, besides atopic dermatitis, psoriasis
• Patients that use systemic medication for their atopic dermatitis, for example ciclosporine
• Patients who are currently treated with phototherapy
• Patients with mild atopic dermatitis
• Patients using trial medication
• Patients using immunosuppressive agents like prednisone or methotrexate
• Patients with relevant co-morbidities
• Patients with a current condition involving an activated immune system, such as the flue or a recent vaccination;Patients with psoriasis will be excluded from this study when any of the following criteria listed below are met:
• Children or adolescents younger than 18 years of age
• Patients with, besides psoriasis, atopic dermatitis
• Patients that use systemic medication for their psoriasis, for example acitretin or biologics
• Patients who are currently treated with phototherapy
• Patients with a mild to moderate psoriasis (Psoriasis Area and Severity Index <=15)
• Patients using trial medication
• Patients using immunosuppressive agents like prednisone or methotrexate
• Patients with relevant co-morbidities
• Patients with a current condition involving an activated immune system, such as the flue or a recent vaccination

The healthy volunteer will be excluded from this study when any of the following criteria listed below are met:
• Children or adolescents younger than 18 years of age
• A volunteer with a history or signs of a relevant skin disease
• A volunteer with a family history of atopic dermatitis or psoriasis
• Volunteers using immunosuppressive agents like prednisone or methotrexate
• Volunteers with relevant co-morbidities
• Volunteers with a current condition involving an activated immune system, such as the flue or a recent vaccination

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:	Recruiting
Start date (anticipated):	01-03-2012
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO Date:	29-09-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-03-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL37430.091.11