Breaking the Barrier: CD8+ T cells in Atopic Dermatitis and Psoriasis Vulgaris

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Investigate the role of CD8+ T cells in AD by:a. Isolation of T cells from the skin and determination of the percentage and phenotype of CD8+ T cells in both acute and chronic AD, using the APT as an in vivo induction model. Comparison with...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Allergic conditions
Study type	Observational invasive

Summary

ID

NL-OMON32531

Source
ToetsingOnline

Brief title
CD8+ T cells in Atopic Dermatitis and Psoriasis Vulgaris

Condition

- Allergic conditions
- Epidermal and dermal conditions

Synonym
atopic dermatitis, eczema

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Atopic Dermatitis, CD8+ T cells, Interleukin-13, Psoriasis Vulgaris, Skin

Outcome measures

Primary outcome

We will determine the percentage of CD8+ IL-13-producing skin resident T cells in acute and chronic AD using the APT as an in vivo model. Results will be compared to data from lesional and non-lesional AD, PV skin and healthy control skin.

Secondary outcome

not applicable

Study description

Background summary

Atopic dermatitis (AD) is an inflammatory disease that is characterized by a dysregulated immune response to exogenous factors causing IgE upregulation and promotion of eosinophilia. Defects in the epidermal permeability barrier play an important role in the pathogenesis of AD. AD skin is characterized by a biphasic infiltration of T cells. In the acute phase of AD, effector T cells are mainly of the T helper-2 (Th2) phenotype. However, in the chronic phase T helper-1 (Th1) cells are more predominant. Researchers have paid little attention so far on the role of CD8+ T cells. Preliminary data show increased numbers of CD8+ T cells in lesional AD skin compared to healthy controls. Furthermore, we found that a significant subset of these CD8+ T cells produce the type-2 cytokine interleukin (IL)-13, which is an important immunomodulatory cytokine that may have an important effect on epithelial barrier function. In this research proposal, we will investigate the role of IL-13-producing CD8+ T cells. We will try to find out in what stage(s) of disease IL-13-producing CD8+ T cells are playing a role, by isolating T cells from the skin and studying T cell phenotype in both acute and chronic AD using the atopy patch test (APT) as an in vivo induction model. We will further investigate the role of IL-13 on epidermal barrier function using human skin equivalents.

Results will be compared with psoriasis vulgaris, another T cell mediated

chronic skin disease. This allows us to determine disease specificity of our results. However, we also expect that our study will contribute to the knowledge of the pathogenesis of psoriasis vulgaris.

Study objective

Investigate the role of CD8+ T cells in AD by:
a. Isolation of T cells from the skin and determination of the percentage and phenotype of CD8+ T cells in both acute and chronic AD, using the APT as an in vivo induction model. Comparison with psoriasis vulgaris.
b. Investigate effects of IL-13 on epidermal barrier function using human skin equivalents

Study design

observational study

Study burden and risks

Patients with AD will have to visit the outpatient department three times. During their first visit an APT will be applied. During a second visit, 24 hours later, the extent of the induced skin reaction will be determined. Skin punch biopsies (4 mm diameter) will be taken from the APT site, from (chronic) lesional and from non-lesional skin (three biopsies in total). To determine disease severity a physical examination will be done to assess a SCORAD and LSS (AD disease severity) and a blood sample will be taken (10 mL) to determine serum thymus and activation regulated chemokine (TARC) levels.
Three days after their first visit (72 hours after application of the APT), another skin biopsy will be taken from an APT site.
Patients with psoriasis vulgaris (PV) will only visit the outpatient department once for biopsies of lesional and non-lesional skin. During the same visit a PASI score (psoriasis severity) will be done and a blood sample will be taken (10 mL). Healthy non-allergic control subjects will visit the the outpatient department for three biopsies of normal skin and collection of a blood sample.
Risks of skin biopsies include infection and the formation of a (hypopigmented) scar. After a biopsy is taken, remaining eczematous lesions induced by the APT can be treated with a topical corticosteroid.

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

Atopic dermatitis patients:
- Adult (18-70 years of age) male or female patients diagnosed with atopic dermatitis
- Positive APT to house dust mite allergen
- Biopsy location (~4 cm2) should not be treated with topical steroids for at least 1 week
- No use of oral antihistamines in the 2 weeks prior to inclusion;Psoriasis vulgaris patients:
- Adult (18-70 years of age) male or female patients diagnosed with psoriasis vulgaris
- Biopsy location (~4 cm2) should not be treated with topical steroids for at least 1 week;Healthy controls:
- Adult (18-70 years of age) male or female volunteers without a history of skin diseases
- Biopsy location (~4 cm2) should not be treated with topical steroids for at least 1 week
- No history of asthma and/or hay fever

Exclusion criteria

- Use of systemic immunosuppressive drugs (i.e., cyclosporin, prednisolone, methotrexate, neotigason, fumaric acid) in the 6 weeks prior to inclusion
- Exposure of biopsy location to (extraordinary) UV sunlight (i.e. UV-therapy, sunny holiday) in the weeks prior to inclusion

- (Secondary) skin infection

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:	Recruitment stopped
Start date (anticipated):	08-04-2009
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO

Date:	09-12-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL23909.041.08