Modelling of human skin diseases using in vitro 3D reconstructed skin

Published: 17-07-2018
Last updated: 10-04-2024

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Epidermal and dermal conditions
Study type	Observational invasive

Summary

ID

NL-OMON46406

Source
ToetsingOnline

Brief title
3D models of human skin diseases

Condition

- Epidermal and dermal conditions

Synonym
inflammatory skin diseases (atopic dermatitis and psoriasis) and genodermatoses (skin diseases caused by genetic disorder)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Atopic dermatitis, Genodermatoses, Psoriasis

Outcome measures

Primary outcome

* The outcome measures of the cell culture experiments include: morphology of the epidermis and gene expression of the epidermal cells, following stimulation of the cells (e.g. by cytokines or microbes). Gene expression analysis will generate quantitative data (delta Ct of qPCR).

* Histology will be scored semi quantitatively (stain intensity and localization).

* We will identify relevant mutations of risk genes for psoriasis and AD. In case of genodermatoses, the causative genes are in general already known.

* The effect of diagnosis and genotype on gene expression and histology will be analysed with multivariate techniques.

Secondary outcome

None

Study description

Background summary

Elucidation of disease aetiology and pathogenesis is often approached using animal models or traditional cell-based in vitro systems. In experimental dermatology, the use of three-dimensional (3D) reconstructed skin models has proven to be a powerful tool to investigate the biology of normal skin and skin diseases. This has prompted us to initiate a research project to develop and apply these models, aiming to resolve the biology underlying genetic risk factors of psoriasis and atopic dermatitis (AD) and to investigate the biological function of genes known to be mutated in rare Mendelian skin

disorders (genodermatoses). The outcome of this project will contribute to understanding the effect of genetic variation on disease and to knowledge on gene function, and it may contribute to personalized therapeutic approaches.

Study objective

In this project we will establish primary keratinocyte cell lines of patient skin biopsies from selected skin diseases, to generate 3D skin constructs. In addition, patient DNA will be genotyped for genetic risk factors (psoriasis and AD) or causative mutations (genodermatoses) to analyze in vitro biological responses in relation to genetic background.

Study design

Patients participating in the study are treated in regular care. Inclusion of patients and collection of samples will be performed at regular outpatient visits as much as possible. If not enough patients can be included, we have a list of volunteers who have registered for participation in research and have agreed to be approached. Patients will be provided with oral and written information about participation in this study and informed consent will be obtained.

* Saliva from each patient will be collected for DNA analysis (to determine disease specific candidate genes, for example the FLG genotype in AD and the HLA-Cw6 and LCE3BC_del genotype in psoriasis). In the case of genodermatosis patients, the causative mutation may already be known, but will be confirmed.
* Four skin biopsies of 4 mm diameter will be collected from patients treated for a chronic inflammatory skin disease (psoriasis and AD) and from patients with a genodermatosis. Primary keratinocytes will be isolated from three biopsies for generation of 3D skin equivalents as previously described. One biopsy will be used for immunohistochemical and morphological analyses. Primary human keratinocytes from healthy controls have already been collected previously. These in vitro skin models will be used to determine the pathogenesis and therapy response in relation to the genetic characteristics of the host. The skin constructs will be analyzed in vitro for gene expression after stimulation with inflammatory, disease-specific cytokines (in case of psoriasis and AD). Analysis by quantitative PCR (qPCR) will be performed on a large panel of genes. The qPCR data will be analyzed with multivariate statistical analysis. Furthermore, the skin constructs will also be analyzed with immunohistochemical stains for protein expression and morphology. Epidermal extracts may be used for biochemical assays to investigate the biological pathways that are affected e.g. in constructs of genodermatosis patients.

Study burden and risks

Skin biopsies pose a very small risk of post biopsy bleeding, infection of the biopsy wound and scar formation. However, despite being performed at a large scale in daily dermatology practice, complications of biopsy-taking are hardly ever encountered. Patients with a tendency to develop hypertrophic scars will be excluded from the studies. Genetic analyses will focus on known genetic risk factors for psoriasis and AD, and on mutations identified to be causative for genodermatoses. Whole exome or whole genome sequencing will not be performed, so there will be no risk of incidental findings.

Contacts

Public
Radboud Universitair Medisch Centrum

Rene Descartesdreef 1
Nijmegen 6525GL
NL
Scientific
Radboud Universitair Medisch Centrum

Rene Descartesdreef 1
Nijmegen 6525GL
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients that suffer from atopic dermatitis, psoriasis and genodermatoses

Exclusion criteria

If it is likely that patients develop hypertrophic scars (patients are asked if they do/don't heal nicely after damage to the skin).

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:	Will not start
Enrollment:	113
Type:	Anticipated

Ethics review

Approved WMO Date:	17-07-2018
Application type:	First submission
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	NL63882.091.18