Single cell analysis in Netherton syndrome

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

Summary

ID

NL-OMON53598

Source
ToetsingOnline

Brief title
SCANS

Condition

- Epidermal and dermal conditions

Synonym
Comel-Netherton Syndrome, Netherton Syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Eigen bijdrage Centrum Kinderdermatologie (gespaard met gelden van trials;presentaties;scholing)

Intervention

Keyword: Gene expression, Netherton syndrome, Pathophysiology, Single cell sequencing technique

Outcome measures

Primary outcome

The main study parameters are the difference in gene expression profile of skin (lesional and non-lesional) of patients with NS (using scRNA-seq, and spatial transcriptomics) from skin of healthy controls and the difference in gene expression profile of NS-ILC and NS-SE. Furthermore, lesional NS skin will be compared with lesional AD skin and lesional psoriasis skin.

Secondary outcome

Secondary endpoints of this study are:

- Comparison of the gene expression profile (using scRNA-seq and spatial transcriptomics) in the lesional skin of NS patients with lesional skin in AD, and lesional skin in psoriasis

- Comparison of the expression profile using scRNA-seq and spatial transcriptomics with bulk-RNA sequencing in and between all previously mentioned subgroups (lesional NS, non-lesional NS, ILC-NS, SE-NS, lesional AD, lesional psoriasis, and healthy controls).

- Comparison of the gene expression profile with immunohistochemistry in the skin of NS, AD, psoriasis, and healthy control skin and to compare immunohistochemical differences amongst subgroups.

- Correlation of the knowledge on the skin inflammation signature of NS with the systemic inflammation signature, analyzed by measured serum cytokine levels

and phenotyping of peripheral blood immune cells (PBMCs) compared to psoriasis,

AD, and healthy controls.

Study description

Background summary

Netherton syndrome (OMIM #256500) (NS) is a rare genetic disorder caused by an autosomal recessive mutation in the serine peptidase inhibitor, Kazal type 5 (SPINK5) gene. Although Netherton is a severe skin disease, sometimes even life-threatening, little is known about therapeutic options and their outcomes, with treatment regimens being only supportive in nature. Lifelong treatment is required, but there are no registered treatments and treatment guidelines available for patients with NS. This is partly due to the fact that the pathogenesis of NS is not yet fully understood. In previous studies, the transcriptomic signature of NS has been investigated using RT-PCR and bulk RNA sequencing. In contrast to these techniques, single cell RNA sequencing (scRNA-seq) and spatial transcriptomics give a more precise understanding of the transcriptome in individual cells and will enable us to map the location of gene activity in the skin. These insights can help to identify potential targets for treatment in NS patients.

Study objective

Our primary objectives are to analyse the gene expression profile of non-lesional and lesional skin of patients with NS (ichthyosis linearis circumflexa (ILC) phenotype and scaly erythroderma (SE) phenotype) using single cell RNA sequencing and spatial transcriptomics, compared to skin of healthy controls. Furthermore, lesional NS skin will be compared with lesional atopic dermatitis (AD) skin and lesional psoriasis skin because of the clinical and the pathophysiological resemblances.

Study design

Multicenter study with an explorative study design. Patients will be included both in France and the Netherlands.

Study burden and risks

The samples will be collected at one time point. A skin excision is a routine dermatological procedure and is generally safe, however there is a small risk of bleeding and infection. Furthermore, the elliptic excision will leave a small linear scar. Blood drawing is a routine clinical procedure and is

generally safe, besides the risk of a local hematoma after blood collection. The participants will not directly benefit from this research, but participation contributes to increasing knowledge about NS, and subsequently improving treatment and care for NS patients. Furthermore, comparison of the gene expression in lesional skin in three different skin diseases (NS, psoriasis, atopic dermatitis) contributes to our knowledge about differences and similarities in these diseases.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Patients with Netherton syndrome:
- A genetic diagnosis of Netherton syndrome
- Aged 18 years or above (adult)

Patients with atopic dermatitis (AD):
- Aged 18 years or above (adult)
- Dermatologist diagnosed atopic dermatitis (AD)
- AD lesion of at least 25x6mm

Patients with psoriasis:
- Aged 18 years or above (adult)
- Dermatologist diagnosed psoriasis
- Psoriasis lesion of at least 25x6mm

Exclusion criteria

Exclusion criteria for Netherton syndrome (NS) patients, atopic dermatitis (AD) patients, and psoriasis patients:
- Use of systemic treatment within a period of 5 half-lives (in the past week to ~3 months depending on the type of medication)
- Bathing within 24-hours prior to the skin excision
- Application of a topical medication (e.g. topical corticosteroids, topical calcineurin inhibitors, topical antibiotics) within 1 week before skin excision
- Active (haematological) malignancy
- Pregnancy or breastfeeding
- No skin lesion of 25x6mm on either trunk or extremities (arms, legs)

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:	Pending
Start date (anticipated):	01-11-2022

Enrollment:	12
Type:	Anticipated

Ethics review

Approved WMO Date:	16-11-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-03-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL81941.078.22