# Expression of cytokeratins and notch in the healthy folliculopilosebaceous unit

Published: 19-08-2015 Last updated: 19-04-2024

1) to examine the expression of cytokeratins and Notch in healthy human FPSUs at different segments. 2) to describe the association between expression of the cytokeratins and Notch 1 in the FPSUs of healthy volunteers.

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

# Summary

#### ID

NL-OMON42336

**Source** ToetsingOnline

Brief title Keratin and Notch in the PSU

## Condition

• Skin appendage conditions

**Synonym** acne ectopica, acne inversa

**Research involving** Human

## **Sponsors and support**

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

#### Intervention

Keyword: FPSU, Keratins, Notch

#### **Outcome measures**

#### **Primary outcome**

The intensity of the stainings will be measured at the 6 segments of the FPSU:

bulb, bulge,

isthmus, sebofollicular junction, infundibulum and interfollicular epidermis.

For each skin sample

the intensity of all performed IF stainings at the aforementioned individual

segments will be

analyzed using Image J software.

#### Secondary outcome

The intensity of the stainings will be measured at the 6 segments of the FPSU: bulb, bulge, isthmus, sebofollicular junction, infundibulum and interfollicular epidermis. For each skin sample the intensity of all performed IF stainings at the aforementioned individual segments will be analyzed using Image J software. Next, the association between expression of the cytokeratins and Notch 1 will be examined. Notch 1 expression will be the independent variable, the expression of the different cytokeratins the dependent variable.

# **Study description**

#### **Background summary**

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease that mainly occurs on the apocrine gland bearing skin. The pathogenesis of HS is largely unknown but

several studies have shown that the initiating event takes place at the hair follicle. Histological studies showed hyperkeratosis of the infundibulum and epidermal psoriatiform hyperplasia. Recently, the European S1 guideline for the treatment of HS was published. In this guideline it is stated that cytokeratin 17 has been shown to be absent from infundibular-like keratinized epithelium, suggesting fragility of the draining sinus epithelium, which may be responsible for rupture. Another recent study showed loss of function mutations in genes encoding components the transmembrane protease gamma-secretase (GS) in HS patients. GS cleaves the intracellular domain of Notch which leads to intracellular Notch signaling. The activation of Notch signaling results in the promotion of growth arrest and onset of differentiation. In mice, it was shown that deficient notch signaling results in occlusion of hair follicles, formation of epidermal cysts and insufficient feedback suppression of innate immunity. In psoriasis, it was hypothesized that decrements in Notch molecules might cause aberrant expression of cytokeratin 10 and cytokeratin 14 leading tot anomalous differentiation of the epidermis. We hypothesize that both cytokeratins and Notch are involved in the pathogenesis of HS. Notch might be responsible for disturbed expression of cytokeratins in the FPSU of HS. The exact expression of Notch and cytokeratins in healthy FPSUs is unknown. In future projects we would like to examine the expression of cytokeratins and Notch in FPSUs of HS patients. To be able to do this, it is first necessary to investigate these proteins in healthy human FPSUs.

#### Study objective

1) to examine the expression of cytokeratins and Notch in healthy human FPSUs at different segments.

2) to describe the association between expression of the cytokeratins and Notch 1 in the FPSUs of healthy volunteers.

#### Study design

Design: observational study

Study duration: four months

Setting: department of Dermatology at the University Medical Center Groningen Procedure:

Healthy volunteers: skin samples of healthy volunteers will be analyzed. A total of 20 subjects will be included; 10 for skin samples of the axilla region

and 10 for skin samples from the groin.

Collecting skin samples: four milimetre (mm) punch biopsies will be taken either from the axilla or the groin under local anesthesia. The biopsy will be taken in the direction of the hair in order to optimize the chance of obtaining the whole PFSU in the biopsy.

Stainings: A hematoxylin and eosin (HE) staining will be performed to evaluate the presence of the different segments of the FPSU. Only if all segments are present, the expression of the different proteins can be examined. From earlier studies we learned that the chance of obtaining a complete FPSU in a biopsy is about 50%. Unfortunately, there is no technique available that increases the chance of obtaining of a complete FPSU. Because we aim at examining 10 biopsies, we ask for permission of taking 20 biopsies. DIF will be performed on the biopsies that include all segments of the FPSU for cytokeratin 1,5, 10,14, 15, 16, 17 and 19 and Notch 1.

Scoring: Image J will be used to analyze the intensity of the IF staining of the different segments.

Evaluation of endpoints:

Primary endpoints: the intensity of the stainings of the different proteins at the different segments of the FPSU

Secondary endpoints: the association between the intensity of the different cytokeratins and Notch 1 in the FPSUs

#### Study burden and risks

The burden and risks associated with participation in the control group is negligible.

Punch biopsies are part of everyday practice at the Dermatology department and seldom

lead to complications like wound infection. The procedure will take approximately 5 to 10

minutes and no further visits are required except for removal of the stitch (takes

approximately 2 minutes).

# Contacts

#### Public

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# **Trial sites**

## **Listed location countries**

Netherlands

# **Eligibility criteria**

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

### **Inclusion criteria**

- Subjects are not affected with HS
- Subjects do not have another skin disease located at the armpits or groins
- Age 18-50 years

## **Exclusion criteria**

- Subjects who have not given informed consent
- Subjects with a skin disease located in the armpits and groins

# Study design

#### Design

Study type: Observational invasive		
Masking:	Open (masking not used)	
Control:	Uncontrolled	
Primary purpose:	Basic science	

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## Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	09-09-2015
Enrollment:	20
Туре:	Actual

# **Ethics review**

Approved WMO	
Date:	19-08-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

# **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 CCMO **ID** NL54117.042.15