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Title: The transcriptome of hand eczema assessed by tape stripping

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Abbreviations

Allergic contact dermatitis (ACD)

Atopic dermatitis (AD)

Differentially expressed gene (DEG)

Gene ontology (GO)

Hand eczema (HE)

Hand eczema severity index (HECSI)

Hand eczema with atopic dermatitis (HE+AD)

Hand eczema without atopic dermatitis (HE-AD)

Irritant contact dermatitis (ICD)

Whole transcriptome sequencing (WTS)
Abstract

**Background:** No biomarkers have been identified that can classify subtypes of hand eczema (HE). Although skin biopsies represent the golden standard for investigations of the skin, the invasive technique is not favorable when investigating skin from sensitive areas. Recent advances in the use of skin tape strips for molecular investigations enable non-invasive investigations of HE.

**Objective:** By using whole transcriptome sequencing (WTS), the molecular profile of HE according to different localizations on the hands, etiologies, and clinical/morphological subtypes was investigated.

**Methods:** Thirty adult, Danish HE patients, 12 with and 18 without concurrent atopic dermatitis (AD), as well as 16 controls were included. Tape strip samples were collected from lesional, non-lesional, and healthy skin. Total RNA was extracted, and WTS was performed.

**Results:** The largest molecular difference of HE patients with and without AD was found in non-lesional skin areas and included a downregulation of CXCL8 for HE patients without AD. Differences between allergic- and irritant contact dermatitis included promising epidermal biomarkers such as EPHA1.

**Conclusion:** Skin tape strip samples could be used to assess the gene expression profile of HE on different localizations of the hands. The skin tape strip method identified new molecular markers that showed promising result for the identification of HE subtypes.

**Key words:** Atopic hand eczema, contact dermatitis, subtypes of hand eczema, tape stripping, transcriptomics
Introduction

Hand eczema (HE) is a prevalent disease with a 1-year prevalence of 9% in the general population. It may affect quality of life, impact work ability, and require treatment periodically or continuously, depending on severity and chronicity.

HE may be a result of different etiologies, which complicates both effective treatment and prevention. HE can be a part of atopic dermatitis (AD), and/or environmental factors, such as exposures to allergens and/or irritants, may result in allergic contact dermatitis (ACD) and/or irritant contact dermatitis (ICD) on the hands. The skin impairment of AD also makes the skin more vulnerable to irritants, sometimes leading to a mixed pattern of AD and ICD.

Diagnostic criteria exist for the different etiological subtypes. ACD can be diagnosed by a combination of patch testing and exposure analysis, AD has distinct disease characteristics, such as early onset, and can be diagnosed by fulfillment of the Hanifin Rajka criteria, while ICD depends on exclusion of ACD and exposure analysis demonstrating significant exposures to irritants. ACD is driven by a type IV hypersensitivity reaction to one or more contact allergens by allergen-specific T-cells releasing pro-inflammatory cytokines. TH1-cells play a major role in the response. It is believed that danger signals induced by the allergen or co-exposures to irritants are important for initiation of the reaction. ICD is caused by agents causing direct damage to the skin barrier initiating the innate immune system. The state of the skin barrier is important for the risk of ICD and persons with current or previous AD in general have an increased risk of developing ICD, especially if filaggrin mutations are present. The immunology of AD is very complex reflecting the heterogeneity of the disease, but in the classical understanding the disease is driven by a TH2 response in the acute phase, that changes towards a TH1 driven response in the chronic phase. Though the molecular profiles related to the various etiologies differ, there are currently no biomarkers in use for supporting the diagnosis of these etiological subtypes in the routine investigation of patients with HE. In addition, subtypes exist, with so far unknown etiology. Some have distinct morphology including palmar hyperkeratotic HE and recurrent vesicular HE, whereas other have no apparent detectable causal factors. Also, anatomical patterns exist, so that some patients primarily have a dorsal and others a palmar pattern.
Recent advances in the use of skin tape strips to obtain valid skin samples now enable research within immunotypes and specific biomarkers. In a previous study, we found that the stratum corneum transcriptome in AD could be assessed by tape stripping of the skin. Based on a paired comparison with skin biopsies from the same patients, we identified established molecular markers of AD in the tape samples. In the current study, we are taking the next step by investigating if differences in the transcriptome can be detected by tape stripping of HE patients with different anatomical patterns, of different etiology, and main morphologies.

Materials and methods

Study population

Thirty adult, Danish, patients with HE were recruited from the Department of Dermatology and Allergy, Herlev-Gentofte hospital, Denmark, between March 2019 and September 2020. The patients included eight patients with current AD, four with a history of AD (HE+AD) and 18 with HE and no history of AD (HE-AD).

Furthermore, 16 age-matched adult controls with no history of inflammatory skin diseases or other atopic diseases (asthma or hay fever) were included. All participants were asked to abstain from use of topical anti-inflammatory treatment and emollients for 24 hours before inclusion. Patients did not use any systemic therapies for their HE or AD. Other exclusion criteria included ongoing infections, pregnancy, lactation, or use of antibiotics, phototherapy, or self-tanners within four weeks of sample collection.

HE+AD included patients with current AD and historical AD. Current AD was diagnosed by the treating physician at the Department of Dermatology and all these patients fulfilled the Hanifin Rajka criteria. Historical AD was based on self-reports from the patients. HE-AD included patients with current HE and no history of AD. Current or previous AD had been ruled out by the treating physician in all HE-AD cases. Clinical severity scores included the Hand Eczema Severity Index (HECSI) for all patients and the Eczema Area and Severity Index (EASI) for patients with concomitant active AD. Furthermore, clinical-morphological subtypes of HE were evaluated according to the classification by Menné et al. All participants answered a detailed questionnaire including questions on use of emollients, and for the patients, the duration of their HE.
Health care data relevant to the patients’ etiological classification of HE was extracted from electronic health records (EPIC). The etiological classification of HE included irritant contact dermatitis (ICD), allergic contact dermatitis (ACD), atopic HE (AHE), and protein contact dermatitis (PCD). If the HE could not be etiologically classified according to these four sub-diagnoses or had more than one sub-diagnosis, the HE was grouped as ‘etiologically unclassifiable’ or ‘mixed etiology’ respectively. The ACD sub-diagnosis was given if the patient had at least one clinically relevant type IV allergy. The ICD sub-diagnosis was given if the patient had a clinically relevant exposure to irritants. In Supplementary Table 1, an overview of the exposures to irritants and/or allergens relevant for the HE can be seen. No patients were diagnosed with PCD.

The characteristics of the study population can be seen in Table 1. Based on the questionnaire, 67% of the HE+AD patients reported that their HE started before the age of two, whereas 89% of the HE-AD patients reported that their HE started when they were 18 years or older. A majority of patients reported that the eczema was present almost all the time (HE-AD 92% and HE+AD 75%), and more than half of the patients reported that the eczema had been present all the time within the last year (HE-AD 56% and HE+AD 58%). A full overview of the self-reported duration of HE can be seen in Supplementary Table 2.

The study was approved by the local ethics committee (H-16050507) and the Danish Data Protection Agency (HGH-2017-073), oral and written consent was gathered before inclusion, and the study followed the Helsinki declaration.

**Skin samples**

Skin samples of both lesional and non-lesional stratum corneum were taken from the patients by tape stripping. The lesional tape strips were taken from a lesion on the most affected area of the hands (palmar or dorsal aspects). The non-lesional skin sample was taken from the upper arm of all patients. From the controls, a healthy skin sample was taken from the hands (palmar or dorsal aspects). From each sample site, two consecutive standard D-squame tape strips (Monaderm, Monaco, France) were collected applying uniform pressure as previously described. For RNA extraction, both tapes were used. The samples were stored and shipped at room temperature, and RNA was extracted within three days from sampling.
RNA extraction and whole transcriptome sequencing

RNA was extracted with the miRNeasy Micro Kit from Qiagen (Qiagen Denmark, Copenhagen, Denmark) following the manufacturer’s instruction. RNA from the two tapes was pooled directly on the column after phase separation.

For whole transcriptome sequencing (WTS), the library build was performed with the SMARTer Stranded Total RNA-Seq Kit v2 - Pico Input Mammalian kit (Takara Bio Europe, Saint-Germain-en-Laye, France) following the manufacturer’s recommendation without fragmentation.

Paired-end sequencing (2 x 100 bp) was performed on a NovaSeq 6000 (Illumina, California USA) using the NovaSeq 6000 S2 Reagent Kit v1 (Illumina, California USA). The sequencing resulted in an average sequencing depth of 82.7M reads per case.

Quality assessment and alignment of sequencing reads were performed as previously described.11

Normalization and differential expression analysis

Gene counts were normalized and analysed by the Bioconductor package DESeq2 (version 1.30.1) using 'apeglm' for LFC shrinkage.17 A gene was considered as a differentially expressed gene (DEG) if an observed difference in normalized read counts between two experimental conditions had a Benjamini-Hochberg adjusted p-value < 0.1 and a log2 fold change > 1 or < -1. For the visual examination, data was transformed by the variance stabilizing transformation (vst) function of DESeq2, with “blind” set to “FALSE”.

Cluster, gene ontology (GO) and keyword analysis were conducted with STRING (Version 11.0, https://version-11-0.string-db.org/).

Data visualization including principal component analysis (PCA), heatmaps, and unsupervised hierarchical clustering were performed in Qlucore Omics Explorer v. 3.6 (Qlucore AB, Lund, Sweden).

Statistics

The statistical analyses were conducted in R (R core team, version 4.0.4, http://www.R-project.org/).
Differential analyses were performed between skin areas in patients (lesional, non-lesional) and compared with controls (healthy skin), anatomical localizations on the hands (palm and dorsum), AD status (HE−AD and HE+AD), HE etiologies (ACD, ICD and AD), and clinical HE subtypes.

For the investigation of the gene expression differences between the etiologies, patients with a single etiology were included (ACD n=5, ICD n=5, and AD n=6) (Table 1). Patients grouped as “etiologically unclassifiable” or having a mixed etiology were not included in this data analysis.

The investigation of clinical HE subtypes included groups with at least three patients and only one clinical subtype, which was only fulfilled by: chronic fissured hand eczema and recurrent vesicular hand eczema.

For the statistical test between RNA parameters and individual biomarker levels, Wilcoxon rank sum test was performed.
Results

Whole transcriptome sequencing on RNA from tape strips from the hands

WTS was performed in a total of 76 tape strip samples (a lesional and non-lesional sample from each HE patient and a healthy sample from each control) (Figure 1A). Seven samples were subsequently excluded due to quality issues as assessed by the FastQC reports (four lesional and three non-lesional samples). With the removal of these, a total of 69 samples were included in the subsequent analyses (26 lesional, 27 non-lesional, and 16 healthy samples).

The mean number of protein coding read counts (having an open reading frame) was 2.7 million for all samples (median [IQR]: 0.7 million [0.4-3.2 million]), with no statistically significant difference (p > 0.05) between the skin areas (average; lesional: 2.2 million, non-lesional: 3.1 million, healthy: 1.1 million) (Supplementary Figure 1A).

The average input read length was the same across skin sites, however, the average mapped read length showed a statistically significant decrease (p < 0.05) from lesional to non-lesional and healthy skin sites, respectively (Supplementary Figure 1B and C). No difference was observed between the number of intronic reads according to skin areas (Supplementary Figure 1D).

Transcriptional differences between dorsum and palm were higher for eczema patients

The 16 control samples included six samples from the dorsum and 10 from the palm. The 26 lesional samples included seven samples from the dorsum and 19 from the palm (AD+HE: 6 dorsal and 5 palmar; AD+HE: 1 dorsal and 14 palmar).

For the healthy skin samples no statistically significant difference in the number of protein coding reads between the localizations (dorsal and palmar aspects) on the hands were observed (p=0.64), however, for the lesional samples, a statistically significant higher number of protein coding reads were observed for the dorsal aspects of the hands (p=0.035) (Supplementary Figure 2).

Only a few DEGs were detected between dorsum and palm (15 for healthy skin samples and 63 for lesional skin samples) (Figure 1B and C respectively), and the genes did not show enrichment for specific biological processes (data not shown). In addition, PCA did not show apparent clustering related to the
dorsal- or palmar aspects of the hands for neither skin area (Supplementary Figure 3A and B respectively).

Tape strip samples show the immunology of lesions on the hands

The main transcriptomic differences between skin areas (healthy, non-lesional, and lesional) were found between lesional and non-lesional as well as healthy skin (PC1: 28%), whereas the non-lesional and healthy skin samples had similar overall gene expression profiles (Figure 2A, and Supplementary Figure 4).

When investigating the number of DEGs between skin areas, the largest difference in gene expression - based on numbers of DEGs between the skin areas - was found between lesional and healthy skin areas (2884 DEGs, 1355 up and 1529 down in lesional skin). The second largest difference was observed between non-lesional and healthy skin areas (1012 DEGs, 697 up, 315 down in non-lesional skin). The difference between patients’ lesional and non-lesional skin areas included 620 DEGs (273 up, 347 down in lesional skin) (Figure 2B). Figure 2C shows the top 25 DEGs between healthy and lesional skin areas. Of these 25 genes, 10 were differentially expressed between all skin contrasts (healthy vs non-lesional, healthy vs lesional, and non-lesional vs lesional). The 10 genes enriched for gene ontologies important for inflammation including “cytokine activity” (GO:0005125) and “antigen processing and presentation of exogenous peptide antigen via MHC class II” (GO:0019886).

Looking at the genes common to the specific skin areas the genes associated with healthy skin included COL4A2, KRT14 and S100A genes (Supplementary Dataset 1), genes associated with to non-lesional skin included hair genes (KRTAPs) and IL18 (Supplementary Dataset 2), and genes associated with lesional skin areas including CXCL8, S100A8 and CCL17 (Supplementary Dataset 3) (Figure 2B and Supplementary Figure 5).

The most prominent difference between HE+AD and HE-AD was at the non-lesional skin sites

Looking at the number of DEGs between HE+AD and HE-AD the greatest difference was observed for the non-lesional skin sites (211 DEGs) as compared to the lesional skin site (28 DEGs) (Figure 3A). The difference between non-lesional skin of HE+AD and HE-AD showed an increase in several inflammatory markers including S100A12, MMP9, CXCL8, and IL1B whereas lesional skin in HE+AD patients showed
a decreased expression of PRLR and PIBPI related to the “activation of Janus kinase activity” (GO:0042976) compared to lesional skin of HE-AD patients.

Next, we investigated if the overall transcriptomic difference between non-lesional and healthy skin was driven by the HE+AD patients (Supplementary Figure 6). In general, the genes specific for the difference between non-lesional and healthy skin for HE+AD and HE-AD respectively, did not enrich for immunologic pathways (data not shown), however, the specific genes for the HE+AD non-lesional and healthy skin difference included known markers of AD and general inflammation such as MMP12, CCL17, CCL27, and several S100A genes.18,19 The 315 genes common to the non-lesional and healthy skin difference of HE+AD and HE-AD included several genes important for the immunology of eczema lesions including SPRR- and S100A genes, IL18, and CCL22.20 Furthermore, the common genes enriched for several immunological processes included interferon-gamma-mediated signaling pathway (GO:0060333) and antigen processing and presentation of exogenous antigen (GO:0019884).

The transcriptome differs between atopic hand eczema and irritant contact dermatitis

When investigating the difference between lesional skin sites according to the etiologies of AD, ACD, and ICD only, we saw that the greatest difference was found between AD and ICD (32 DEGs), followed by the difference between ACD and ICD (six DEGs). Only one (NRK), and not skin relevant gene, was differentially expressed between AD and ACD.

Of the 32 DEGs between AD and ICD, 25 genes were upregulated, and seven genes were downregulated in AD (Supplementary table 3). When investigating the gene ontologies related to the 25 upregulated genes, the top three GO enrichment was related to response to interferon-alpha and mast cell activation (cellular response to interferon-alpha; GO:0035457, response to interferon-alpha; GO:0035455, and mast cell activation; GO:0045576). For the two other differences, too few genes were differentially expressed to conduct gene enrichment analysis.

When looking at the six genes differentially expressed in our study between ACD and ICD we found markers that could have potential for the distinction between ACD and ICD, including EPHA1 and ACTN3. The genes, however, did not distinguish e.g. ACD from AD and the mixed etiologies (Supplementary Figure 7).
The tape strip samples detect gene expression differences between clinical subtypes of hand eczema.

Next, we investigated if the tape strip samples detected gene expression differences according to the clinical subtypes of HE.

A total of 248 DEGs were detected between chronic fissured and vesicular eczema (240 upregulated and eight downregulated in chronic fissured eczema) (data not shown). The 240 upregulated genes did not correlate to any gene enrichment, however, the eight downregulated genes enriched for epidermis development (GO:0008544), cornification (GO:0070268), and tissue development (GO:0009888), mainly due to the involvement of *KRT4, KRT78, RPTN*, and *EMP1*. 
Discussion

Tape strip skin samples can be used to assess the gene expression profile of different localizations on the hands. We showed that the most notable differences between HE-AD and HE+AD were found in non-lesional skin areas. The tape strip skin samples detected transcriptomic differences between etiologies of HE as well as some clinical-morphological subtypes. There seems to be a potential use of non-invasive tape strip samples for detecting new biomarkers to facilitate the molecular investigation of the different subtypes of HE.

To our knowledge, the transcriptomic differences according to localizations on the hands have not yet been investigated in spite of apparent differences such as the epidermis of the palm being thicker than at other localizations on the hands. We saw no difference in the number of protein coding reads from the tape strip samples of healthy skin from different localizations on the hands (palm and dorsum). In contrast, for lesional samples, a statistically significant higher number of protein coding reads was detected from the dorsal samples, but the transcriptomic profile of the palm as compared to the dorsum did not show differences related to specific biological processes from either skin area. This shows that the tape strip samples can be used to investigate the transcriptome of the hands independent of the localization.

When investigating the molecular markers related to the different skin areas (lesional, non-lesional, and healthy) we found that S100A genes were expressed in both lesional and healthy skin. S100A genes are known to be important for the inflammatory process of AD, and have also been shown to be increased in lesions of HE, however they are also expressed in epidermis of healthy skin. The expression of various S100A genes of both lesional and healthy skin on the hands suggests that these genes play a role not only in the pathogenesis of HE, but also in the healthy skin of the hands. Therefore, further studies are needed to establish the role of different S100A genes in healthy and diseased skin of the hands.

The genes related to lesional skin also included CCL17, one of the most reliable biomarkers of AD. Though CCL17 has also been shown to correlate to severity of AD in tape strip samples, we did not see a correlation between CCL17 and HECSI in this study (data not shown). Whether this is due to the scoring system or the biomarker level of CCL17 from the hands needs further investigation.
A recent study by Kumari et al. investigated the protein expression of selected molecular markers of HE and their relation to treatment with alitretinoin. In that study, they found CLDN1, LOR, FLG, KRT10, and TSLP to be related to the lesional skin of HE. In our study, we only rediscovered a difference between healthy and lesional skin for CLDN1. If this is due to the difference in study population, sample type (biopsy versus tape stripping) or proteins versus mRNA is not known. It should be noted that differences in LOR and FLG expression between lesional AD skin and healthy skin has previously been shown by tape strip samples, and therefore the differences are most likely not due to the sampling method.

The largest difference between HE with and without AD was found at the non-lesional skin sites. Non-lesional skin areas of AD patients have previously been shown to have a distinct molecular pattern as compared to healthy skin. We therefore tested if the difference between non-lesional and healthy skin was greater for the HE^{+AD} group. When investigating the difference between non-lesional and healthy skin for the two HE subtypes we could see that the HE^{+AD} group indeed showed common markers of AD, however the genes showing enrichment for inflammatory processes were shared between the two HE subtypes. This indicates that in the HE^{AD} patients, a general skin inflammation was observed even at skin areas distant from the active eczema on the hands.

In this study, HE^{+AD} was defined as HE in patients with current or previous AD. This definition includes historic AD in the HE^{+AD} group though it might not be the cause of their current HE. When considering the etiology of the current HE lesion, only current AD was considered, however, for only two HE^{+AD} patients their AD was not considered relevant for their HE lesion supporting the importance of the impaired skin barrier of AD patients.

When investigating the patients’ current etiologies, we found that the largest transcriptomic difference was between AD only and ICD only. This difference included an upregulation of genes that enriched for the biological process of response to interferon-alpha and mast cell activation, both important for an inflammatory process. This finding suggests that AD^{+HE} patients have a larger activation of mast cells as well as interferon-alpha.

A recent study investigated if machine-learning-driven biomarker discovery could differentiate ACD from ICD. The study was based on applications of known allergens or irritants and was therefore not based on samples from a clinical setting. Furthermore, the skin samples were obtained by skin biopsies,
and therefore included the deeper layers of epidermis and dermis. The study identified 21 genes that in combination made up 28 gene-sets that were able to distinguish the two etiologies. In our study we did not rediscover transcriptomic differences between the biomarkers identified in this study (Supplementary Table 4). This could be due to the differences between gene expression of full biopsy samples vs. stratum corneum tape samples where a major global difference is expected.11

Six genes were differentially expressed between ACD and ICD. These genes included EPHA1, which has been found to be an important marker for a normal epidermal differentiation.34,35 Though the role of EPHA1 in contact dermatitis is not known, the results may have importance for the distinction between ACD and ICD. A study by Tam et al. found LOR as a candidate gene to distinguish ACD from ICD. The study, however, were performed on patch test samples and not on a hand eczema lesion as in our study.36 It should be noted, however, that the biomarkers found in this study had difficulty distinguishing ACD and ICD to the mixed etiologies. Therefore, to study this in detail, larger, more homogenous patient groups should be included to validate this based on the specific etiologies, as well as PCD, which was not included in the current study.

There are some limitations to our study; first, sample size, even though we aimed at fairly large groups for a study of this nature, the mixed etiologies and morphologies meant that the number of patients with some pure forms were limited. The HE+AD group included patients with a history of AD (both current and historical AD). However, only patients with active AD received the AHE etiological sub-diagnosis. We took the non-lesional sample distant from the lesional samples, this may have caused confounding effects, however it can be difficult to be sure that samples are truly non-lesional, if obtained from skin areas adjacent to the inflammatory area on the hands. Patients were asked to abstain from topical anti-inflammatory treatment and emollients for 24 hours before inclusion in the study. A longer wash out period would have been preferable; however, many patients are not willing to abstain from topicals for longer periods and therefore compliance might have been lower with a longer wash out period.

This study shows that the tape strip method is a valuable tool to investigate the transcriptomic differences between HE with and without AD independent of the localization of the lesion. The use of non-invasive skin sampling of the hands enables large-scale studies of HE with no harm to the patients. Furthermore,
the non-invasive tape strip samples show potential for the investigation of the molecular profile related to different etiologies as well as clinical subtypes of HE.
References


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### Tables

**Table 1. Characteristics of study participants.** The study included 12 hand eczema (HE) patients with a history of AD (HE+AD), 18 HE patients with no history of AD (HE-AD), and 16 age matched controls. Severity of the eczema was measured by the Hand Eczema Severity Index (HECSI) and Eczema Area and Severity Index (EASI).

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<td>59.0 [37.0; 66.0]</td>
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<td>58.5 [37.5; 144.5]</td>
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<tr>
<td>EASI, median [IQR]</td>
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**Etiologies of HE**

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<th>HE-AD</th>
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Figure legends

Figure 1. A) Tape strip samples were taken from the hands (a lesional from the patients and a healthy from the controls). Furthermore, a non-lesional tape strip sample was taken from the upper arm of the patients. Whole transcriptome sequencing was performed on RNA extracted from the first two tapes, shipped, and stored at room temperature. B) Differential analysis of dorsum versus palm of healthy skin samples resulted in 15 differentially expressed genes (5 up and 10 down) (adjusted p-value < 0.1, Fold change > 2). B) Differential analysis of dorsum versus palm of lesional skin samples resulted in 63 differentially expressed genes (4 up and 59 down) (adjusted p-value < 0.1, Fold change > 2). Created with Biorender.

Figure 2 A) The principal component analysis (PCA) shows that the largest difference (PC1) between skin areas (lesional (LS), non-lesional (NL) and healthy (NN) skin is found between lesional and healthy/non-lesional skin. B) A total of 2 884 genes are differentially expressed between lesional and healthy skin, 1 012 genes between healthy and non-lesional, and 620 genes between non-lesional and lesional skin areas. The diagram also shows that 364 genes were related to lesional skin, 598 to healthy skin, and 27 to non-lesional skin areas. C) The heatmap shows the mean normalized count of the different skin areas for the top 25 genes differentially expressed between lesional and healthy skin (defined by the smallest Benjamini-Hochberg corrected p-values and a fold change>2) scaled by gene. The table show the adjusted p-values (**=<0.001). Ten of the 25 genes are differentially expressed between all skin area differences. Created with Biorender.

Figure 3 A) Up- and downregulated genes of lesional and non-lesional skin of HE^+AD and HE^-AD respectively. B) Diagram showing the difference between HE^+AD and HE^-AD for non-lesional and lesional skin respectively. C) Schematic of the difference between non-lesional and healthy skin for HE^+AD and HE^-AD respectively, as well as the common differentially expressed genes (DEGs). Created with Biorender.
A

RNA extraction of tape 1 and 2

B

Dorsum vs palm healthy skin samples
45 differentially expressed genes (5 up and 10 down)

C

Dorsum vs palm lesional skin samples
63 differentially expressed genes (4 up and 59 down)

-log(D) (adjusted p-value)

log2FoldChange

-5.0  -2.5  0.0  2.5  5.0

-7.0  -4.0  -1.0  2.0  5.0

Blue: Down-regulated
Gray: Not significant
Red: Up-regulated

COD_14015_Figure1.jpg
A. Up- and downregulated genes between HE^AD versu HE^AD

B. HE^AD versus HE^AD

- Non-lesional skin: Inflammatory response
  - CXCL8
  - S100A12
  - IL1B

- Lesional skin: Activation of Janus kinase activity
  - PRKRA
  - PRKRF

C. Hand eczema with AD

- 1,063 DEGs
- Non-lesional versus healthy skin
- 315 shared DEGs

Hand eczema without AD

- 621 DEGs
- Enrich for immunologic processes

COD_14015_Figure3.jpg