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**Citation for published version (APA):**

Felix Garza, Z. C., Lenz, M., Liebmann, J., Born, M., Arts, I. C. W., Hilbers, P. A. J., & van Riel, N. A. W. (2017). *Gene expression-based cellular profiling of skin in health and inflammatory dermatological conditions*. Abstract from 3rd Dutch Bioinformatics & Systems Biology Conference (BioSB 2017), April 04-05, 2017, Lunteren, The Netherlands, Lunteren, Netherlands.

**Document license:**

Unspecified

**Document status and date:**

Published: 01/01/2017

**Document Version:**

Author's version before peer-review

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# Gene expression-based cellular profiling of skin in health and inflammatory dermatological conditions

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## 1. Introduction

Gene expression has long been used for molecular profiling of a large diversity of conditions including cancer<sup>1</sup>, heart and dermatological diseases<sup>2</sup>. In the field of dermatology, it has led to the discovery of complex gene expression patterns underlying the activation of specific cells infiltrating in skin lesions of chronic inflammatory conditions<sup>3</sup> like psoriasis and atopic dermatitis. The combination of gene expression-based studies with techniques like flow cytometry has allowed the identification of cell types and signalling pathways involved in these diseases. However, the detailed cellular profile, i.e. the number and nature of specific cells, in the lesional and non-lesional phenotypes of these dermatological diseases is not fully characterized. Recently, robust methodologies have been implemented for fast and accurate cellular profiling of diverse diseases based on gene expression data<sup>4,5</sup>. One promising approach is CIBERSORT<sup>6</sup>, which yields the relative fraction of various cell types in a given tissue, using microarray data and a predefined signature matrix as input. In this study, we apply CIBERSORT to inflammatory skin conditions and derive phenotype specific cellular profiles for healthy and diseased skin.

## 2. Materials & Methods

CIBERSORT was originally developed for deconvolution of blood cell types and the study of immune cell infiltration in cancers<sup>7</sup>; thus the signature matrix used by the method did not account for skin-specific cell types. Here, those cell types were first added to the signature matrix based on publicly available expression data from basal and suprabasal epidermal cells. Then, raw microarray data from five studies was gathered from Gene Expression Omnibus. Pooled data comprised skin biopsies from healthy, lesional and non-lesional tissue of patients with psoriasis or atopic dermatitis (Figure 1). The deconvolution analysis was implemented for each dataset and the relative fraction of twenty-six different cell types found in the skin was derived for them.

## 3. Results

To verify an adequate classification of the data by the deconvolution method, the correlation between the cell types included in the signature matrix was first analysed. Based on the correlation analysis, it was concluded that distinguishing

between immune system cells, basal and suprabasal epidermal cells is feasible based on their gene expression. Additionally, cell type specific genes were identified for epidermal cells.

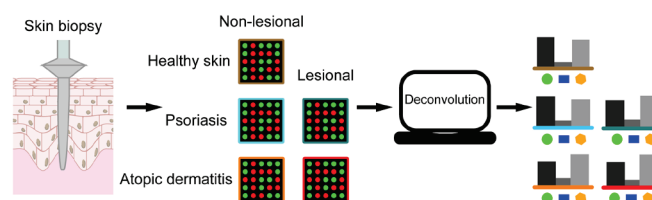


Figure 1. Overview of gene expression-based deconvolution of skin biopsies in healthy and diseased phenotypes.

The deconvolution analysis confirmed the characteristic changes in cellular infiltrates known to be involved in skin lesions of psoriasis and atopic dermatitis. Further, it shed light on the key differences between the lesional and non-lesional phenotypes of these diseases, which differ from healthy skin.

## 4. Discussion

The computer-based cellular profiling of inflammatory skin conditions represents a strong, fast and effective alternative to current experimental methods, which only account for a fraction of the cell types found in the skin<sup>8</sup>. However, the use of this tool in dermatology is currently limited by the signature matrix. In the future other cell types could be included in the signature matrix to strengthen the approach. The application of deconvolution analysis to dermatological diseases is of great interest for tracing the effect of diverse therapeutic approaches.

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