Single-cell analysis of human skin identifies CD14+ type 3 dendritic cells co-producing IL1B and IL23A in psoriasis

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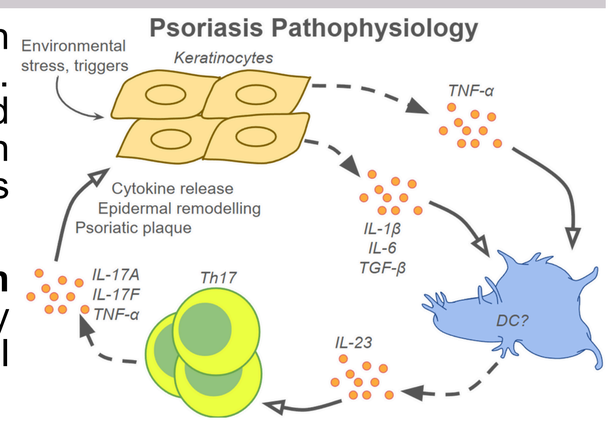
INTRODUCTION

Atopic Dermatitis (AD) and Psoriasis (PSO) are two of the most prevalent chronic inflammatory skin conditions characterized by the presence of activated T cell subtypes secreting pro-inflammatory cytokines. Dendritic cells (DCs) act as a bridge between innate and adaptive immunity by presenting antigens and producing cytokines to shape T cell responses[1]. Previous studies have hinted at a role for DC subsets in inflammatory conditions[2], but the heterogenity of DC populations, cellular sources and functional contributions to PSO pathogenesis have yet to be fully elucidated[3].

The aim of this study was thus to **comprehensively map dendritic cell and macrophage populations in healthy, non-lesional, and lesional skin of PSO and AD patients** at the single-cell level; as well as identify specific subsets of immune cells enriched in diseased skin and characterize their molecular and functional properties.



METHODS

Sample Collection

Biopsies (4mm) were taken from lesional and non-lesional skin of 21 PSO and 15 AD patients, along with healthy controls. The samples were processed into single-cell suspensions.

Analytical Techniques

1. *Flow Cytometry and CyTOF:* Surface protein expression of immune cells was assessed based on the expression of characteristic patterns of surface markers and proteins. This is to generate an unbiased profile of DCs and macrophages
2. Sin*gle-Cell RNA Sequencing (scRNA-seq):* RNA sequencing, via Smart-seq2 protocol, was applied to index-sorted cells to profile gene expression at single-cell resolution. Data integration was performed using Seurat V3[4], enabling unbiased clustering of immune subsets.

RESULTS

Creation of a skin DC and macrophage atlas

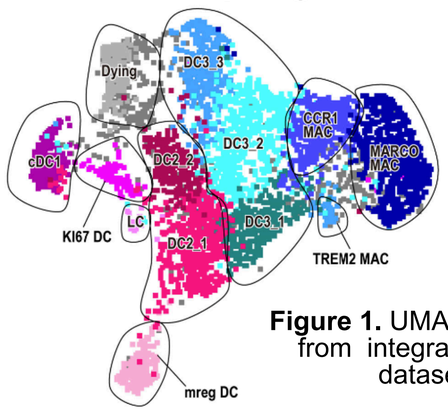


Figure 1. UMAP generated from integration of the datasets.

Increased levels of CD14+ DC3s in PSO lesions

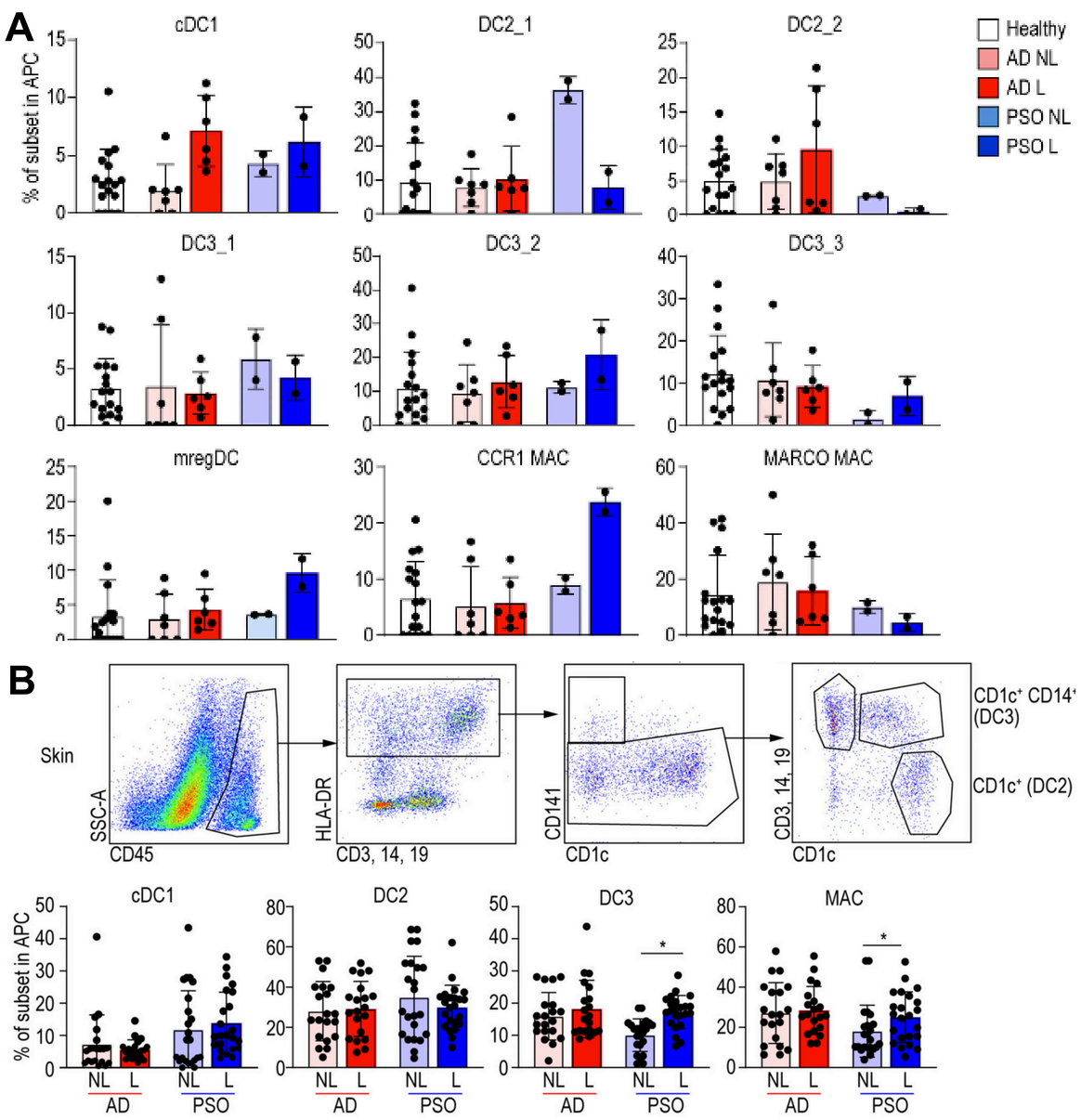


Figure 2. (A) Bar graph of the percentage of each DC and macrophage subset in healthy, nonlesional (NL), and lesional (L) skin from integrated scRNA-seq data **(B)** Flow-cytometric analysis of each DC and macrophage in skin of healthy subjects and AD (14 samples) and PSO (16 samples) patients.

Production of cytokines IL1B and IL23A by CD14+ DC3s in PSO lesional skin

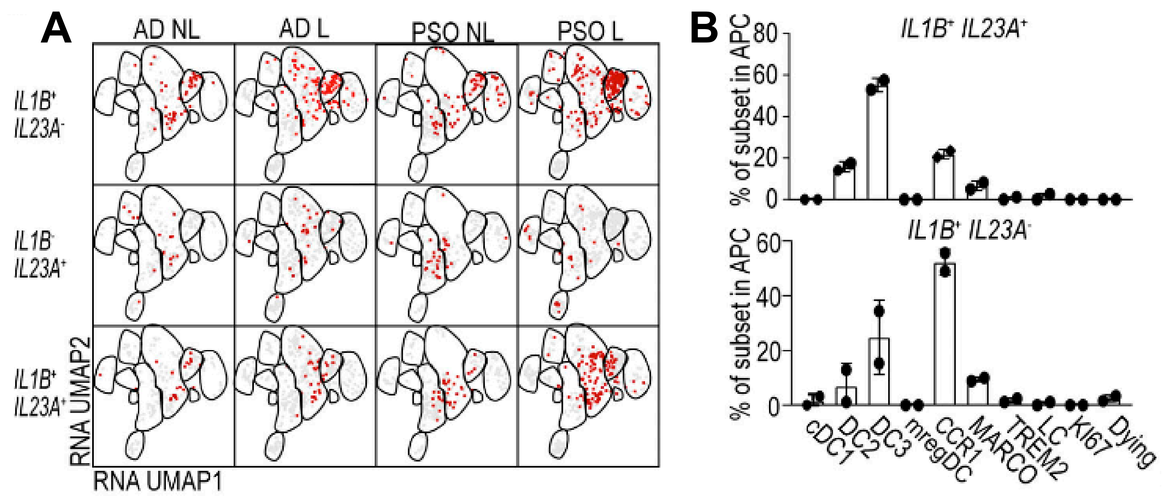


Figure 3. (A) Dot plot of IL1B- and IL23A-producing cells in nonlesional and lesional skin from AD and PSO patients. **(B)** Bar graph of the percentage of IL1B and IL23A double-positive and IL1B single-positive cells within each DC and macrophage subset in PSO lesional skin.

IL1B/IL23A double positive CD14+ DC3s express SLC2A3 (GLUT3)

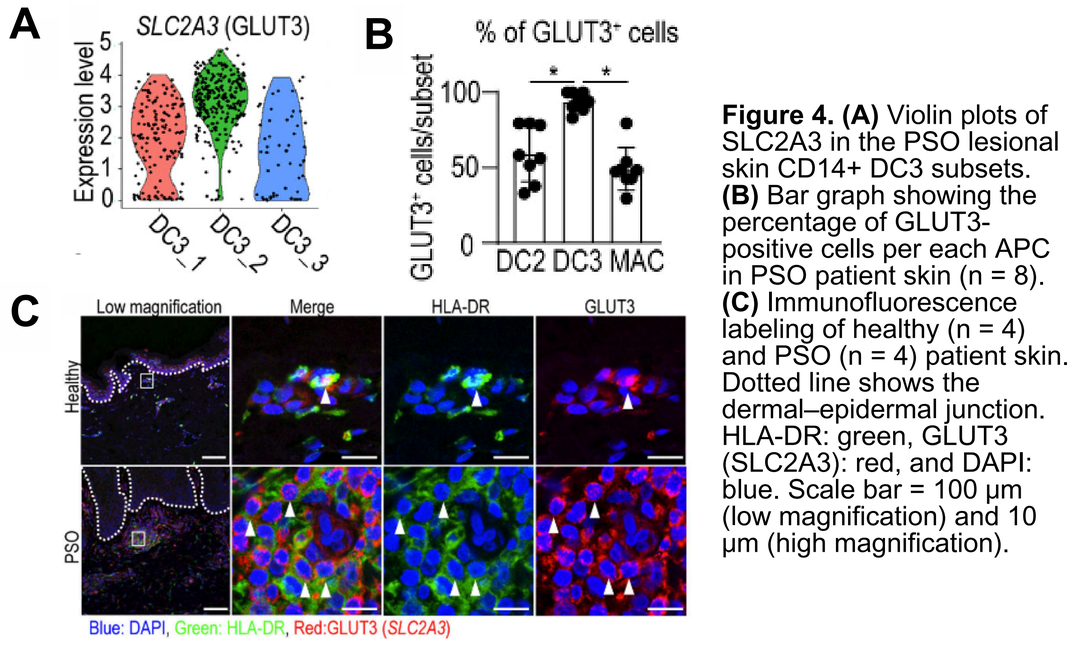
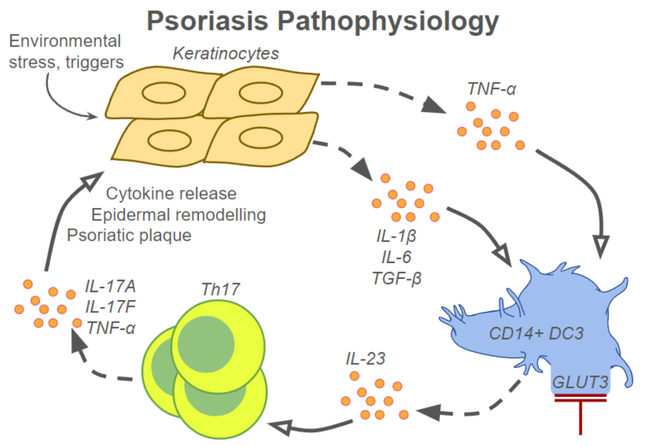


Figure 4. (A) Violin plots of SLC2A3 in the PSO lesional skin CD14+ DC3 subsets. **(B)** Bar graph showing the percentage of GLUT3-positive cells per each APC in PSO patient skin (n = 8). **(C)** Immunofluorescence labeling of healthy (n = 4) and PSO (n = 4) patient skin. Dotted line shows the dermal–epidermal junction. HLA-DR: green, GLUT3 (SLC2A3): red, and DAPI: blue. Scale bar = 100 μm (low magnification) and 10 μm (high magnification).

CONCLUSION

- Psoriasis skin shows increased populations of DC3
- In lesional PSO skin, CD14+ DC3s coexpressed IL1B and IL23A, cytokines at the centre of PSO pathophysiology[5]
- Majority of CD14+ DC3s express SLC2A3 (GLUT3)
- GLUT3 expressing cells have been validated in situ in lesional skin using immunofluorescence

Figure 5. Illustration of the pathophysiology of PSO, and the potential pharmacological applications of the paper's findings on GLUT3 positive CD14+ DC3s.



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