

Integrated microbiome–metabolome analysis identifies a *Staphylococcus aureus*-associated decanoic acid inflammatory pathway in seborrheic dermatitis

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Abstract

Seborrheic dermatitis (SD) is a common inflammatory dermatosis whose pathogenic drivers remain incompletely understood. We integrated bacterial 16S rRNA gene and fungal ITS1 amplicon profiling with scalp metabolomics in patients with SD and healthy controls. Lesional skin showed *Staphylococcus* enrichment and *Cutibacterium* depletion, without a corresponding increase in *Malassezia*. Decanoic acid (DA) was elevated in SD scalp and showed positive nominal associations with *Staphylococcus* abundance and qPCR-measured *S. aureus*. In a tape-stripped mouse model, *S. aureus* exposure was accompanied by increased cutaneous DA and remodeling of the fatty-acid profile. Topical DA phenocopied several features observed after *S. aureus* exposure, including epidermal thickening, inflammatory-cell recruitment, and increased IL-1 β staining. RNA sequencing identified 1,134 differentially expressed genes shared by DA- and *S. aureus*-treated skin, involving inflammatory, chemotactic, and epidermal-differentiation programs. Together, these data identify an *S. aureus*-associated DA response and provide functional evidence that DA can contribute to cutaneous inflammation and perturbed epidermal differentiation in SD.

Introduction

Seborrheic dermatitis (SD) is a chronic inflammatory disorder that preferentially affects sebaceous-rich areas of the skin, including the scalp and face. Although microbial dysbiosis has been suggested to play a role in SD, the exact mechanisms linking cutaneous microbial ecology to epidermal inflammation remain incompletely understood.¹ Current models emphasize the interaction among sebaceous lipids, epidermal susceptibility, and host immune responses, but the microbial metabolites that connect these processes have not been clearly defined.²

Malassezia (*M.*) has traditionally been regarded as a central contributor to SD. However, the quantity of *Malassezia* species on the skin does not consistently parallel disease activity, and clinical improvement after antifungal treatment is not always accompanied by a proportional reduction in *Malassezia* abundance.^{3–4} These observations suggest that fungal abundance alone is insufficient to explain SD and that other microbial communities or microbial functions may participate in disease-associated inflammation.

Increasing evidence indicates that bacterial community composition is also altered in SD, with changes involving *Staphylococcus* (*S.*), *Cutibacterium*, and other members of the skin microbiota⁵. Nevertheless, sequencing-based observations do not establish whether an enriched bacterial taxon is functionally connected to the host lipid environment. This distinction is particularly relevant for *Staphylococcus*, because genus-level enrichment does not identify the responsible species or define the metabolic pathway involved. *S. aureus* can interact with sebum-derived substrates and has the enzymatic capacity to modify extracellular lipids, raising the possibility that bacterial activity may influence the microenvironment of SD lesions.^{6–7}

Skin-surface fatty acids are not only structural components of the epidermal barrier but can also influence keratinocyte differentiation and innate immune signaling.⁸ Alterations in fatty-acid composition may therefore provide a mechanistic link between microbial dysbiosis and cutaneous inflammation.^{2,9} However, whether a specific fatty acid is associated with *Staphylococcus* expansion in SD, whether this association extends to *S. aureus*, and whether the metabolite is sufficient to reproduce SD-like inflammation remain unknown.

In this study, we integrated bacterial and fungal community profiling with scalp metabolomics and microbe–metabolite correlation analysis in patients with SD and healthy controls. We then examined the effects of *S. aureus* exposure on the cutaneous fatty-acid profile in mice and tested whether topical application of a specific fatty acid could reproduce inflammatory and epidermal-differentiation abnormalities observed after *S. aureus* exposure.

Materials and methods

1. Recruitment of participants

A recruitment cohort comprising 44 patients with scalp SD, 31 patients with facial SD, and 41 age- and sex-matched healthy controls (HC; 26 scalp and 15 facial controls) was enrolled at Peking University First Hospital between March 2021 and May 2022. SD was diagnosed clinically by dermatologists using predefined diagnostic criteria. Participants with other inflammatory or infectious dermatoses, systemic malignancy, severe uncontrolled chronic disease, recent systemic antibiotics, corticosteroids, or immunosuppressants (within 3 months), or topical treatment (within 4 weeks) were excluded. The study was approved by the Institutional Review Board of Peking University First Hospital (2021-006), and written informed consent was obtained from all participants. Clinical trial number: not applicable.

2. Clinical sampling and sample processing

At each sampling site, sterile PBS-moistened swabs were collected from SD lesional skin (LS) and, when available, matched non-lesional skin (NLS); HC samples were collected from the corresponding anatomical site. Participants refrained from shampooing and from applying topical products for 24 h before sampling. Each area was sampled using a standardized number of firm strokes. Parallel swabs were collected for microbial DNA and metabolomics, placed into sterile tubes, and immediately stored at – 20°C or snap-frozen in liquid nitrogen and stored at – 80°C, respectively. Sample identity, anatomical site, lesion status, processing time, and assay allocation were recorded before laboratory analysis. The individual participant, rather than the technical replicate, was treated as the biological experimental unit.

3. Bacterial and fungal amplicon sequencing

Genomic DNA was extracted using the DNeasy Blood and Tissue Kit (Qiagen, Hilden, Germany) according to the manufacturer's instructions. The fungal ITS1 region and bacterial 16S rRNA gene V3–V4 region were amplified using ITS1 primers (5'-GGAAGTAAAAGTCGTAACAAGG-3' and 5'-GCTGCGTTCTTCATCGATGC-3') and 16S primers (5'-CCTACGGGNGGCWGCAG-3' and 5'-GACTACHVGGGTATCTAATCC-3'), respectively^{10–11}. Amplicons were sequenced on an Illumina HiSeq 2500 platform (Novogene, Beijing, China)¹². Reads were quality filtered, denoised, merged, and screened for chimeras using QIIME 2¹³ with DADA2-based processing. Taxonomy was assigned using UNITE v8.0 for fungi and SILVA for bacteria. A subset of samples overlapped with or was cross-referenced to previously published datasets^{5,14}.

4. Species-specific qPCR

Species-specific SYBR Green qPCR was used to quantify *S. aureus* and *S. epidermidis* in scalp samples. The *S. aureus* nuc assay used the forward primer 5'-GTTGCTTAGTGTTAACTTTAGTTGTA-3' and reverse primer 5'-AATGTGCGCAGGTTCTTTATGTAATTT-3'¹⁵. The *S. epidermidis* *sodA* assay used the forward primer 5'-TCAGCAGTTGAAGGGACAGAT-3' and reverse primer 5'-CCAGAACAATGAATGGTTAAG-3'¹⁶. Species-specific signals were normalized to the bacterial 16S rRNA gene signal and expressed as 16S-normalized relative quantities calculated as $2^{-\Delta Cq}$, where $\Delta Cq = Cq(\text{target}) - Cq(16S)$. Values were not converted to percentages.

5. Untargeted metabolomics

Swab samples were resuspended in 1,000 μL pre-chilled 80% methanol, vortexed, incubated on ice for 5 min, and centrifuged at $15,000 \times g$ for 20 min at 4°C. The supernatant was lyophilized and reconstituted in 10% methanol. UHPLC–MS/MS was performed using a Vanquish UHPLC system coupled to an Orbitrap Q Exactive HF-X mass spectrometer (Thermo Fisher Scientific, Germany). Chromatographic separation used a Hypersil Gold column (100 $\times$ 2.1 mm, 1.9 μm) with a 12-min gradient. Positive-mode mobile phases were 0.1% formic acid and methanol; negative-mode mobile phases were 5 mM ammonium acetate (pH 9.0) and methanol. Raw files were processed in Compound Discoverer 3.1 for peak detection, alignment, and quantification. Metabolites were annotated using mzCloud, mzVault, and MassList databases, and pathway annotation was performed using KEGG. Differential metabolites were evaluated using prespecified effect-size and statistical thresholds with Benjamini–Hochberg false-discovery-rate control.

6. Mouse topical-exposure model

S. aureus (ATCC 25923) and *M. globosa* (ATCC 96807) were cultured on blood agar (37°C, 48–72 h) and Dixon agar (37°C, 72–96 h), respectively. C57BL/6 wild-type female mice (specific-pathogen-free grade), aged 6–8 weeks, were purchased from Sybf (Beijing) Biotechnology Co., Ltd. and acclimated in a

specific-pathogen-free facility. Dorsal skin was mildly tape-stripped three times before topical exposure. Mice were randomly assigned to vehicle, decanoic acid (DA), *S. aureus*, or *M. globosa* groups. DA was applied at 1 mM and microorganisms at 5×10^6 CFU/mL, with 100 μ L applied once daily for 7 consecutive days; vehicle-treated mice received PBS. Animals, cage allocation, intervention timing, and assay-specific sample sizes are reported in the relevant figure legends. Investigators performing histological, flow-cytometric, and image-based quantification were blinded to treatment group whenever feasible. Mice were anesthetized with 2.5% isoflurane during the experimental procedures. At the final sampling, skin was collected under anesthesia for lipidomics, RNA sequencing, flow cytometry, histology, and immunohistochemistry. Following skin collection, mice were euthanized by cervical dislocation.

7. RNA sequencing

Total RNA was extracted from mouse skin using TRIzol Reagent (Invitrogen). RNA concentration and integrity were assessed using an Agilent 5300 Bioanalyzer and NanoDrop ND-2000 spectrophotometer. Libraries were prepared using the Illumina Stranded mRNA Prep kit and sequenced on a NovaSeq X Plus platform. Reads were aligned to the appropriate mouse reference genome, and transcript abundance was quantified with RSEM¹⁷. Differential expression was analyzed using DESeq2 with prespecified contrasts of DA versus vehicle, SA versus vehicle, and MG versus vehicle. Differentially expressed genes were defined as $|\log_2 \text{ fold change}| \geq 1$ and $\text{FDR} < 0.05$. Gene Ontology and KEGG enrichment analyses were performed using GOATOOLS and KOBAS^{18–19}.

8. Targeted fatty-acid quantification

Targeted fatty-acid quantification was performed using a UHPLC–QTRAP 6500 + system (AB SCIEX, USA). Skin homogenates were extracted with isopropanol/acetonitrile (1:1) containing isotopically labelled or otherwise specified internal standards. Chromatographic separation was performed on a Waters ACQUITY UPLC BEH C18 column maintained at 50°C, and analytes were acquired in negative-ion multiple-reaction-monitoring mode. Decanoic acid was quantified using the same prespecified analytical workflow as the other fatty acids.

9. Skin-cell isolation and flow cytometry

Skin was minced and digested for 1 h at 37°C in collagenase (0.4 mg/mL), trypsin (1 mg/mL), and DNase I (0.1 mg/mL; Solarbio, China). Cell suspensions were filtered through a 70- μ m mesh, subjected to red-blood-cell lysis, and blocked with anti-CD16/32 (BioLegend, USA). Cells were stained with fluorochrome-conjugated antibodies against CD45, CD3, CD4, CD11b, Ly6G and Siglec-F, filtered through a 40- μ m mesh, and analyzed using a BD LSRFortessa II. FlowJo v10.8 was used for analysis.

10. Histology and immunohistochemistry

Skin specimens were fixed in 10% neutral-buffered formalin, paraffin-embedded, and sectioned at 4–5 μm . Sections were subjected to the prespecified antigen-retrieval procedure, treated with 3% H₂O₂ to block endogenous peroxidase, and blocked with 5% BSA. Primary antibodies against IL-1 β , cytokeratin 1 (CK1), and cytokeratin 10 (CK10) were incubated overnight at 4°C, followed by enzyme-conjugated secondary antibodies, chromogenic development, and haematoxylin counterstaining. Images were acquired using a NanoZoomer S60 scanner and analyzed with NDP.view2 (Hamamatsu, Japan). H-scores were calculated using a prespecified intensity-by-positive-area method from blinded image measurements; the number of sections and fields analyzed per animal is reported in the figure legends.

11. Statistical analysis and reproducibility

All tests were two-sided and were performed in R (v4.1.2) or GraphPad Prism 9. Data distribution was assessed before selecting parametric or non-parametric tests. Paired LS–NLS comparisons used the Wilcoxon signed-rank test; independent two-group comparisons used Welch's t-test or the Wilcoxon rank-sum test, as appropriate; and comparisons among four mouse groups used one-way ANOVA with Tukey correction or Kruskal–Wallis testing with Dunn's correction, according to distribution and variance assumptions. Associations were assessed using Spearman's rank correlation. Partial least squares-discriminant analysis (PLS-DA) was performed to visualize the metabolic differences among groups. Multiple comparisons were adjusted using the Benjamini–Hochberg procedure. Results are reported as mean $\pm$ standard deviation, as indicated in the figure legends, with individual biological replicates. A *p*-value of less than 0.05 was considered statistically significant.

Results

1. Lesional SD skin exhibits a bacterial dysbiosis centered on

1. Lesional SD skin exhibits a bacterial dysbiosis centered on *Staphylococcus*

We first profiled scalp and facial microbial communities using bacterial 16S rRNA gene V3–V4 and fungal ITS1 amplicon sequencing. Bacterial NMDS ordinations showed partial overlap among SD.LS, SD.NLS and HC samples, whereas genus-level profiles suggested a lesion-associated shift at both anatomical sites (Fig. 1a,b). *Cutibacterium* and *Staphylococcus* were the dominant bacterial genera. *Staphylococcus* relative abundance was higher in SD.LS than in SD.NLS and HC skin, whereas *Cutibacterium* showed the reciprocal pattern in scalp and facial samples (Fig. 1a-c). Species-specific qPCR showed that 16S-normalized *S. aureus* relative quantity was higher in SD than in HC scalp, whereas *S. epidermidis* did not differ significantly (Fig. 1d).

Fungal communities were dominated by *Malassezia*, but its relative abundance did not differ significantly among groups (Fig. 1e,f; Supplementary Fig. 1a). Fungal NMDS plots showed broad overlap (Fig. 1e,f). Within the limits of relative-abundance profiling and the available sample size, these data indicate a more prominent bacterial compositional shift than a lesion-associated expansion of *Malassezia* in this cohort.

2. Scalp metabolomics nominates decanoic acid as an SD-associated metabolite

We next analyzed untargeted LC–MS/MS profiles from 22 SD and 22 HC scalp samples. The PLS-DA score plot showed separation between groups (Fig. 2a). The observed R^2 was 0.810 and the permutation-test p value was 0.004 (Fig. 2b). Differential-feature analysis indicated broad metabolic differences, including fatty-acid features (Fig. 2c). DA was higher in SD than in HC samples ($p < 0.001$), and eicosapentaenoic acid was also increased ($p < 0.05$; Fig. 2d).

3. and abundance track with decanoic acid

3. *Staphylococcus* and *S. aureus* abundance track with decanoic acid

We integrated microbiome and metabolome profiles in the scalp cohort. A correlation matrix comprising the five most abundant bacterial genera and 15 fatty acids showed a positive nominal association between *Staphylococcus* relative abundance and DA and predominantly inverse associations for *Cutibacterium* ($\rho = 0.325$, nominal $p = 0.036$; Fig. 3a,b).

A positive association was also observed using species-specific qPCR: 16S-normalized *S. aureus* relative quantity correlated with DA ($\rho = 0.441$, nominal $P = 0.004$; Fig. 3c). In contrast, the dominant fungal genera showed weaker associations with the fatty-acid panel, and *Malassezia* was not correlated with DA ($\rho = -0.086$, $p = 0.588$; Supplementary Fig. 2).

5. Decanoic acid reproduces key inflammatory and tissue-remodeling features of exposure

5. Decanoic acid reproduces key inflammatory and tissue-remodeling features of *S. aureus* exposure

We next asked whether exogenous DA was sufficient to reproduce tissue features observed after *S. aureus* exposure. DA- and *S. aureus*-treated skin showed erythema/scaling, epidermal thickening, and increased dermal inflammatory-cell infiltration relative to vehicle, whereas *M. globosa* produced a milder phenotype (Fig. 5a,b; Supplementary Fig. 3a). Immunohistochemistry showed increased IL-1 β staining in the DA and *S. aureus* groups (Fig. 5b). Flow cytometry identified increased neutrophil recruitment in both groups, and additional analyses indicated increased CD3 + T-cell accumulation after DA or *S. aureus* exposure compared with vehicle and *M. globosa* controls (Fig. 5c; Supplementary Fig. 3b). Eosinophil abundance did not differ significantly among groups (Supplementary Fig. 3b).

Together, the histological, immunohistochemical and flow-cytometric results show that exogenous DA is sufficient to reproduce several inflammatory features observed after *S. aureus* exposure in this tape-stripped mouse model.

6. DA and converge on inflammatory, chemotactic, and epidermal-differentiation programs

6. DA and *S. aureus* converge on inflammatory, chemotactic, and epidermal-differentiation programs
To define the host programs associated with these phenotypes, we performed RNA-seq across the DA-, *S. aureus*-, *M. globosa*-, and vehicle-treated mice skin. PCA showed clear treatment-associated structure in the transcriptomes (Fig. 6a). Relative to vehicle, DA treatment yielded 1,573 differentially expressed genes (DEGs), *S. aureus* yielded 1,776 DEGs, and *M. globosa* yielded 888 DEGs (Fig. 6b). DA and *S. aureus* shared 1,134 DEGs, indicating substantial convergence between the metabolite- and bacterium-induced responses (Fig. 6c).

The shared-expression heatmap highlighted genes involved in inflammation and chemotaxis, including *Il1b*, *Il6*, *Cxcl1*, *Cxcl2*, *Cxcl13*, *S100a8*, and *S100a9*, together with epidermal differentiation-associated keratins (Fig. 6d). The concordant DA/*S. aureus* signature provides a molecular bridge between DA accumulation and the inflammatory phenotype observed in the tissue assays.

We further examined CK1 and CK10 expression in mouse skin. CK10 immunostaining and H-score analysis showed lower CK10 expression following DA exposure ($p = 0.019$; Fig. 6e,f). CK1 staining likewise showed a numerically lower signal in the DA-treated group, although the difference did not reach statistical significance in the available samples ($p = 0.082$; Supplementary Fig. 3d).

The combined transcriptomic and histological evidence therefore supports a model in which *S. aureus* exposure and exogenous DA are associated with overlapping inflammatory responses and perturbed epidermal differentiation.

Discussion

Our study identifies a bacteria–lipid–host response pattern that extends the conventional *Malassezia*-centred view of SD. Across scalp and facial skin, SD lesions showed increased *Staphylococcus* and reduced *Cutibacterium* relative abundance, whereas *Malassezia* remained dominant but did not show a consistent lesion-associated expansion. This pattern is compatible with previous studies indicating that SD is not explained by fungal abundance alone and that bacterial community structure can distinguish lesional from healthy skin^{2,4,20}. Species-targeted qPCR linked the genus-level *Staphylococcus* signal specifically to *S. aureus*, whereas *S. epidermidis* was not significantly altered. These data identify a lesion-associated bacterial feature without implying that every member of the *Staphylococcus* genus is pathogenic.

The metabolomic analysis provided the second component of this model. We prioritized DA because it was elevated in scalp SD and showed positive associations with *Staphylococcus* relative abundance and qPCR-measured *S. aureus*. This selection is biologically plausible because skin lipids participate in barrier integrity and antimicrobial defence, and *S. aureus* can interact with and remodel host-associated

fatty acids^{21–24}. Importantly, the human correlations are cross-sectional and do not establish that *S. aureus* produces DA, that the association is independent of compositional effects or clinical confounding, or that DA is the only metabolite contributing to the phenotype.

The mouse experiments provided functional support for the association. Topical *S. aureus* exposure was accompanied by an altered cutaneous fatty-acid profile and increased DA, whereas exogenous DA reproduced several features observed after *S. aureus* exposure, including epidermal thickening, IL-1 β induction, and recruitment of neutrophil and CD3 + T-cell populations. The directionally similar inflammatory responses are consistent with previous work showing that *S. aureus* can amplify epithelial danger signalling and leukocyte recruitment in barrier-disrupted skin²⁵. Nevertheless, increased DA after *S. aureus* exposure could reflect direct bacterial metabolism, host lipid remodeling, or both. The tape-stripped topical-exposure model is a mechanistic reduction of SD biology rather than a complete reconstruction of human disease.

The RNA-sequencing data further connected the microbial and metabolite perturbations. DA- and *S. aureus*-treated skin shared 1,134 DEGs involving inflammatory, chemotactic and epidermal-differentiation programs. Expression patterns involving IL1b, IL6, CXCL1, CXCL2, S100A8, S100A9 and keratin-associated genes, together with reduced CK10 immunoreactivity, are consistent with overlapping effects on a keratinocyte–myeloid inflammatory circuit. However, shared DEG membership alone does not demonstrate concordant direction or establish mediation; replicate-level expression and fold-change concordance analyses are needed. The more limited response to *M. globosa* under these experimental conditions suggests that the dominant signal in this model was associated with bacterial/lipid exposure, but it should not be interpreted as excluding a role for *Malassezia* in human SD.

Several limitations define the scope of these conclusions. First, the human cohort was cross-sectional, so the temporal sequence linking dysbiosis, DA accumulation and inflammation cannot be established, and residual clinical confounding is possible. Second, relative-abundance and genus-level analyses are vulnerable to compositional effects and do not resolve strain-specific functions; paired and composition-aware sensitivity analyses are required. Third, the correlation screen involved multiple taxa–metabolite comparisons, and its interpretation depends on FDR-adjusted results. Fourth, neither direct microbial production of DA nor the necessity of DA for *S. aureus*-induced inflammation was tested using isotope tracing, bacterial mutants, enzyme inhibition, or rescue/blockade experiments. Fifth, the mouse model used controlled topical exposure after tape stripping and requires confirmation of microbial burden, vehicle equivalence, and quantitative epidermal-thickness outcomes. Finally, the small sample size of individual histological assays, particularly CK10/CK1 H-score analyses, limits precision. Future work manipulating fatty-acid production or signalling and characterizing keratinocyte responses will be needed to test causality.

Taken together, our findings support a testable model in which lesion-associated *S. aureus* is coupled to DA accumulation and overlapping inflammatory and epidermal-differentiation responses. This framework does not replace the established role of *Malassezia*; rather, it places fungal and bacterial

components within a metabolically connected skin ecosystem. The *S. aureus*-associated DA pathway is therefore a candidate mechanism and potential therapeutic target that requires direct production and intervention studies before causal or translational conclusions can be drawn.

Declarations

Competing interests: The authors declare no competing interests.

Author Contributions

Rong Tao and Ruojun Wang performed the research. Rong Tao, Ruojun Wang, and Ruoyu Li designed the study. Rong Tao, Ruojun Wang, and Zhe Wan contributed essential reagents or tools. Rong Tao and Ruojun Wang analyzed the data. Rong Tao wrote the original draft. Ruojun Wang and Ruoyu Li reviewed and edited the manuscript.

Ethics approval and consent to participate: The human study was approved by the Institutional Review Board of Peking University First Hospital (2021-006) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants, which included consent for data sharing. All animal procedures were approved by the Biomedical Research Ethics Committee of Peking University First Hospital (Approval No. 2025-069).

Consent for publication: Not applicable.

Availability of data and materials: The bacterial 16S rRNA gene and fungal ITS amplicon sequencing data generated during this study are publicly available in the NCBI BioProject repository under accession numbers PRJNA1513736 (16S rRNA) and PRJNA1513469 (ITS).

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Figures

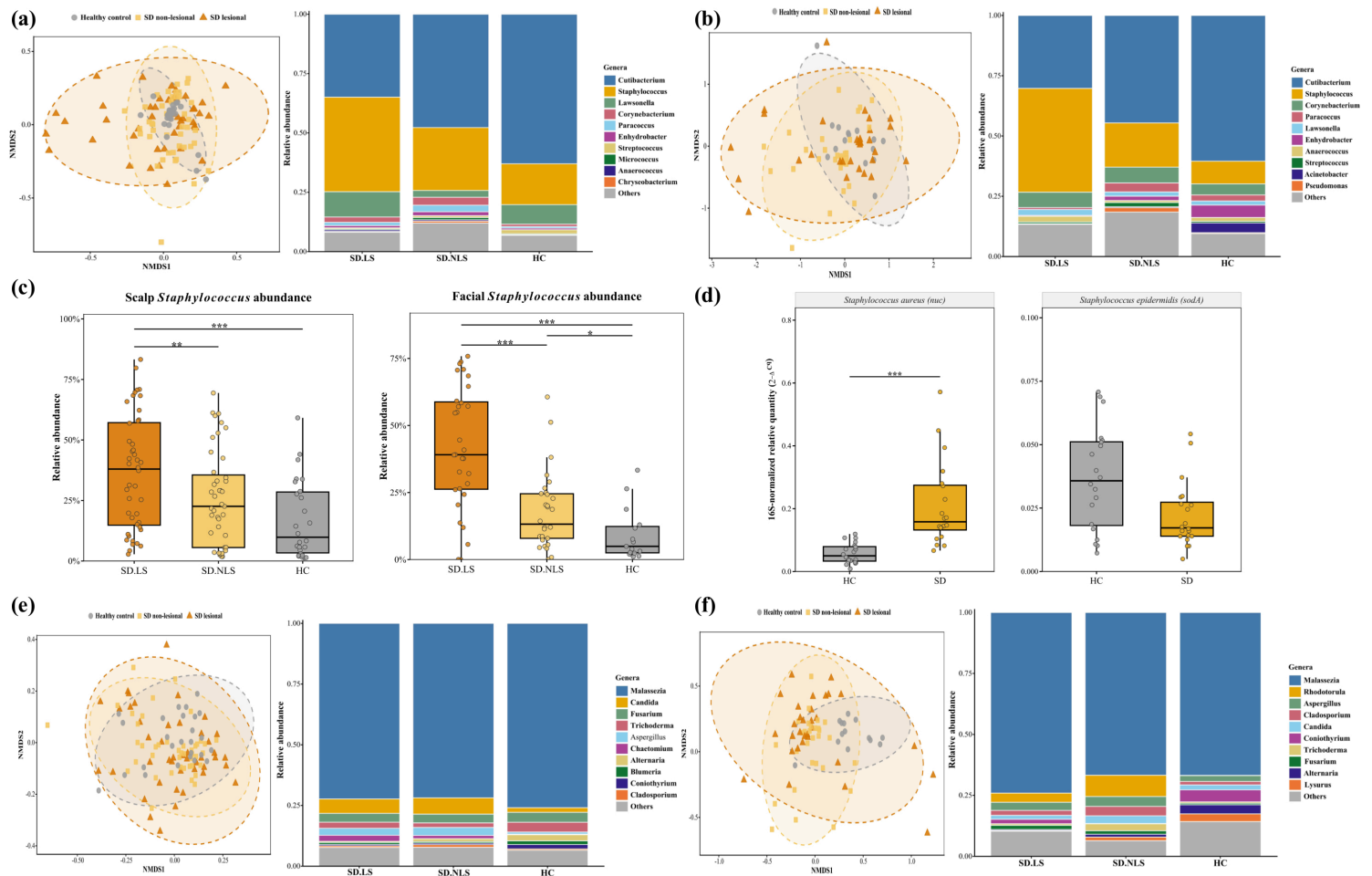


Figure 1

Skin microbial community structure and *Staphylococcus* abundance in scalp and facial seborrheic dermatitis. (a) Scalp bacterial NMDS ordination and group-level genus relative-abundance profile. (b) Facial bacterial NMDS ordination and group-level genus relative-abundance profile. (c) Boxplots with individual observations showing *Staphylococcus* relative abundance in scalp and facial samples. (d) Boxplots with individual observations showing 16S-normalized relative quantities ($2^{-\Delta C_q}$) of *S. aureus* (nuc) and *S. epidermidis* (sodA) in scalp samples. (e) Scalp fungal NMDS ordination and genus relative-

abundance profile. (f) Facial fungal NMDS ordination and genus relative-abundance profile. SD, LS, lesional SD; SD, NLS, non-lesional SD; HC, healthy control.

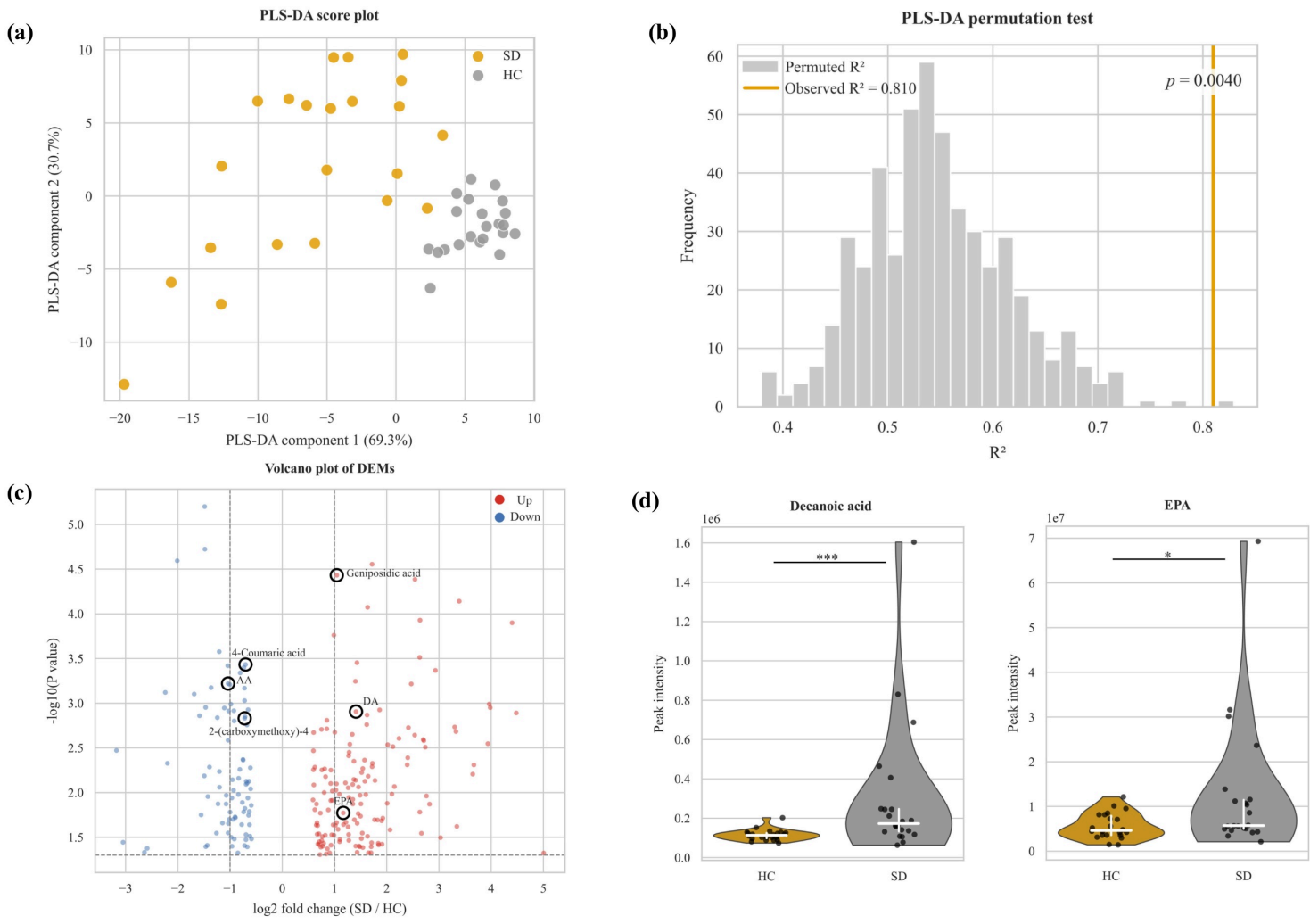


Figure 2

Scalp metabolomic profiles in participants with seborrheic dermatitis and healthy controls. (a) PLS-DA score plot. (b) Permutation test for the PLS-DA model. (c) Volcano plot of differential metabolic features, with selected annotations highlighted. (d) Violin plots with individual observations for DA and eicosapentaenoic acid. SD, seborrheic dermatitis; HC, healthy control; PLS-DA, partial least-squares discriminant analysis

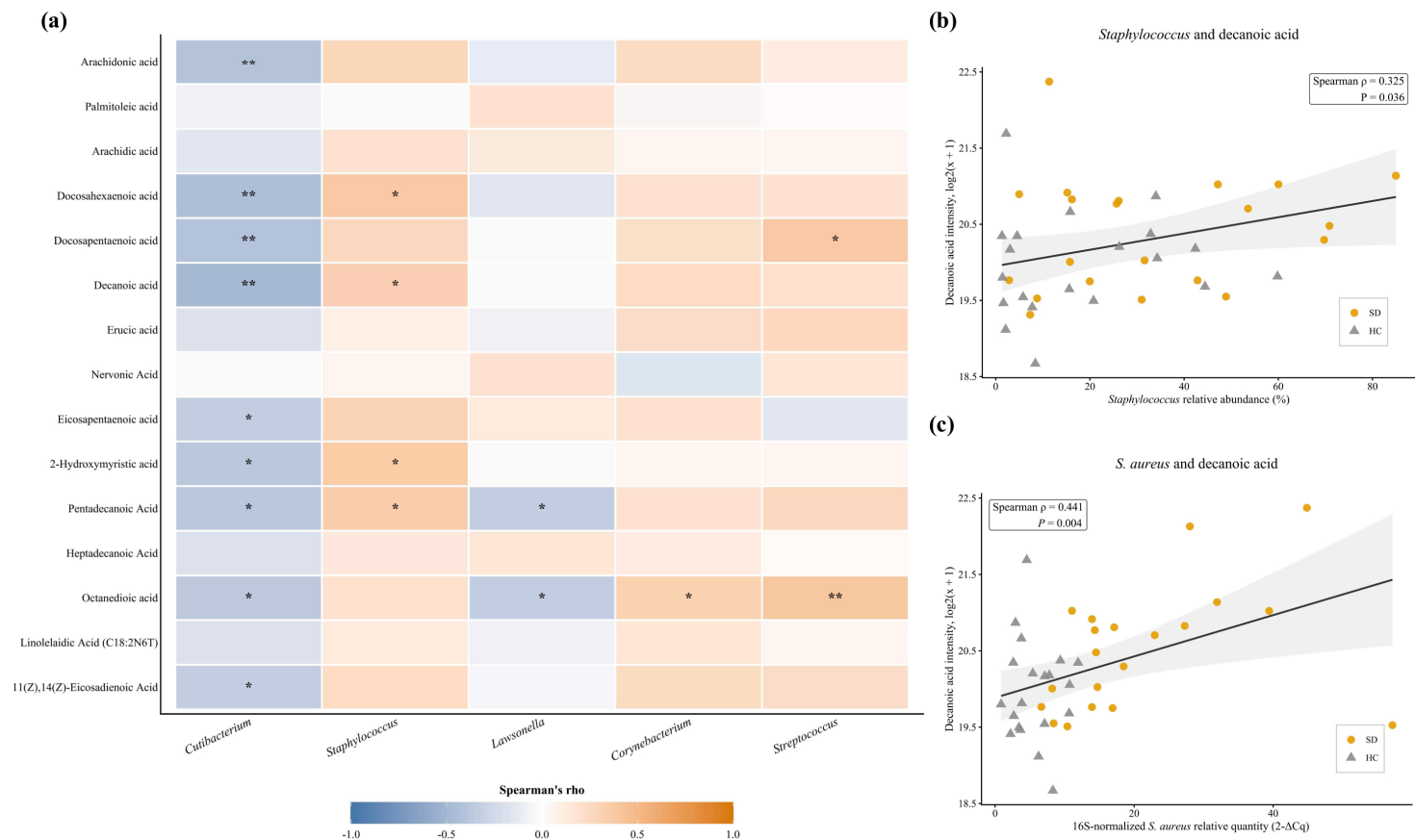


Figure 3

Integrated bacterial–metabolite associations in the pooled scalp cohort. (a) Spearman correlation heatmap between the five most abundant bacterial genera and 15 fatty acids. (b) Association between *Staphylococcus* relative abundance and DA. (c) Association between 16S-normalized *S. aureus* relative quantity ($2^{-\Delta Cq}$) and DA. Shaded bands denote 95% confidence intervals for the displayed fitted lines; inference was based on Spearman correlation.

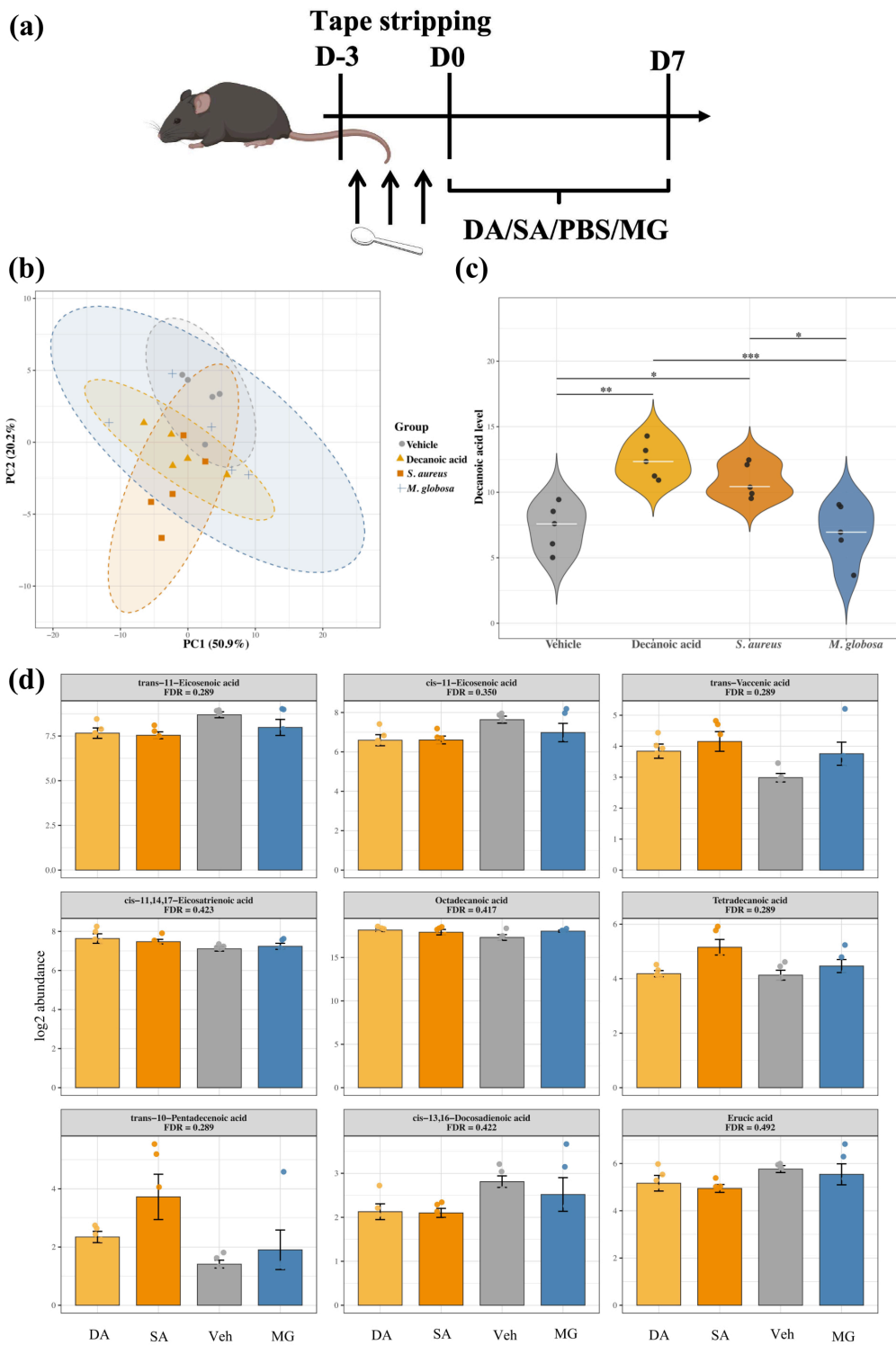


Figure 4

Cutaneous fatty-acid profiles after topical exposure in mice. (a) Experimental exposure scheme. (b) PCA of targeted fatty-acid profiles. (c) DA abundance across vehicle-, DA-, *S. aureus*- and *M. globosa*-treated groups. (d) Group comparisons for the displayed fatty acids. DA, decanoic acid; SA, *S. aureus*; MG, *M. globosa*.

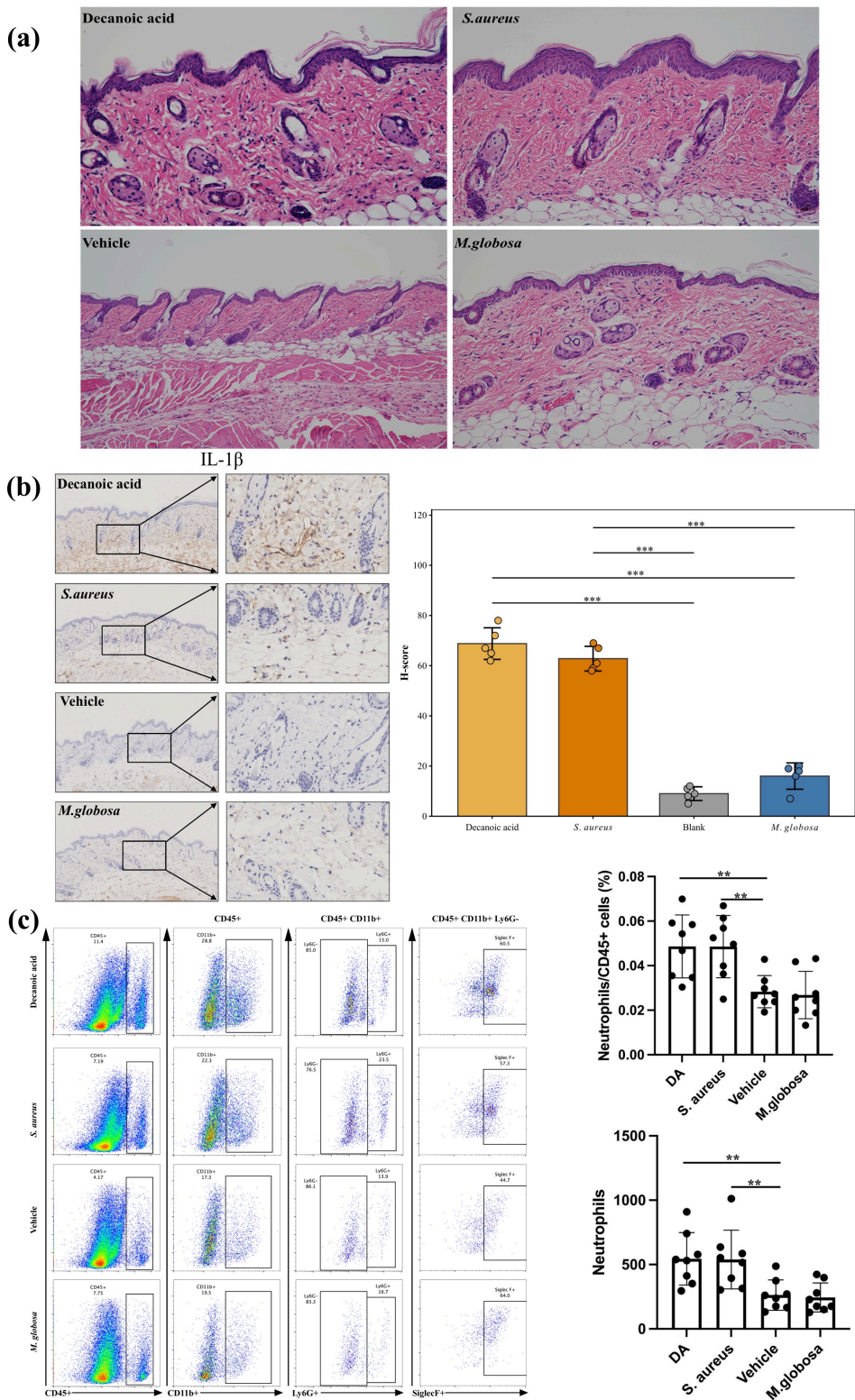


Figure 5

Decanoic acid and *S. aureus* induce inflammatory changes in tape-stripped mouse skin. (a) Representative haematoxylin-and-eosin-stained skin sections from DA-, *S. aureus*-, vehicle- and *M. globosa*-treated mice, showing epidermal and dermal morphology. (b) Representative IL-1 β immunohistochemistry at low and higher magnification, with corresponding H-score quantification. (c) Representative flow-cytometric gating strategy used to identify CD45+ leukocytes, CD11b+ myeloid cells,

Ly6G+ neutrophils and Siglec-F+ cells, with quantification of neutrophil frequency among CD45+ cells and absolute neutrophil number. DA, decanoic acid.

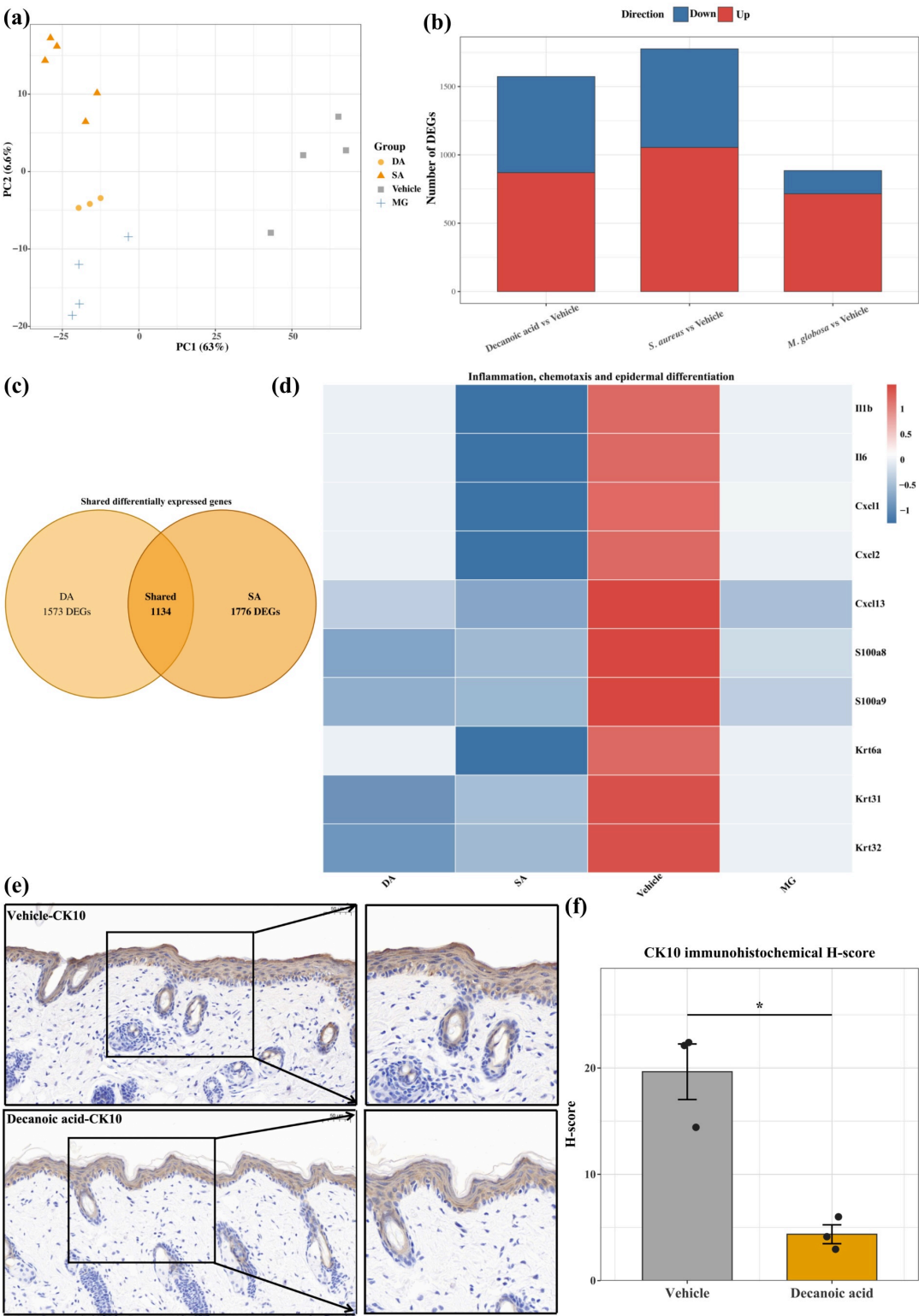


Figure 6

Transcriptomic and epidermal-differentiation responses to DA and *S. aureus* in mouse skin. (a) PCA of RNA-sequencing profiles across treatment groups. (b) Numbers of up- and downregulated DEGs for DA

versus vehicle, *S. aureus* versus vehicle and *M. globosa* versus vehicle. (c) Overlap of DA- and *S. aureus*-associated DEGs. (d) Heatmap of representative inflammatory, chemotactic and epidermal-differentiation genes. (e) Representative CK10 immunohistochemistry. (f) CK10 H-score quantification, showing lower CK10 immunoreactivity following DA exposure. DEG, differentially expressed gene.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryFigurelegends.docx](#)
- [sFigure1.jpg](#)
- [sFigure2.jpg](#)
- [sFigure3.jpg](#)