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Life Sciences Reporting Summary

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For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study.
For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

Experimental design

1. Sample size

   Describe how sample size was determined.

   No statistical methods were used to predetermine sample size.

2. Data exclusions

   Describe any data exclusions.

   For the epidermal tissue metabolomite profiling, the Glut1fl/fl control group contained 8 mice, and Glut1fl/fl K14-Cre group contained 8 mice. One mouse in the Glut1fl/fl K14-Cre group showed inefficient Glut1 knockout as assessed by RT-PCR; thus, it was excluded from the data analysis.

3. Replication

   Describe the measures taken to verify the reproducibility of the experimental findings.

   For all the cell culture experiments, each experiment was repeated in at least 3 independent experiments. For primary cultured keratinocytes, each independent experiment used cells derived from different mice. All animal experiments (UV irradiation, wound healing, psoriasiform dermatitis) were repeated independently at least 3 times in different groups of mice. For gene expression analyses (microarray), samples were analyzed from a total of 8 mice, with RNA pooled from 2 independent mice. We confirmed the expression of genes of interest by RT-PCR in independent samples from at least 3 independent mice.

4. Randomization

   Describe how samples/organisms/participants were allocated into experimental groups.

   For primary cultured mouse keratinocytes, we isolated keratinocytes from littermates and determined the genotype of each cell line and confirmed the genotype by RT-PCR or Western blot after samples were collected or the experiments were completed.
   For mouse experiments, Glut1fl/fl females were crossed with Glut1fl/fl K14-Cre male which allowed for the gnerattion of similar ratios of WT and conditional KO mice mice. Mice were gender and age matched for experiments. For experiments, gender and age matched mice were randomly allocated into groups for for the experiments.

5. Blinding

   Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

   For allocation into groups, treatments, and data collection, investigators were blinded to the genotypes of the mice. For all histological analyses, the rater was blinded to the genotype and/or and treatment condition.

Note: all in vivo studies must report how sample size was determined and whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ A statement indicating how many times each experiment was replicated
☐	☒ The statistical test(s) used and whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☐	☒ Test values indicating whether an effect is present *Provide confidence intervals or give results of significance tests (e.g. P values) as exact values whenever appropriate and with effect sizes noted.*
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒ Clearly defined error bars in all relevant figure captions (with explicit mention of central tendency and variation)

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.

GraphPad Prism Version 7.0A
MetaboAnalyst 3.0 (http://www.metaboanalyst.ca/)
Affymetrix Expression Console Software (https://www.thermofisher.com/us/en/home/life-science/microarray-analysis/microarray-analysis-instruments-software-services/microarray-analysis-software/affymetrix-transcriptome-analysis-console-software.html)

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a third party.

No unique materials were used in this study.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

Glut1 (Thermo, RB-9052-P0, LOT #:9052P 1311L) Western Blot, both mouse and human samples in this study.
Glut1 (Millipore, 07-1401, LOT #: 2794923) western blot
Anti-Cytokeratin 10 antibody [EP1607IHCY] (Abcam, ab76318, LOT #: GR202189-16) Western Blot and IHC, both mouse and human samples in this study.
Anti-Cytokeratin 14 antibody (Santa Cruz, SC-53253, LOT #: I0109) Western Blot and IHC, both mouse and human samples in this study.
Loricrin (BioLegend, 905104, LOT#: B243235). IHC, mouse samples in this study.
p-ACC Ser79 (CST, 3661. LOT#: 10) and p-S6 Ser240/244 (CST, 5364, LOT #: 6), Western Blot, both mouse and human samples in this study.
Ki-67 (Abcam, ab16667, LOT #: GR289011-2), IHC, mouse samples in this study.
CD45 (BioLegend 147701, LOT#: B181434), IHC, mouse samples in this study.
F4/80 (BioLegend 122602, LOT #: B226028) IHC, mouse samples in this study.
CD11c (BioLegend 117301, LOT #: B191076), IHC, mouse samples in this study.
Gr-1 (BD Biosciences 550291, LOT #: 7152722), IHC, mouse samples in this study.
CD4 (Thermo, 4SM95, LOT #: 4307663), IHC, mouse samples in this study.
HSP90 (CST, 4877, LOT #: 4), Western Blot, both mouse and human samples in this study.
Involucrin (Thermo, MA5-11803, LOT #: RA2147064), Western Blot, human samples in this study.
ACC (CST, 3662, LOT #: 4), Western Blot, mouse samples in this study.
COX IV (CST, 4844, LOT #: 3), Western Blot, mouse samples in this study.
Secondary antibodies conjugated to HRP at a dilution of 1:2500
(Santa Cruz, Donkey anti-Rabbit: SC2077, Donkey anti-mouse: SC2096) For IHC and Western Blots in this study.
IF secondary antibody: Alex Fluor 546 goat-anti-rabbit or Alex Fluor 488 goat-anti-mouse secondary antibody (Life Technology, A11001, A11010). IF in this study.
Biotinylated Goat Anti-Rat IgG (Vector BA-9400, LOT #: ZB1216)
Biotinylated Goat Anti-Hamster IgG (Vector BA-9100, LOT #: ZB0702)
Antibodies were validated in house by Western blot and/or staining pattern. Antibodies performing as reported according to published literature (25, 30, 31, 34, 52) or the manufacturer's description were used in the study.

10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used.

Primary cultured mouse cell lines were harvested from the experimental mice around 1 week old. Primary cultured human keratinocytes were harvested from excess tissues obtained from excisions. HEK001 (ATCC CRL-2404) was purchased from ATCC. Squamous cell carcinoma cells (SCCT8) were provided by Andrew South.

b. Describe the method of cell line authentication used.

For the mouse/human primary cultured keratinocytes, we confirmed the cells by both the morphology and keratinocyte marker staining.

c. Report whether the cell lines were tested for mycoplasma contamination.

The cell lines were not tested for mycoplasma contamination.

d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use.

No commonly misidentified cell lines were used .

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide all relevant details on animals and/or animal-derived materials used in the study.

For animal experiments, we used C57BL/6 background mice, both male and female. Age and gender matched mice were used for experiments. Primary keratinocytes were derived from ~7 day old mice. For other experiments, all the mice were ~2 months old when experiments were initiated unless otherwise specified.

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants.

Human research participants were recruited from University of Texas Southwestern Medical Center outpatient clinics. Written, informed consent was obtained from all subjects. The study was approved by the UTSW institutional review board (STU 082010-241). Exclusion criteria included patients on subcutaneous and intravenous systemic immunosuppressant medications. Patients were clinically evaluated for psoriasis subtype and PASI score, and they completed a clinical questionnaire about demographics and current and past psoriasis treatments. 4-mm punch skin biopsy samples (from lesional skin) were procured. Human primary keratinocytes were pooled together for studies regardless of the gender/age.

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☐ Initial submission ☐ Revised version ☒ Final submission

Flow Cytometry Reporting Summary

Form fields will expand as needed. Please do not leave fields blank.

Data presentation

For all flow cytometry data, confirm that:

☒ 1. The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ 2. The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ 3. All plots are contour plots with outliers or pseudocolor plots.

☒ 4. A numerical value for number of cells or percentage (with statistics) is provided.

Methodological details

5. Describe the sample preparation.	Cells were typically grown in 6 well in the indicated media, stained with 5 µM DCFDA for 30 min. Next, cells were washed, trypsinized, collected on ice, washed and resuspended in FACS buffer (DPBS, 2% FBS, and 0.2 mM EDTA).
6. Identify the instrument used for data collection.	BD FACSCalibur
7. Describe the software used to collect and analyze the flow cytometry data.	CellQuestPro was used to collect cells. FlowJo was used to analyze the data.
8. Describe the abundance of the relevant cell populations within post-sort fractions.	Not applicable
9. Describe the gating strategy used.	Not applicalbe

Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information. ☐