Supplemental Data

Mast cells are required for full expression of allergen/SEB-induced skin inflammation

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Top similarity-contributing genes (Table S1) were mostly found in the following categories:

Similarly regulated epidermal growth/differentiation genes: Hyper-proliferation of epidermis was reflected in the increase of keratin 16 (KRT16 [human gene], Krt16 [mouse gene]) and its binding partner keratin 6 (KRT6A, Krt6b), which are selectively induced in the suprabasal layers under stressful conditions, such as wounding or chronic inflammation (Paladini et al., 1996). Downregulated keratins include keratin 15 (KRT15, Krt15), 77 (KRT77, Krt77), and 13 (KRT13, Krt13). Keratin 15 downregulation has been observed in two hyper-proliferating situations, psoriasis and hypertrophic scars (Waseem et al., 1999). Mutations in keratin 13 and keratin 4 have been associated with the autosomal dominant keratotic disorder white sponge nevus (OMIM #193900). Genes related to the cell cycle and survival were also found as top similarity-contributing genes, such as FOXM1 (Foxm1), HOXA10 (Hoxa10), MCM10 (Mcm10), KIAA1199 (RIKEN 9930013L23), BCL2A1 (Bcl2a1d), CDC6 (Cdc6), BUB1 (Bub1), BIRC5 (Birc5), and G0S2 (G0s2). Interestingly, FOXM1 and BUB1 are selectively upregulated in AD skin, not in psoriasis (Guttman-Yassky et al., 2009).

Besides hyper-proliferation, differential expression of the genes related to keratinocyte terminal differentiation (i.e., cytoplasmic compaction, cornification, and lipid release) has been implicated in the pathogenesis of AD (De Benedetto et al., 2012; Guttman-Yassky et al., 2009). During the formation of cornified cell envelopes, transglutaminases cross-link precursors, such as elafin, filaggrin, keratin intermediate filaments, loricrin, and small proline-rich proteins 1 and 2 (Steinert and Marekov, 1995). Among these, Sprr2k (murine ortholog of human SPRR2A, B, D, E, F, G), Sprr1b (human SPRR3), and transglutaminase 3 (TGM3, Tgm3) were commonly upregulated in human AD and our model. Consistent with this, E74-like factor 3 (ELF3, Elf3), an epithelial-specific transcription factor required for the expression of genes such as small proline-rich proteins, transglutaminase-3, and profilaggrin during terminal differentiation of keratinocytes (Andreoli et al., 1997; Sark et al., 1998), was also commonly increased. While most of the late cornified envelope (LCE) genes are not orthologous between human and mouse, Lce1m (human LCE1D) was a commonly downregulated gene, indicating an impairment of terminal differentiation of keratinocytes in our model. Other genes implicated in the terminal differentiation, such as ets-homologous factor (EHF, Ehf), retinoic acid receptor responder 1 (RARRES1, Rarres1), Serine protease 27 (PRSS27, Prss27), Trypsinogen 1, 3 (PRSSI, 3, Prss2) were also found among the top similarity-contributing genes. Interestingly, although the filaggrin-2 gene, whose expression was reduced, was found among the similarity-contributing genes (Table S1), filaggrin and loricrin were not. Loricrin mRNA level was lower at the steady state and further downregulated by AD induction in NC/Nga mice, in line with the high susceptibility of these mice to AD-like dermatitis.

Similarly regulated skin barrier-related genes: Consistent with human AD, Der f/SEB-induced mice had impaired skin barrier, as revealed by high levels of TEWL (Fig. S2). Epidermal barrier function is controlled by layers of cells and intercellular spaces, a fine-tuned balance between proteinases and proteinase inhibitors, lipid metabolism, and
adhesion molecules (Cork et al., 2009; De Benedetto et al., 2012; Elias and Schmuth, 2009). Epidermal corneocytes are tightly bound with corneodesmosomes, desmosomes modified with corneodesmosin (CDSN). Kallikrein (KLK)-related peptidases degrade CDSN and other desmosome proteins leading to desquamation. Among eight KLKs expressed in epidermis (Lundwall and Brattsand, 2008), KLK8, KLK6, and KLK13 were commonly upregulated in human AD and our model. KLK6 and KLK13 degrades desmoglein-1, one of the adhesive proteins in the corneodesmosome (Borgono et al., 2007). KLK8 has been implicated in terminal differentiation of keratinocytes (Kuwae et al., 2002). However, expression of the KLK inhibitor LEKTI (lymphoepithelial Kazal-type-related inhibitor), encoded by AD-associated SPINK5 gene (Walley et al., 2001), was not changed in our model, suggesting a shift of protease-inhibitor balance towards desquamation. Another group of serine protease inhibitors expressed in skin, SERPINB3, 4, 13 (Serpinh3d, 3a, 13a in mouse), related to carcinogenesis (Meyer-Hoffert, 2009), were all highly upregulated.

The second barrier under the stratum corneum is tight junction in the stratum granulosum. Although the claudins were not found as the top similarity-contributing genes, claudin-1 (CLDN1, Cldn1) was downregulated in AD-induced B6 mice (but unchanged in NC/Nga mice), and claudin-23 (CLDN23, Cldn23) was downregulated in both strains. Both were selectively downregulated in AD non-lesional skin compared to psoriasis non-lesional skin (De Benedetto et al., 2012). Non-lesional skin of AD patients is known to have an altered gene expression profile similar to that of lesional skin (Leung et al., 2004; Suarez-Farinas et al., 2011). Comparison with the changes in non-lesional epidermal tissue from AD patients (Table 1) revealed that many of similarly expressed genes in whole AD skin tissues are also expressed in non-lesional epidermal tissue, suggesting the substantial contribution of epidermal changes to gene expression in the whole skin samples. Interestingly, the similarity score between AD-induced mice and non-lesional epidermal tissue from psoriasis patients was lower than those between AD-induced mice and AD patients (Table 1). Another intercellular junction protein, connexin-26 (GJB2, Gjb2), was commonly upregulated in the AD patients and our model, which was also selectively observed in AD non-lesional epidermis compared to psoriasis (De Benedetto et al., 2011). Increased expression of aquaporin 3 (AQP3, Aqp3), which transports water as well as glycerol, and water-selective aquaporin 5 (AQP5, Aqp5) might also contribute to the change in epidermal barrier function (Table S1).

**Similarly regulated lipid/energy metabolism genes:** Interestingly, the similarity-contributing genes related to lipid metabolism were downregulated in human AD and mouse models. These include fatty acid transport proteins (SLC27A2 (Slc27a2) and FABP4 (Fabp4)), regulators of lipid metabolism (PRKAA2 (Prkaa2) and THRSP (Thrsp)); lipid metabolic enzymes (ACACB (Acacb), FA2H (Fa2h), FASN (Fasn), and FAR2 (Far2)); a transcription coactivator/phosphatidase phosphatase (LPIN1 (Lpin1)) implicated in adipose tissue development; and obesity-related hormones (LEP (Lep) and ADIPOQ (Adipoq) and a downstream molecule NNAT (Nnat)). Importantly, fatty acid 2-hydroxylase (FA2H, Fa2h) accounts for the synthesis of sphingolipids in keratinocytes required for extracellular lamellar membrane formation, which is important for the epidermal permeability barrier (Uchida et al., 2007). Top similarity-contributing genes also include other metabolic enzymes (PCK1 (Pck1), GPD1 (Gpd1) and ALDH1A1.
(Aldh1a1)) and a transcriptional coactivator that regulates genes involved in energy metabolism (PPARGC1A (Ppargc1a)).

Similarly regulated immune response genes: Growth factors, cytokines, and chemokines secreted from keratinocytes, leukocytes, and stromal cells regulate inflammatory responses in the skin (Yamanaka and Mizutani, 2011). A commonly downregulated gene, betacellulin (BTC, Btc) is one of the seven EGF receptor ligands (Shing et al., 1993). Mice lacking the EGF receptor in keratinocytes develop AD-like skin inflammation (Franzke et al., 2012). Interestingly, blockade of the EGF receptor signaling results in enhanced chemokine expression in keratinocytes (Mascia et al., 2003). Such chemokines as CCL2 (mouse Ccl12), CCL5 (mouse Ccl5), and CXCL10 (mouse Cxcl10) were all upregulated and found among top similarity-contributing genes in our models. Keratinocytes also produce alarmins S100A8 and S100A9, which have both intracellular and extracellular functions. As secreted proteins, they regulate leukocyte functions such as adhesion and transendothelial migration (Ryckman et al., 2003) through binding to Toll-like receptor-4 (Vogl et al., 2007) and the receptor for advanced glycation end products (Boyd et al., 2008). Other chemokines and cytokines or their receptors found among top similarity-contributing genes include CXCL1 (Cxcl3), CCL4 (Ccl4), CXCL2 (Cxcl1), IL1F9 (Il1f9), IL1F5 (Il1f5), IL1F8 (Il1f8), IL4R (Il4ra), and CXCR4 (Cxcr4). As described previously (Kawakami et al., 2007), IL-4, IL-5 and IL-17 were upregulated in both mouse strains, IL-13 was upregulated only in B6 mice; IL-33 and interferon γ were upregulated in NC/Nga mice; IL-25 was downregulated in both strains.

Similarly regulated extracellular matrix genes: Matrix metalloproteinases (MMPs) play an important role in tissue remodeling during inflammation (Page-McCaw et al., 2007). MMP12, 9, and 3 were upregulated by AD induction and found as top similarity-contributing genes. In the skin, eosinophils, mast cells, Langerhans cells, and keratinocytes express MMP-9 and MMP-3. MMP-9, but not MMP-3, was shown to be upregulated in keratinocytes in response to IL-13 (Purwar et al., 2008). Tissue inhibitor of metalloproteinases-4 (TIMP4, Timp4), which can bind MMP-3 and MMP-4, were also upregulated. Other upregulated proteins related to extracellular matrices include tenascin C (TNC, Tnc), which is a large extracellular matrix glycoprotein, and periostin (POSTN, Postn). Tenascin C expression was induced by patch tests in skin of atopic individuals (Phipps et al., 2004), where the tenascin C-positive cells were identified morphologically as fibroblasts. Periostin expression was shown to be increased in human AD and house dust mite extract-induced mice, where periostin secreted from Th2 cytokine-stimulated skin fibroblasts induced TSLP expression in keratinocytes and TSLP in turn induced dendritic cells to differentiate T cells into Th2 cells, thus forming a vicious cycle to amplify Th2 inflammation (Masuoka et al., 2012).

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**Supplementary Materials and Methods**

**Determination of transepidermal water loss (TEWL)**

TEWL was measured on lesional skin and the dorsal skin of shaved mice by using a Tewameter™ 300 (Courage-Khazaka Electronics, Cologne, Germany) as described (Li *et al.*, 2010).

**Microarray analysis of gene expression**

Total RNA was extracted from skin using Trizol One Step RNA Reagent (BioPioneer Inc., San Diego, CA). We combined four RNA samples for AD-induced B6, three RNA samples for naive B6 mice, and two RNA samples each for naive and AD-induced NC/Nga mice. The same amount of RNA from 2-4 mice were mixed and cleaned by RNeasy Total RNA Mini Kit (Qiagen). A microarray analysis was performed using 200 ng of total RNA from each cohort and SurePrint G3 Mouse Gene Expression 8x60K arrays (Agilent Technologies) according to the manufacturer’s instructions. The microarray data will be deposited in Gene Expression Omnibus upon acceptance of this manuscript ([http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE_](http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE_)). Data analysis was performed with GeneSpring software (version 11.5.1). Signal intensity was normalized by 75 percentile shift and reduced difference in the levels of beta-actin and 18S ribosomal subunit was confirmed. To eliminate genes containing only a background signal, genes were selected only if the raw values of “Expression” were more than 100. A total of 29,573 probes met this criterion and were subjected to further analysis.

Detection of similarity in expression pattern between different species was detailed elsewhere (Hoffmann *et al.*, 2007; Lottaz *et al.*, 2006; Yang *et al.*, 2006). Briefly, orthologs were collected from human and mouse microarray data sets according to the HomoloGene database build 65 (NCBI). These genes were listed in the order of fold changes, and the gene lists were compared for human and mouse data using OrderedList package on R software version 2.14.1. Similarity score is defined as follows: for a gene list $G$, let the flipped gene list is denoted by $f(G)$. For two gene lists $G_1$ and $G_2$, let $O_n(G_1, G_2)$ equal the number of common genes in top $n$ ranks of both lists. Large $O_n$ indicate that the same genes accumulate in the top $n$ ranks, which suggests commonly upregulated genes. On the flipped gene lists, $O_n(f(G_1), f(G_2))$ detect commonly downregulated genes. A similarity score is calculated as:

$$S'_\alpha(G_1, G_2) = \sum_{n} e^{-\alpha n} \{O_n(G_1, G_2) + O_n(f(G_1), f(G_2))\}$$

where $\alpha$ is a parameter which determines the weight on both ends of the lists. Therefore, if an ortholog is ranked high at either top (upregulated) or bottom (downregulated) end in both human and mouse gene list, this ortholog contributes highly to the similarity score. By comparing a similarity score with the random distribution of the scores (the similarity scores calculated on two randomized lists) ([Fig. S1B](#fig:S1B)), $p$-value for the significance of similarity is obtained (Table 1). Computation was performed at alpha=0.01151 (max rank=1000), with 1000 permutations for random distribution.
**Real-time RT-PCR**
RNA was extracted from skin and spleen samples. cDNA was prepared with SuperScript II reverse transcriptase (Invitrogen, Carlsbad, CA). Primers (sequences to be provided upon request) were tested for the amplification efficiency along with 18S ribosomal RNA as an internal control. Real-time RT-PCR was performed using LightCycler® 480 System (Roche Applied Science). Relative expression levels were determined using ΔΔCt method.

**Histological analysis**
Dorsal skin samples were fixed in 10% formaldehyde, paraffin embedded and cut into 6 μm sections. Deparaffinized sections were stained with hematoxylin and eosin (H&E), toluidine blue (pH 4.0), Congo red, or Masson Trichrome (Sigma Aldrich). The remaining part of the skin was embedded in an OCT compound, snap frozen in liquid nitrogen and stored at −80°C until use. Frozen sections cut at 6 μm were incubated with primary antibodies at 4°C overnight, followed by fluorochrome-conjugated secondary antibodies. Antibodies for keratin 5, keratin 1, and loricrin were generated in the Jamora laboratory (Lee et al., 2009). E-cadherin antibody was purchased from Invitrogen; keratin 6 antibody from Covance and collagen antibody from Chemicon. Anti-TSLP antibody was provided by Amgen. Coverslips were mounted with Prolong Gold antifade reagent with DAPI (Invitrogen). Fluorescence was observed under Zeiss Axiovert 200M Marianas system. Cells were counted under a microscope at a magnification of x400 and expressed as the total number of the cells in five high power fields per section.

**Bone marrow-derived mast cells (BMMCs) and their engraftment**
BMMCs were generated by culturing bone marrow cells in IL-3 (Kawakami et al., 1992). Expression (>95% of the cells) of c-Kit and FcεRI was confirmed by flow cytometry before use. Engraftment of Kit<sup>W-sh/W-sh</sup> mice with BMMCs was performed 6 weeks before the Der f/SEB experiments (Nakano et al., 1985).

**Serum IgE**
Serum IgE levels were measured using an enzyme-linked immunoassay kit purchased from BD Biosciences Pharmingen.

**Statistical Analysis**
Data are expressed as mean ± SEM. One-way ANOVA with Tukey post-hoc test (Fig. 1A) and Student’s t test (all other comparisons) was used for mean comparisons. Differences were considered statistically significant at P values < 0.05.
## Table S1. Similarity-contributing genes.

| Human Data Set | AD Ilexical / normal | AD Ilexical / non-lexical | AD Non-lexical / normal | AD Non-lexical / non-lexical | Mouse Gene Symbol | Mouse Dendritic Change | Mouse Fold Change | Mouse Fold Change | Mouse Fold Change |
|----------------|----------------------|--------------------------|-------------------------|-----------------------------|-------------------|------------------------|------------------|------------------|------------------|
| (mouse H1D)    |                      |                          |                         |                             |                   |                        |                  |                  |                  |
| 74496          | SERPINB4             | Serpinb3a                | 7.385                   | 7.17                        | serine (or cysteine) peptidase inhibitor, clade B (ovotransaminase), member 3A |
| 20547          | MMP12                | Mmp12                    | 2.248                   | 2.175                       | matrix metalloproteinase 12 |
| 20665          | S100A6               | S100a6                   | 8.346                   | 7.142                       | S100 calcium binding protein A6 (calgranulins) B |
| 2285           | S100A8               | S100a8                   | 6.027                   | 5.856                       | S100 calcium binding protein A8 (calgranulins A) |
| 1174           | LTP                   | Ltf                      | 4.796                   | 2.842                       | decorin |
| 31145          | KRT18                 | Krt18                    | 3.501                   | 6.198                       | keratin 18 |
| 37380          | SLCO2A2               | Slc2a2                   | 2.250                   | 5.181                       | solute carrier family 27 (fatty acid transporter), member 2 |
| 36028          | KRT16                 | Krt16                    | 5.583                   | 9.763                       | keratin 88 |
| 48584          | SERPINB3             | Serpinb3d                | 4.508                   | 7.218                       | serine (or cysteine) peptidase inhibitor, clade B (ovotransaminase), member 3D |
| 55530          | TNC                   | Tnc                      | 3.159                   | 5.968                       | tenascin C |
| 68655          | IL22RA               | Ilt2a                    | 2.234                   | 4.484                       | interleukin 22 receptor, alpha |
| 62724          | CXCL1                 | Cxcl1                    | 1.593                   | 2.327                       | chemokine C-X-C motif ligand 1 |
| 105184         | DZMB                 | Dmrtb                    | 1.352                   | 3.768                       | granulocyte |
| 5218           | GALNT6               | Galnt6                   | 1.726                   | 3.633                       | O-Linked N-acetylglucosaminyltransferase B |
| 31413          | SPPR2A, B, D, E, F, G | Spp2k                    | 5.631                   | 7.122                       | small proline-rich protein 2K |
| 7321           | BTF                  | Btf2                     | 1.669                   | 2.644                       | etv homologous factor |
| 21125          | EPHI                 | Eph1                     | 1.436                   | 2.249                       | Eph receptor-like |
| 43530          | BIRC5                | Birc5                    | 4.224                   | 6.812                       | baculovirus IAP repeat-containing |
| 1159          | Bcl2                  | Bcl2                     | 1.305                   | 2.095                       | b-cell lymphoma/leukemia 2 |
| 2975           | CCL1                 | Ccl1                     | 1.179                   | 2.349                       | chemokine C-C motif ligand 1 |
| 45905          | TPSMB                | Tspam                    | 2.794                   | 2.140                       | transcriptase |
| 37256          | CA2                   | Car2                     | 3.300                   | 6.940                       | carbonic anhydrase 2 |
| 11748          | SAM51                | Samd51                   | 1.405                   | 2.937                       | SAM domain, SH3 domain and nuclear localization signals 1 |
| 36995          | MMP3                 | Mmp3                     | 1.372                   | 2.487                       | matrix metalloproteinase 3 |
| 194            | SGCG                  | Sgcp2                    | 1.690                   | 1.900                       | saposin 2 |
| 4551           | PRKAA                 | Prkaa2                   | 1.772                   | 2.203                       | protein kinase A, protein-activated, alpha 2 catalytic subunit |
| 139            | LEF2                  | Lef2                     | 2.034                   | 2.032                       | lymphoid enhancer factor 2 |
| 81738          | ECL3                 | Ecl3                     | 1.620                   | 2.405                       | b-cell leukemia/lymphoma 3 |
| 45490          | KRT77                | Krt77                    | 2.722                   | 6.925                       | keratin 77 |
| 7794           | POU2F1               | POU2F1                   | 1.279                   | 2.267                       | POU domain containing 1 |
| 7318           | FOXN1                | Foxn1                    | 1.332                   | 2.127                       | forkhead box M1 |
| 2975           | CCL1                 | Ccl1                     | 1.568                   | 2.063                       | chemokine C-C motif ligand 1 |
| 35605          | CLEC7A                | Clec7a                   | 1.002                   | 2.999                       | colony-stimulating factor receptor |
| 28716          | SERPINB13             | Serpinb13                | 1.626                   | 1.889                       | serine (or cysteine) peptidase inhibitor, clade B (ovotransaminase), member 13 |
| 117632         | CCL2                 | Ccl2                     | 1.367                   | 2.413                       | chemokine C-C motif ligand 2 |
| 7784           | IL1R                 | Il1r1                    | 1.286                   | 2.068                       | interleukin 1 receptor, alpha |
| 67285          | CXCL6               | Cxcl6                    | 1.203                   | 2.371                       | chemokine C-X-C motif ligand 6 |
| 52452          | S100A6               | S100a6                   | 5.571                   | 7.186                       | S100 calcium binding protein A6 (calgranulins) B |
| 8599          | NR1D1                | Nrd1                     | 1.860                   | 3.841                       | neuregulin 1 |
| 11748          | NKX5.1               | Nkx5.1                   | 1.428                   | 2.410                       | transcription factor 5, directly regulated 18 |
| 1944           | PCK1                 | Pck1                     | 2.317                   | 2.020                       | phosphoenolpyruvate carboxykinase 1, cytosolic |
| 10922         | MS447                | Ms447                    | 1.836                   | 3.567                       | membrane-spanning 44A, subfamily A, member 7 |
| 4056           | PPPR1A                | Pppr1a                   | 1.378                   | 3.180                       | protein phosphatase 1A, regulatory (inhibitor) subunit 1A |
| 20960          | TGM1                 | Tgm1                     | 2.068                   | 1.134                       | transglutaminase 3, E polypeptide |
| 50385         | RIL5                 | Ril5                     | 1.625                   | 3.034                       | ribosomal protein L5 |
| 30738          | COCH                 | Cogh1                    | 1.609                   | 2.563                       | chemokine (C-X-C motif) receptor 4 |
| 388            | SEL4                 | Sel4                     | 3.867                   | 4.983                       | selectin, endothelial cell |
| 4510           | DAO3                 | Daus1                    | 0.730                   | 2.118                       | 2-o-furaldehyde dehydrogenase 3 |
| 68256          | MMY4                 | Myo4                     | 0.711                   | 2.039                       | myosin heavy polypeptide 4B, smooth muscle |
| 31036          | HNL1                 | Hnl1                     | 2.346                   | 1.648                       | hair and a half LIN1 |
| 47947          | ATP5A2               | Atp5a2                   | 1.046                   | 2.046                       | ATPase, Na+/K+ transporting, alpha 2 ATPase |
| 7784           | A22A                 | A2a2                     | 1.174                   | 2.007                       | ATPase, Na+/K+ transporting, alpha 2 ATPase |
| 7365           | MOX1                 | Mox1                     | 2.868                   | 2.957                       | homeobox 450 |
| 38377          | DSC2                 | Dsc2                     | 0.810                   | 2.722                       | desmocollin 2 |
| Gene Name | Description | Gene Name | Description |
|-----------|-------------|-----------|-------------|
| TMEM132A | transmembrane protein 132A | ZWILCH | ZW1 linear chaperone homolog |
| IN10B1 | | ED39 | E3 ubiquitin-protein ligase |
| MAPK6 | mitogen-activated protein kinase 6 | ARHGAP4 | Rho GTPase activating protein 4 |
| NNT | nicotine receptor, alpha 9 | NUP210 | nucleoporin 210 |
| CAS2 | DnaE2 | | |
| SLC3A1A | solute carrier family 3 (sodium/pendrin/crude exchanger), member 2 | PHLDA2 | PHL domain containing 2 |
| MX1 | | PRSS2 | proprotein convertase subtilisin/kexin type 2 |
| RASG1 | RasG1 | CXCL9 | C-X-C motif chemokine 9 |
| UAP5 | | ADAM9 | ADAM metalloprotease (disintegrin and metalloproteinase) domain 9 |
| SLN12 | | | |
| TUBB8 | | | |
| CYBA | | | |
| PLSCR1 | | | |
| HDX1C13 | | | |
| LUMN | | | |
| HER1 | | | |
| CD290 | | | |
| TPK2 | | | |
| FUT7 | | | |
| PC2D2 | | | |
| CCH2 | | | |
| 1372 | | | |
| PIGH | | | |
| C10Q1 | | | |
| 853 | | | |
| 68902 | | | |
| 56497 | | | |
| 62175 | | | |
| 89676 | | | |
| HCLS1 | | | |
| TSER1A | | | |
| TSC22D3 | | | |
| RAB89b | | | |
| MLYK | | | |
| HSD3B1 | | | |
| GAPB3 | | | |
| GRK1 | | | |
| GABP5 | | | |
| CRC2 | | | |
| MYC1 | | | |
| NEDD4L | | | |
| HCV | | | |
| INOS | | | |
| TSFNT1 | | | |
| IFIT1 | | | |
| TAP2B1 | | | |
| PKH1 | | | |
| MRP | | | |
| PCED4 | | | |
| C1orf51 | | | |
| RUNK2 | | | |
| CIDEB | | | |
| DUSP1 | | | |
| PTG1 | | | |
| C0BL | | | |
| AGR2 | | | |
| SERPINF2 | | | |
| SCN2B | | | |
| SPAG11B | | | |
| PLCP | | | |
| AATT | | | |
| SPRI5 | | | |
| PIN3L3 | | | |
| ARM3 | | | |
| CYP2J2 | | | |
| RA2 | | | |
| HOWER2 | | | |
| HMV1 | | | |
| AHK4 | | | |
| PKNOX2 | | | |
| INTC7 | | | |
| MTERF1 | | | |
| SOC3 | | | |
| FLBG | | | |
| Gene Name | Description |
|-----------|-------------|
| TMD01    | Transmembrane domain 1 |
| SHBG     | Sex hormone-binding globulin |
| BRMS     | BRM-related protein |
| LRR2     | LRR-domain containing 2 |
| MMP13    | Matrix metalloproteinase 13 |
| COL5A1   | Collagen, type V, 1 |
| COL5A2   | Collagen, type V, 2 |
| Sema3A   | Semaphorin domain-containing 3A |
| LRR3C    | LRR-domain containing 3C |
| MYB2     | Myb-domain containing 2 |
| AP1D1    | AP1 domain-containing 1D |
| LOC289489 | Locus tag LOC289489 |
| LRR3C    | LRR-domain containing 3C |
| BCL2L11  | Bcl-2-like 11 |
| KCNH1    | Potassium voltage-gated channel, subfamily H (Kv) member 1 |
| ASPN     | ASPN domain-containing protein |
| HLA-C    | Histocompatibility antigen, C |
| SLCO5A1  | Solute carrier organic anion transporting polypeptide 5A1 |
| PDE6C    | Phosphodiesterase 6C |
| MLK4     | MLK interacting protein |
| COL5A5   | Collagen, type V, 5 |
| CLEC8     | C-type lectin domain-containing 8 |
| GNL3L    | GTPase-activating like 3L |
| CYP11B1   | Cytochrome P450, family 11, subfamily B, polypeptide 1 |
| MCT10    | Multicarrier 10 |
| KRT7     | Keratin 7 |
| EMT    | E-cadherin |
| TACR1    | Tachykinin receptor 1 |
| CASZ1    | Cazpin |
| GGT1     | Glutamyltransferase 1 |
| CYB58    | Cytochrome b58 |
| CAPN8    | Calpain 8 |
| ELF7     | Endoplasmic reticulum enzyme, family F, member 7 |
| GSTT3    | Glutathione S-transferase T3 |
| CDH17    | Cadherin 17 |
| NINBB    | Ninbin |
| TBC1D30  | TBC1 domain, family D, member 30 |
| ST6GALN4 | ST6 alpha-galactosaminyltransferase 4 |
| NINBB    | Ninbin |
| ILR6     | Interleukin 6 receptor, alpha |
| GAB5     | GABA A receptor, gamma 5 |
| SLC4A8   | Solute carrier organic anion transporting polypeptide 4A8 |
| SLC4A8   | Solute carrier organic anion transporting polypeptide 4A8 |
| SGK2     | Serine/threonine kinase 2 |
| VWA2     | VWA domain-containing protein 2 |
| PTP1B    | Protein tyrosine phosphatase 1B |
| KRT18    | Keratin 18 |
| ECHS1    | Enolase 1 |
| AVPR1A   | V2 vasopressin receptor 1A |
| PRKG1    | Protein kinase G, type 1 |
| GPRK1    | G protein-coupled receptor 1 |
| DUSP1    | Dual-specific protein phosphatase 1 |
| MGC12540 | MGC 12540 |
| MYOT     | Myotube |
| TAF12    | TAF1 domain-containing protein 12 |
| ATP2B2   | ATPase, Ca++ transporting, plasma membrane 2 |
| PKA      | Protein kinase, cyclic AMP-regulated, alpha |

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In comparison between human AD and mouse models, a gene that has higher fold changes in expression both in human and mouse contributes more to the similarity score. Each comparison gives a list of the top genes that contribute to a total of 95% of a similarity score. Twenty comparisons were performed between ten human AD datasets and two mouse models, and the genes appearing in similarity-contributing gene lists of this Table were sorted by the frequency appearing in these comparisons. A filled box indicates that the gene is listed among the top similarity-contributing genes in the comparisons. Two additional comparisons between psoriasis non-lesional epidermis and mouse models are also shown. HID, HomoloGene ID.
Figure S1. Clustering analysis of global gene expression and confirmation by quantitative RT-PCR.
(A) Among 29,573 gene probes, 7,475 probes were upregulated or downregulated by 2-fold or more through AD-induction in at least one strain of B6 and NC/Nga. These genes were subjected to hierarchical clustering. (B) An example of random distribution of similarity scores and observed scores in comparison between GSE32924 data set and B6 data set. Three observed similarity scores were off the random distribution, indicating a significant similarity. Random distribution was calculated by 1000 permutations. (C) RT-qPCR analysis of the selected genes. Each symbol represents one mouse.
Figure S2. Impaired skin barrier in Der f/SEB-induced skin lesions.
Der f/SEB induction experiments were done on NC/Nga mice and TEWL was assessed as described in the Materials and Methods. Each symbol represents one mouse.

Figure S3. Expression of epidermal differentiation markers in allergen-induced eczematous mice.
Immunofluorescence microscopy was performed before and after Der f/SEB induction on WT, μMT, TCRβ+, and Rag1−/− mice, as described in Materials and Methods. k1, keratin 1; k5, keratin 5; k6, keratin 6; lor, loricrin; Ecad, E-cadherin; Col, collagen.
**Figure S4.** Numbers of mast cells in inflammatory skin are correlated with the clinical skin score.

Mast cells were counted in Toluidine-blue stained skin sections. (A) Mast cell numbers per the entire skin section with surface area of 1 mm$^2$ are presented. *, p<0.05; **, p<0.01; ***, p<0.001; ****, p<0.0001; n.s., not significant. (B) Weak correlation was detected between mast cell numbers and clinical scores. Linear regression line is shown. Each symbol represents one mouse.
Figure S5. Mast cell-deficient Cpa3-Cre;Mcl-1<sup>fl/fl</sup> mice exhibited attenuated skin inflammation.

Der f/SEB induction experiments were performed on Cpa3-Cre;Mcl-1<sup>fl/fl</sup> mice. (A) Clinical skin scores. (B) Macroscopic features. (C,D) H&E staining of the lesional or non-lesional skin sections. The rectangle portions are enlarged below. The epidermal-dermal borders are shown by dotted lines. Bar, 200 μm. (E) Toluidine blue staining was also done. Only a few mast cells were detected in lesional and non-lesional skin areas of Cpa3-Cre;Mcl-1<sup>fl/fl</sup> mice. Each symbol represents one mouse. *, p<0.05; ***, p<0.001.
Figure S6. Numbers of neutrophils in inflammatory skin are correlated with the clinical skin score.
Neutrophils were counted in Congo red-stained skin sections. (A) Their numbers per high power field are presented. *, p<0.05; ***, p<0.001; n.s., not significant. (B) Significant correlation was detected between neutrophil numbers and clinical scores. Linear regression line is shown. Each symbol represents one mouse.