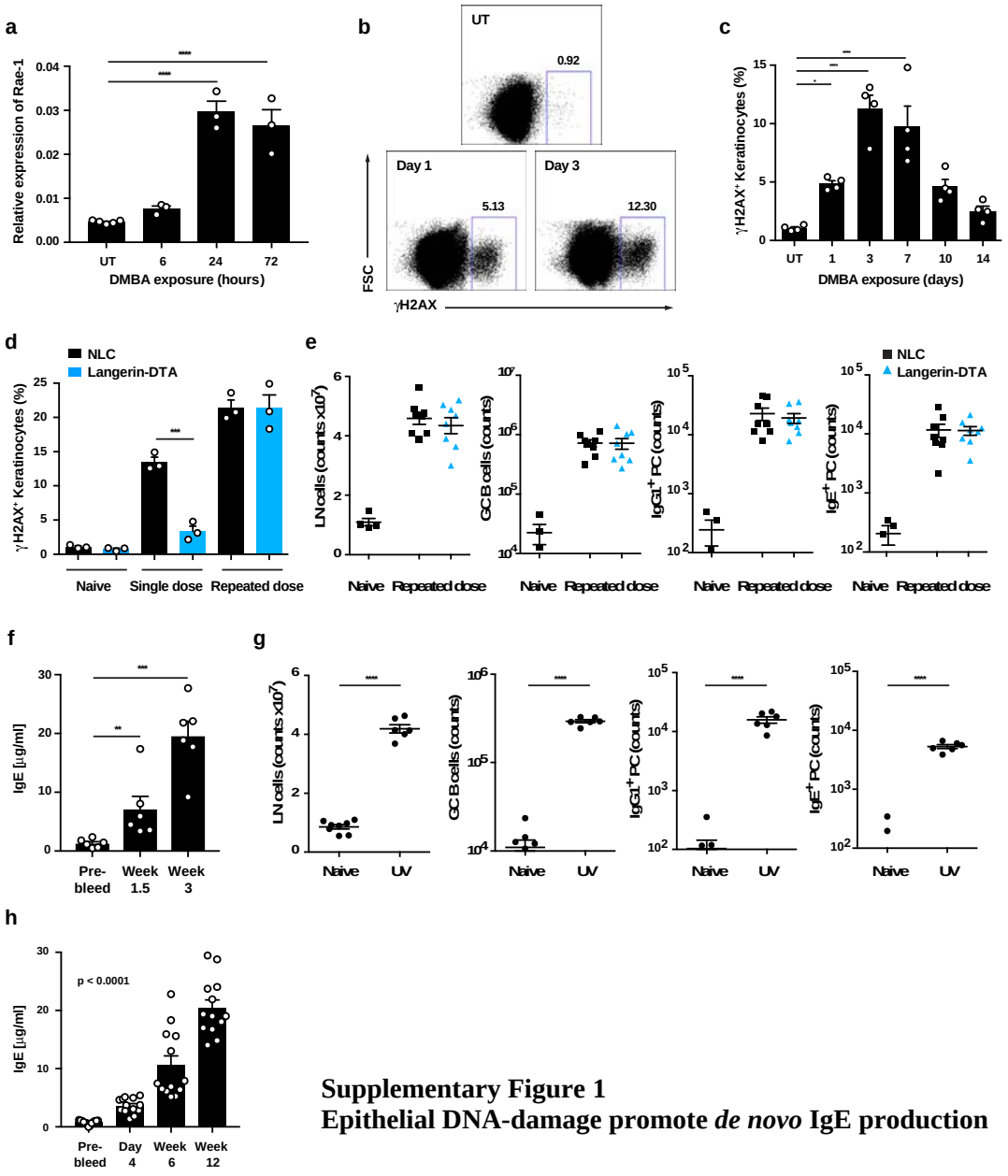
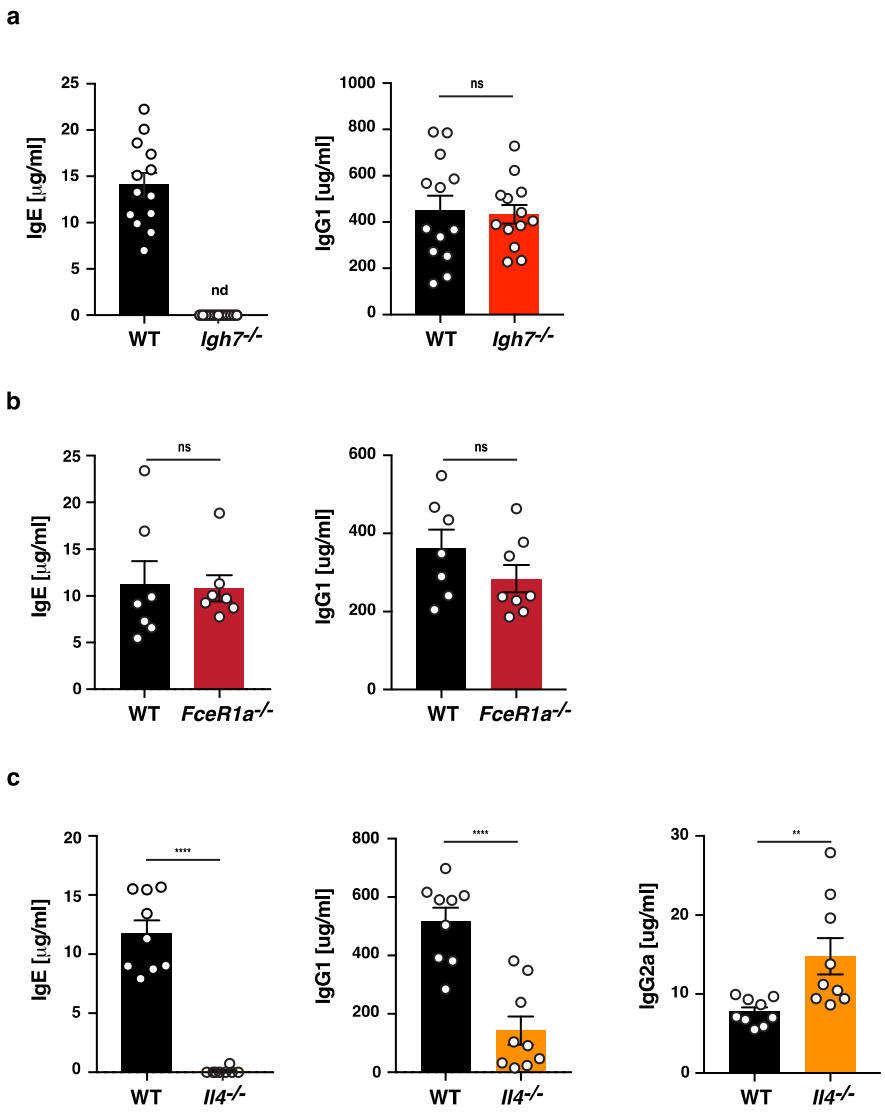


Supplementary Figure 1
Epithelial DNA-damage promote *de novo* IgE production

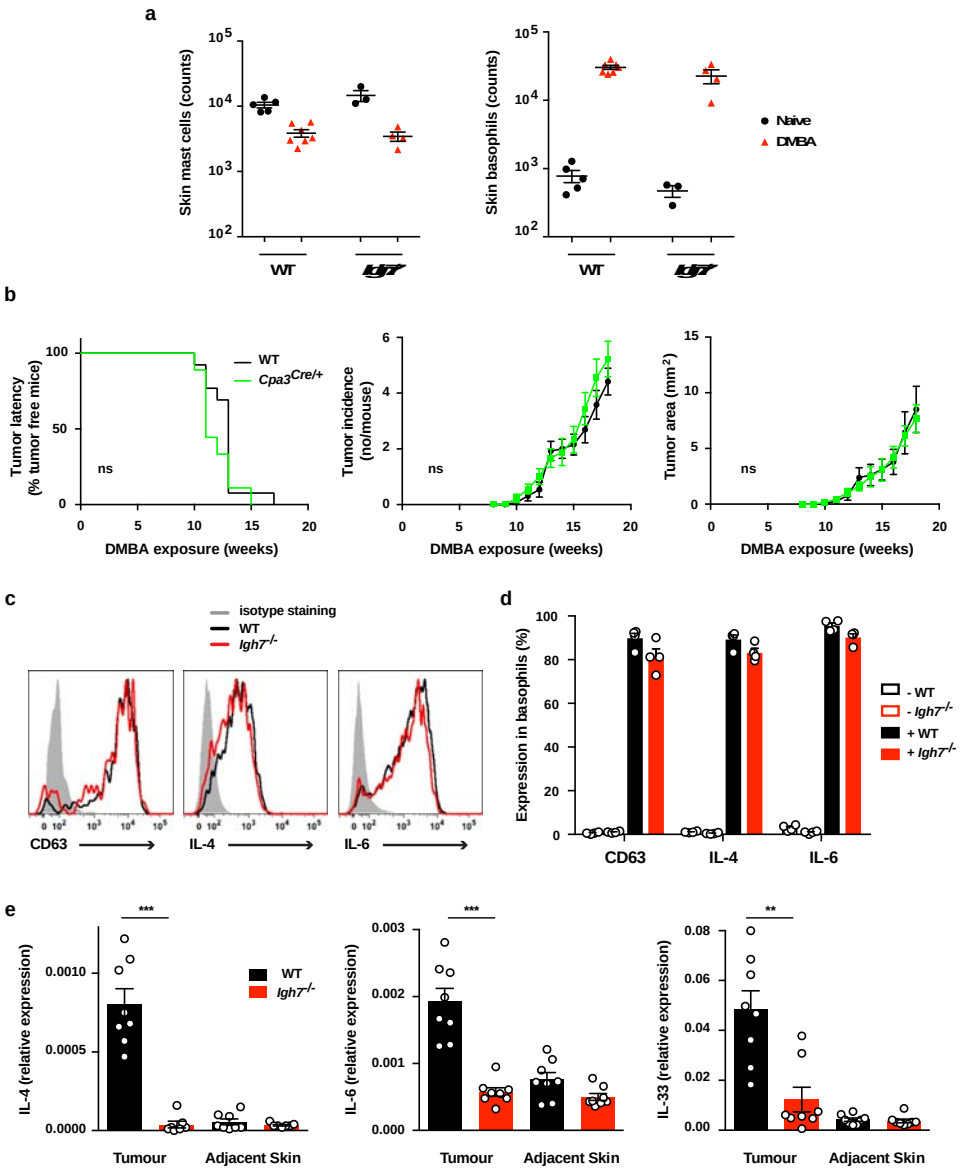
(a) Quantitative RT-PCR analysis of Rae-1 relative to cyclophylin in skin epithelial cells (n=3) and (b-c) FACS analysis of γH2AX, as a measure of ds-DNA breaks, in skin epithelial cells (n=4), at indicated time-points after topical exposure to a single dose of DMBA to the dorsal ear skin of wild-type FVB mice. UT = untreated (n=4-5). (b) Representative FACS plots of γH2AX staining in $CD45^-$ epidermal cells. (d) FACS analysis of $\gamma H2AX^+$ $CD45^-$ skin epithelial cells from Langerin-DTA mice and non-transgenic littermate controls (NLC) (n=3/group) after a single or repeated topical DMBA treatment, analysed 3 days after last exposure and (e) FACS analysis of humoral immunity in the skin-draining LNs 7 days after the last DMBA exposure. Total LN cells, $B220^+CD95^+GL7^+$ GC B cells and $IgG1^+$ and IgE^+ $FSC^{hi}CD95^+CD138^+$ PCs were enumerated (n=8/group). (f) ELISA of serum IgE and (g) FACS analysis of humoral immunity as in (e) in wild-type FVB mice exposed to UV light on shaved back skin at 100mJ/cm^2 2-3x a week (n=6). Mice were bled after 4 exposures (week 1.5) and again at the end of the experiment (week 3) after 8 exposures. (h) ELISA of serum IgE in wild-type mice exposed to 200nmol DMBA for 5 consecutive days and then left without further exposure. Mice were bled prior to exposure and at indicated time-points after the last DMBA-treatment (n=13). Some mice started to develop tumors around week 6. Statistics by two-tailed Student's t-test for unpaired data (d and g), one-way ANOVA multiple comparison (a, c, f) and one-way ANOVA with testing for linear trend of IgE increase with time (h); **p<0.01, ***p<0.001 and ****p<0.0001. All data are expressed as mean ± SEM.



Supplementary Figure 2

Antibody levels in wild-type, *Igh7*$^{-/-}$, *FceR1a*$^{-/-}$ and *Il4*$^{-/-}$ mice following DMBA carcinogenesis

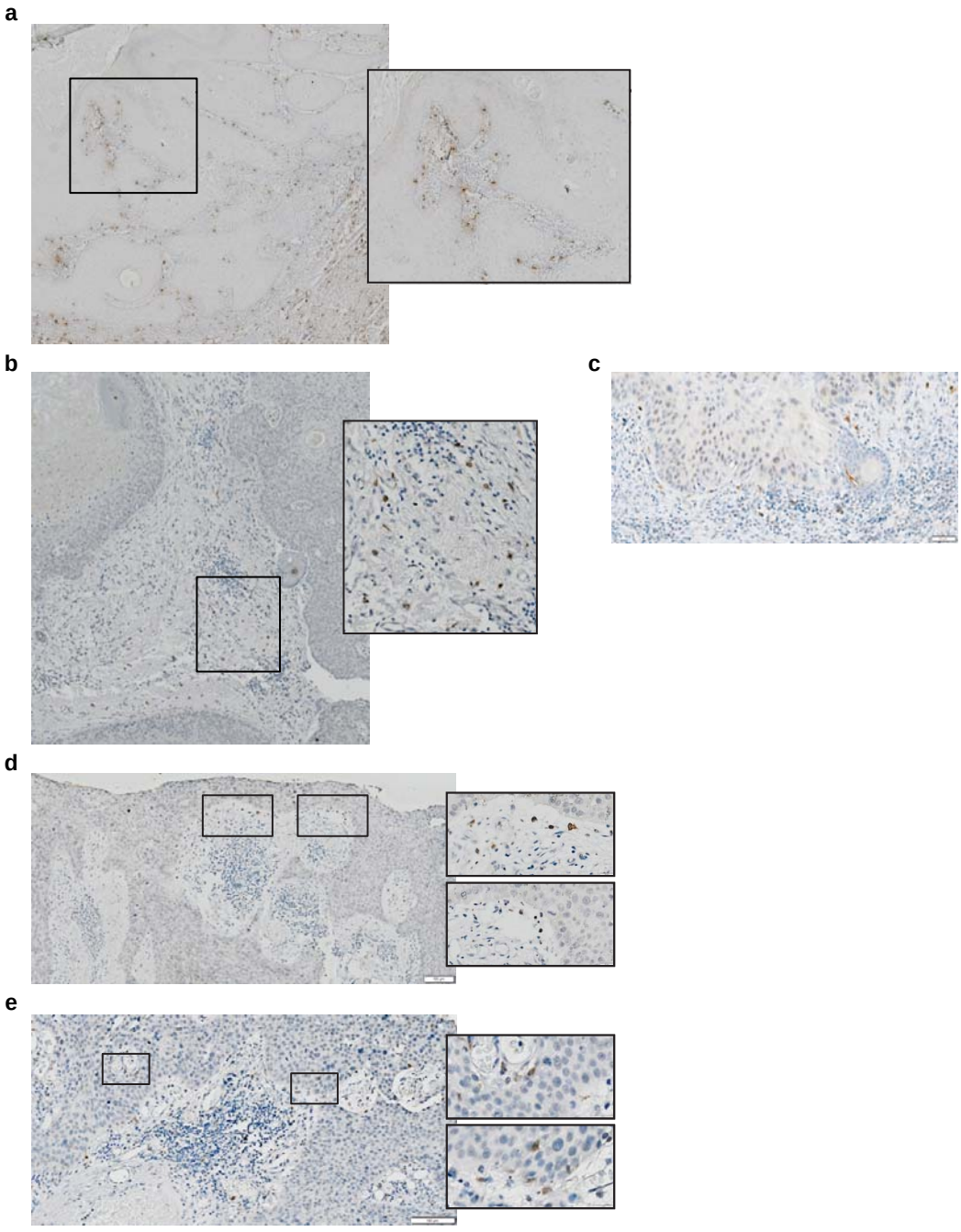
(a-c) ELISA of serum antibodies in mice subjected to DMBA carcinogenesis by once weekly exposure to DMBA on shaved back skin. Mice were bled and sera collected at the end of the carcinogenesis experiment. Data are expressed as mean antibody amount ± SEM in sera from (a) BALB/c wild-type and *Igh7*$^{-/-}$ mice (n=13/group), (b) BALB/c wild-type and *FceR1a*$^{-/-}$ mice (n=7/group) and (c) FVB wild-type and *Il4*$^{-/-}$ mice (n=9/group). Statistical analysis in (a-c) was determined using two-tailed Student's t-test for unpaired data; **p<0.01 and ****p<0.0001. nd = not detected. ns = not significant. WT = wild-type.



Supplementary Figure 3

FcεRI-signaling in basophils is sufficient to protect against carcinogenesis and alters the tumor microenvironment

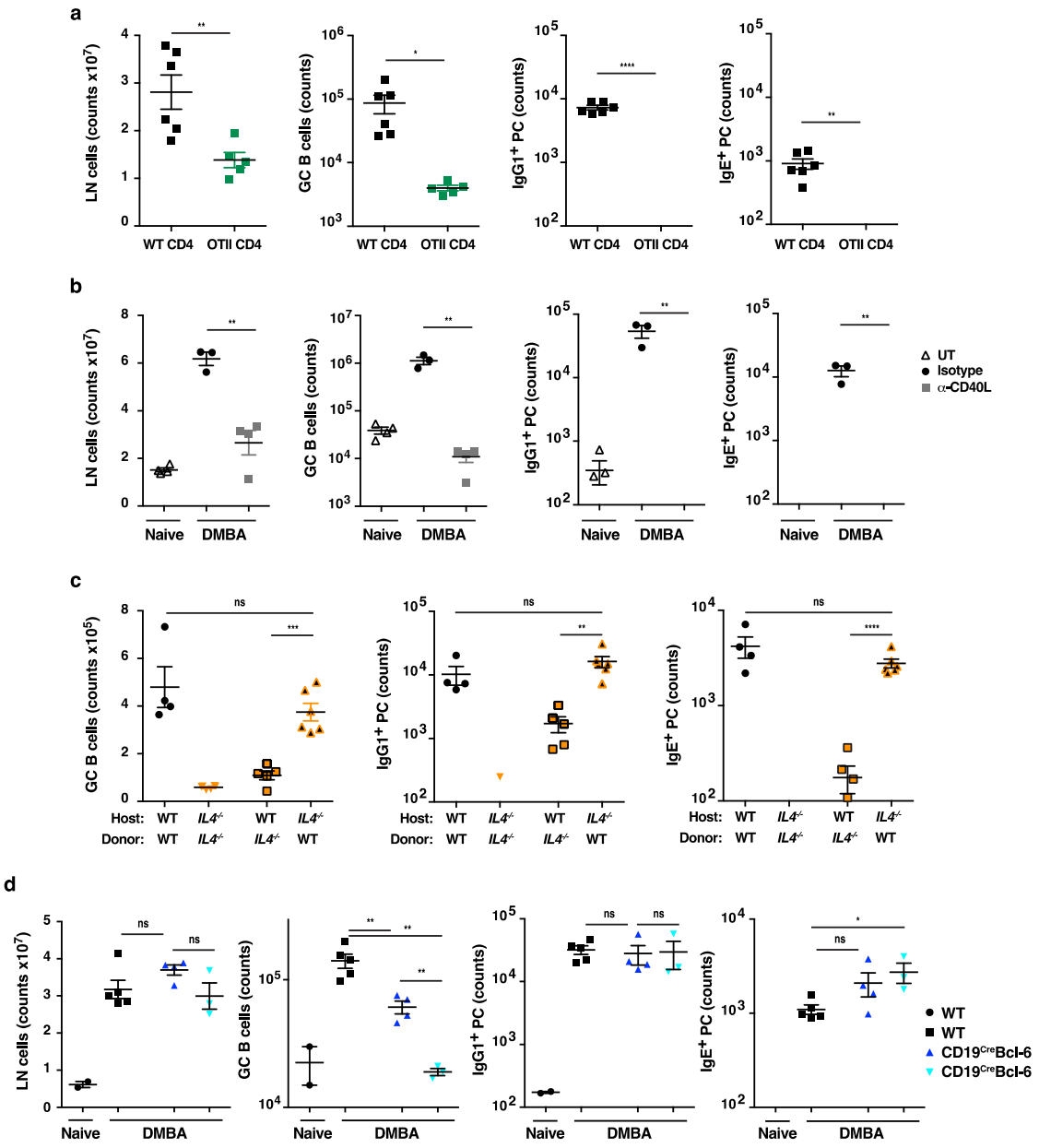
(a) FACS analysis of CD45^{hi}cKit^{+}FcεRI^{+} skin mast cells and CD45^{lo}cKit^{-}FcεRI^{+} skin basophils in wild-type and *Igh7*$^{-/-}$ mice after twice topically treatment with DMBA compared to naïve mice (wild-type naïve n=6, wild-type DMBA n=7; *Igh7*$^{-/-}$ naïve n=3, *Igh7*$^{-/-}$ DMBA n=4). (b) Tumor susceptibility expressed as tumor latency (time to appearance of first tumor), tumor incidence (average number of tumors per mouse) and tumor area (average tumor size per mouse) in *Cpa3*$^{Cre/+}$ (n=10) and *Cpa3*$^{+/+}$ (wild-type) littermates (n=13) following DMBA-induced carcinogenesis. Data are expressed as mean ± SEM and statistical significance assessed using Log-rank (Mantel-Cox) test for tumor latency and linear regression for tumor incidence and area. ns = not significant. (c-d) FACS analysis of the degranulation marker CD63 and intracellular cytokine staining in splenic CD45^{+}cKit^{-}CD41^{+}FcεRI^{+} basophils from wild-type and *Igh7*$^{-/-}$ mice (n=4/group) left unstimulated (-) or stimulated *ex vivo* with PMA and ionomycin (+). (c) Representative histograms and (d) enumeration of % basophils positive for indicated marker. (e) Quantitative RT-PCR analysis of selected cytokines relative to cyclophylin in tumor tissue and adjacent skin from wild-type and *Igh7*$^{-/-}$ mice (n=8/group) treated topically with DMBA once weekly and analysed at week 17. Data are expressed as mean ± SEM. Statistics by two-tailed Student's t-test for unpaired data; **p<0.01 and ***p<0.001. WT = wild-type.



Supplementary Figure 4

FcεRI^{+} cells in human skin SSCs accumulate at the interface between the stroma and the neoplastic keratinocytes

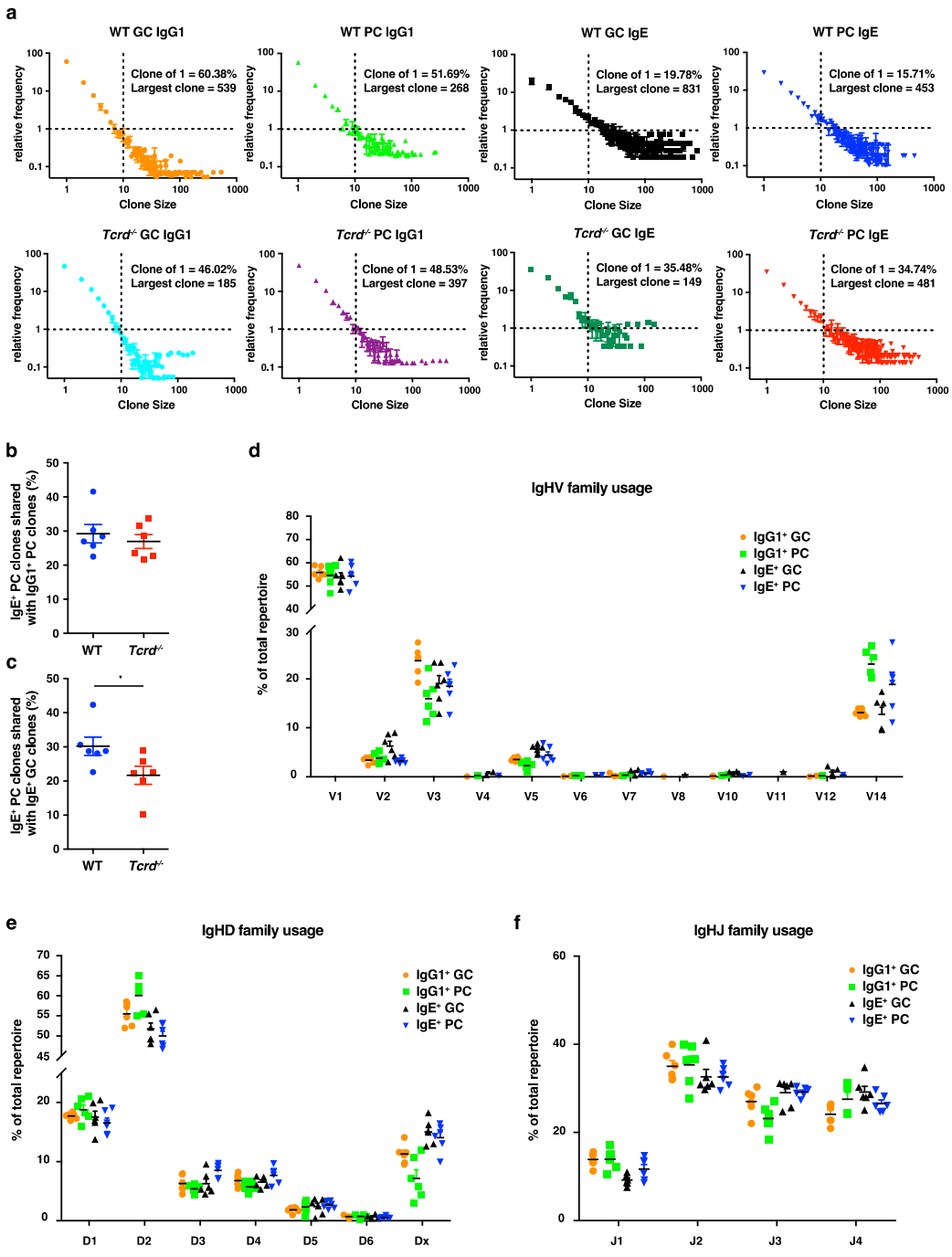
(a-e) Representative SSC histology from 5 patients showing FcεRI staining in brown. 5 µm tissue sections were cut from formalin-fixed paraffin-embedded samples, stained against FcεRI and counterstained with Mayer's Haematoxylin. Slides were imaged at 20x magnification using an Olympus Dotslide microscope and analysed using OlyVIA software. Insets show zoom of outlined areas.



Supplementary Figure 5

Carcinogen-induced antibody responses require TCR signaling, CD40L and LN IL-4 but not GC B cells

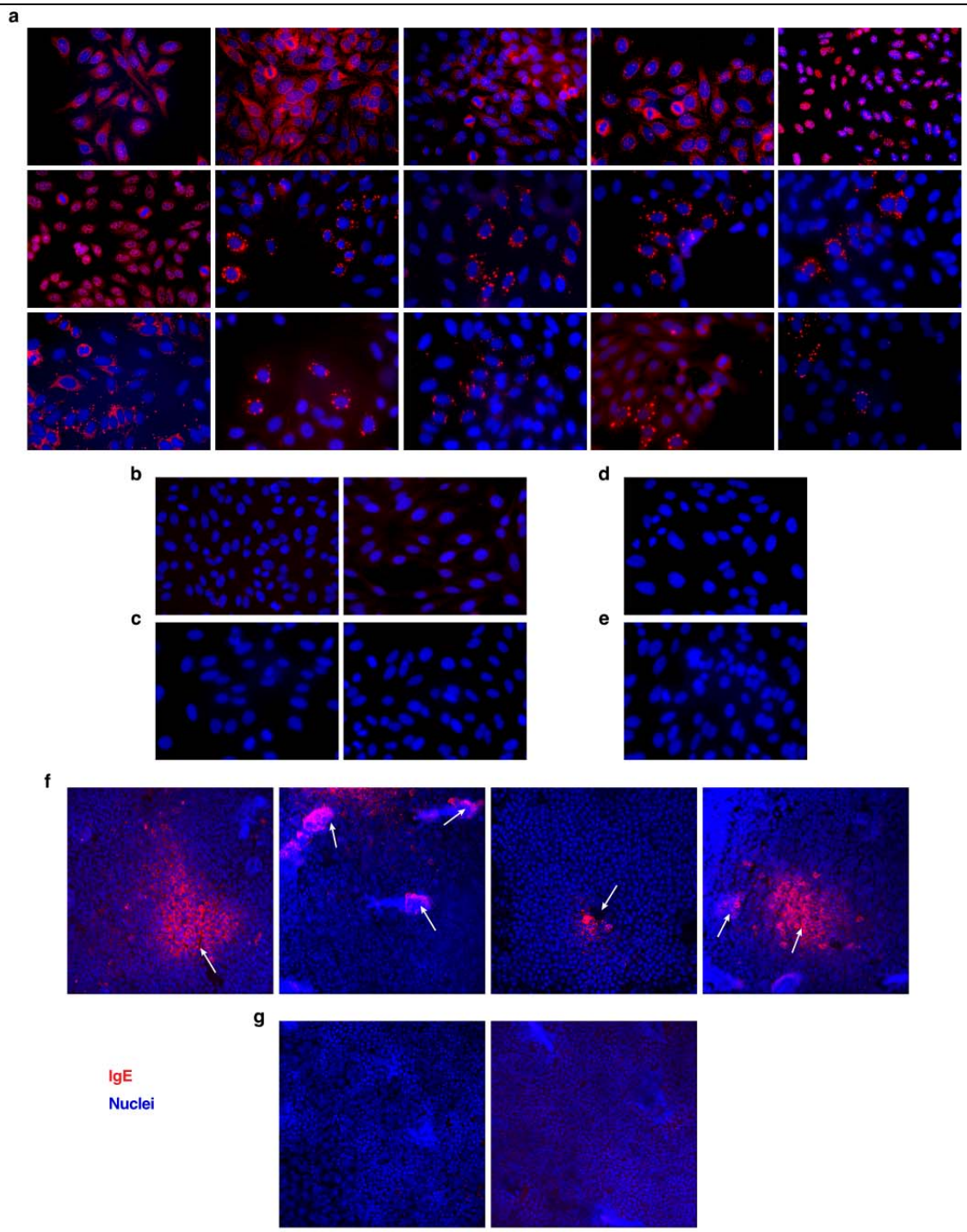
(a-d) FACS analysis of humoral immunity in the skin draining LNs analysed 7 days following twice topical exposure to DMBA on the dorsal ear skin. (a) C57BL/6 *Tcrb*$^{-/-}$ mice were reconstituted with wild-type (n=6) or OTII TCR-restricted CD4^{+} αβ T cells (n=5) 1 day prior to DMBA exposure. (b) Wild-type FVB mice were injected with α-CD40L blocking Ab (MRI clone) (n=4) or isotype control Ab (n=3) prior to DMBA exposure and 3 further times during induction of the response. (c) Lethally irradiated FVB wild-type or *Il4*$^{-/-}$ mice were reconstituted with either wild-type or *Il4*$^{-/-}$ BM cells and exposed to DMBA 8 weeks after BM transplant (n=4-6/group). (d) C57BL/6 wild-type mice and mice with a heterozygous or homozygous deletion of Bcl-6 in B cells (CD19^{cre}Bcl-6$^{fl/wt}$ and CD19^{cre}Bcl-6$^{fl/fl}$ respectively) were exposed to topical DMBA (n=3-5/group). Graphs show number of total LN cells, B220^{+}CD95^{+}GL7^{+} GC B cells and IgG1^{+} or IgE^{+} FSC^{hi}CD95^{+}CD138^{+} PCs presented as mean ± SEM. Statistics by two-tailed Student's t-test for unpaired data; *p<0.05, **p<0.01, ***p<0.001 and ****p<0.0001. ns = not significant. WT = wild-type. UT = untreated.



Supplementary Figure 6

Analysis of the IgG1 and IgE repertoires induced by topical carcinogen exposure on wild-type and *Tcrd*$^{-/-}$ mice

(a-f) High-throughput sequencing and heavy-chain repertoire analysis of IgG1 and IgE in sorted B220^{+}CD95^{+}GL7^{+} GC B cells and FSC^{hi}CD95^{hi}CD138^{+} PCs from skin draining LNs of wild-type and *Tcrd*$^{-/-}$ mice 7 days after the last of two topical exposures to DMBA (n=6/group). (a) Average frequency of a given clone size in the entire repertoire is shown for wild-type and *Tcrd*$^{-/-}$ IgG1^{+} and IgE^{+} GC B cells and IgG1^{+} and IgE^{+} PCs. (b) Proportion of IgE^{+} PC clones shared with the IgG1^{+} PC clones and (c) the fraction of IgE^{+} PC clones shared with the IgE^{+} GC B cell clones. (d-f) Total IgHV, IgHD and IgHJ family gene usage within the wild-type IgG1^{+} GC B cells and PCs as well as wild-type IgE^{+} GC B cells and PCs. Statistics in (c) by two-tailed Student's t-test for unpaired data; *p<0.05. WT = wild-type.



Supplementary Figure 7

Autoreactivity of IgE in serum from DMBA-treated wild-type mice

(a-e) Examples of autoreactive binding to HEp-2 cells of IgE in serum from (a) DMBA-treated wild-type mice (1:25 dilution), (b) DMBA-treated *Tcrd*$^{-/-}$ mice (1:5 dilution), (c) TPA-treated wild-type mice (1:5 dilution), (d) DMBA-treated *Igh7*$^{-/-}$ mouse (1:5 dilution) and (e) naïve wild-type mouse (1:5 dilution). (f-g) Examples of autoreactive binding of IgE to clusters of epithelial cells in acutely DMBA damaged epidermis from *FceR1a*$^{-/-}$ mice exposed to 200nmol DMBA once on the dorsal ear skin and epidermal sheets isolated 24hr later and stained with serum from (f) DMBA-treated wild-type or (g) *Igh7*$^{-/-}$ mice (1:25 dilution). Arrows point to hair follicles. IgE binding (red) and nuclei (blue). Each image represents an individual mouse.

1