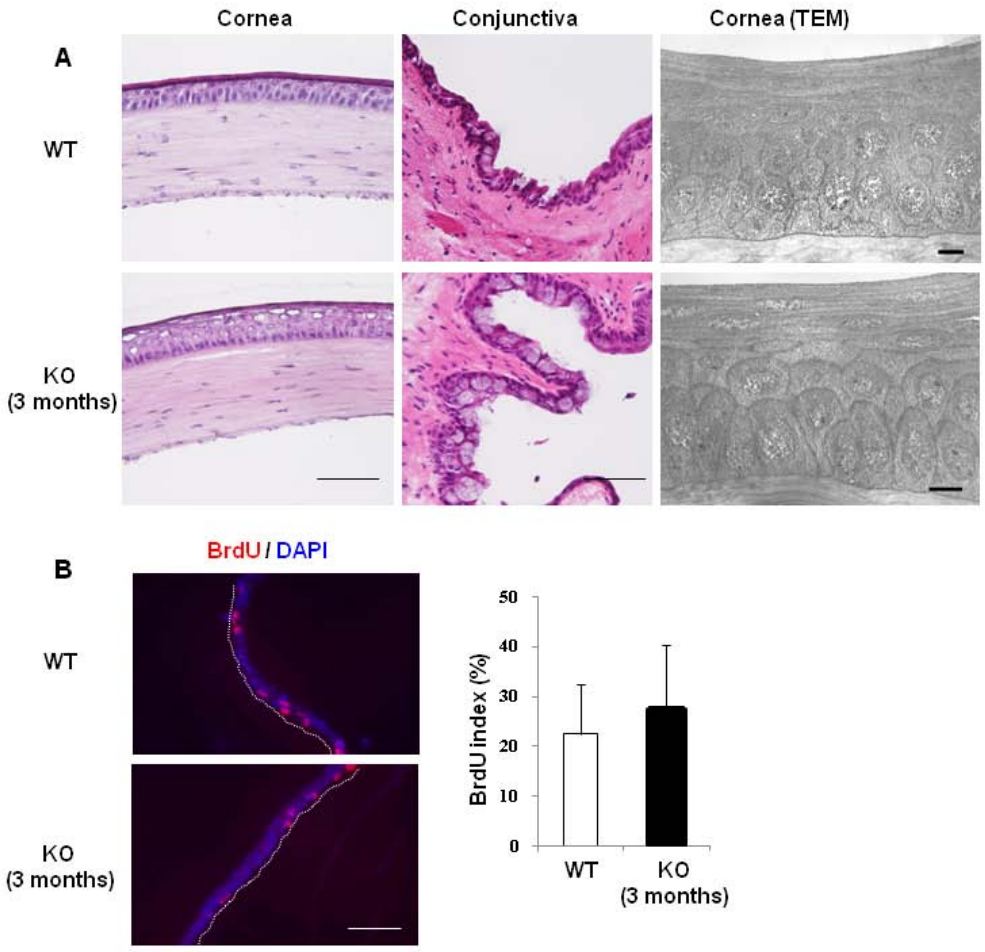
Supplemental Table1. Up-regulated genes in holoclone-type corneal keratinocytes (selected)

Gene Symbol	Gene Title	Proposed Function
•*NLRP2*	NLR family, pyrin domain containing 2	Aactivation of proinflammatory caspases
•*IL24*	Interleukin 24	Anti-proliferative property
•*PTX3*	Pentraxin-related gene, rapidly induced by IL-1 beta	Regulation of innate resistance to pathogens
•*CALD1*	Caldesmon 1	Actin- and myosin-binding protein
•*KLK6*	Kallikrein 6 (neurosin, zyme)	Serine protease
•*CRISP2*	Cysteine-rich secretory protein 2	Regulation of ion channels' activity
•*JPH3*	Junctophilin 3	Stabilization of the junctional membrane
•*MUM1*	Melanoma associated antigen (mutated) 1	DNA damage response pathway
•*Lrig1*	Leucine-rich repeats and Ig-like domains 1	Epidermal and intestinal stem cell marker
•*MTSS1*	Metastasis suppressor 1	Cancer progression
•*KRT19*	Keratin 19	Organization of myofibers
•*LRP11*	Low density lipoprotein receptor-related protein 11	Receptor activity
•*DEFB4*	Defensin, beta 4	Antibacterial activity
•*LGR5*	Leucine-rich repeat-containing G protein-coupled receptor 5	Intestinal and hair follicule stem cell marker
•*KRT24*	Keratin 24	Structural constituent of cytoskeleton

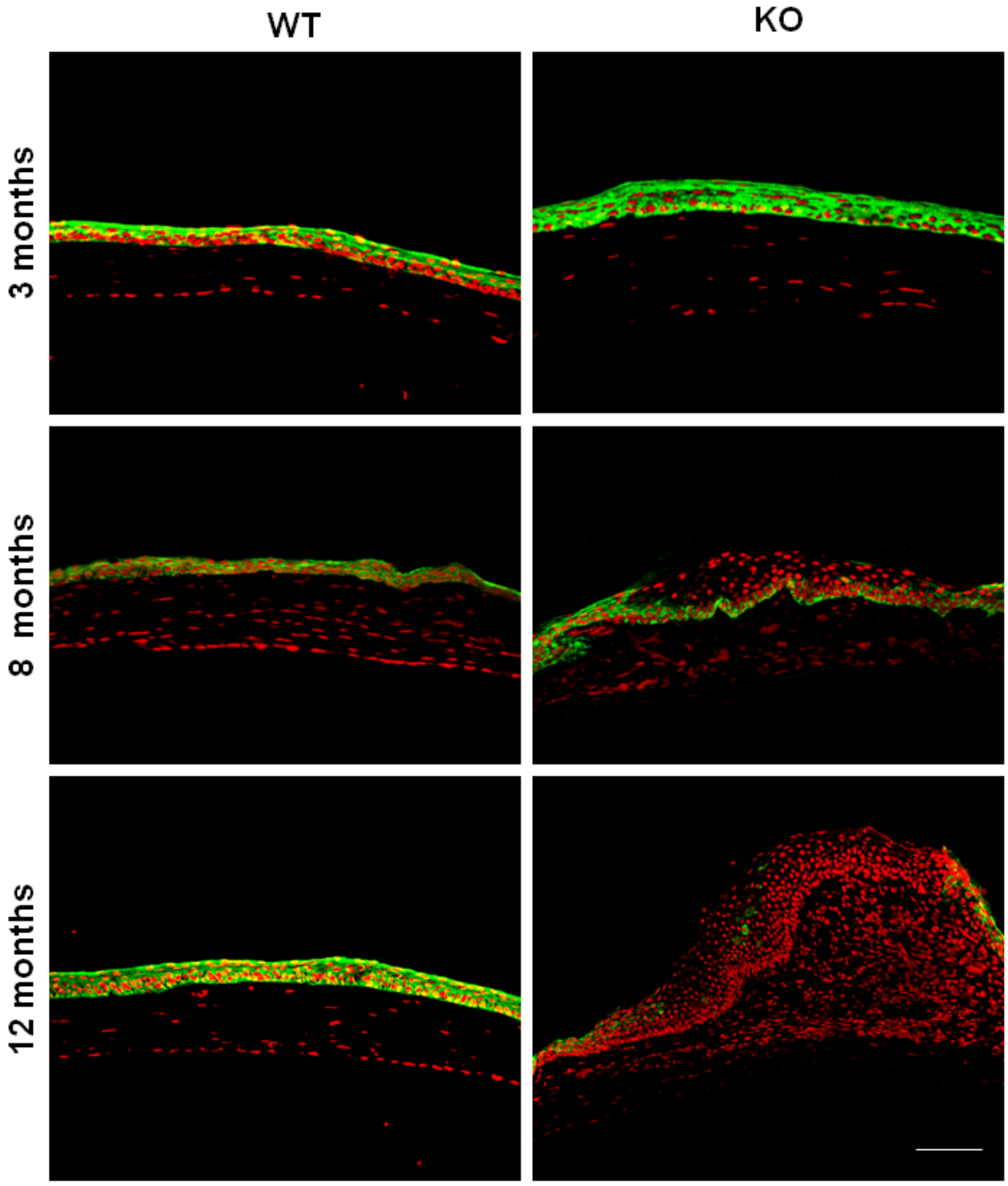
Supplemental Table 3. Sequences for PCR

mouse *Lrig1*	F	ACACCTGTGGCTTCATTGCAG
	R	TAGCAGAGAGCAATAGTGTGTC
	Neo	AGAACCTGCGTGCAATCCATC
mouse *TNFα*	F	CCCTCACACTCAGATCATCTTCT
	R	GCTACGACGTGGGCTACAG
mouse *MCP1*	F	CCAGCACCAGCACCAGCCAA
	R	TGCTCCAGCCGGCAACTGTG
mouse *IFNγ*	F	CGGCACAGTCATTGAAAGCCTA
	R	GTTGCTGATGGCCTGATTGTC
mouse *IL17*	F	ACGCGCAAACATGAGTCCAG
	R	CTCAGCAGCAGCAACAGCATC
mouse *TSLP*	F	AATGACCACTGCCCAGGCTA
	R	TTGTGAGGTTTGATTCAGGCAGATG
mouse *IL33*	F	CCGTTCTGGCCTCACCATAAG
	R	AATGTGTCAACAGACGCAGCAA
mouse *IL25*	F	CTCAACAGCAGGGCCATCTC
	R	GTCTGTAGGCTGACGCAGTGTG
mouse *IL10*	F	GACCAGCTGGACAACATACTGCTAA
	R	GATAAGGCTTGGCAACCCAAGTAA
mouse *IL13*	F	TGTCTCTCCCTCTGACCC
	R	TACAGAGGCCATGCAATATCC
mouse *Stat3*	F	CAATACCATTGACCTGCCGAT
	R	GAGCGACTCAAACTGCCCT
mouse *gp130*	F	ATTTGTGTGCTGAAGGAGGC
	R	AAAGGACAGGATGTTGCAGG
mouse *SOCS3*	F	AGACCTTCAGCTCCAAAAGC
	R	ACCAGCTTGAGTACACAGTCG
mouse *JAK1*	F	CGGAACCAATGACAACGAACAGTC
	R	CCAAGGTAGCCAGGTATTTCACC
mouse *JAK2*	F	GCAGCAGCAGAACCTACAGATACG
	R	TCCTTATGTTTCCCTCTTGACCAC
mouse *β-actin*	F	CATCCGTAAAGACCTCTATGCCAAC
	R	ATGGAGCCACCGATCCACA

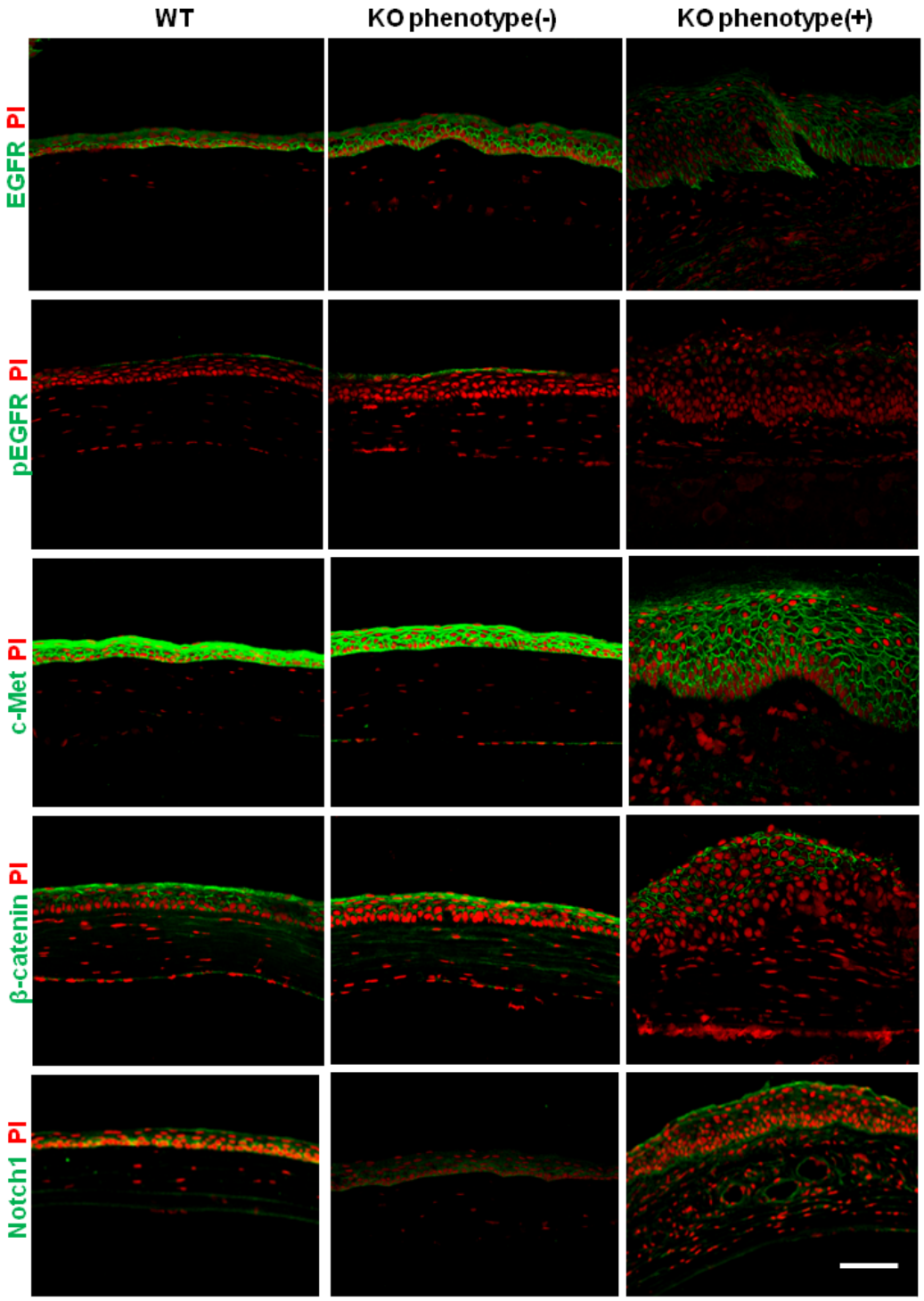
F: Forward, R: Reverse



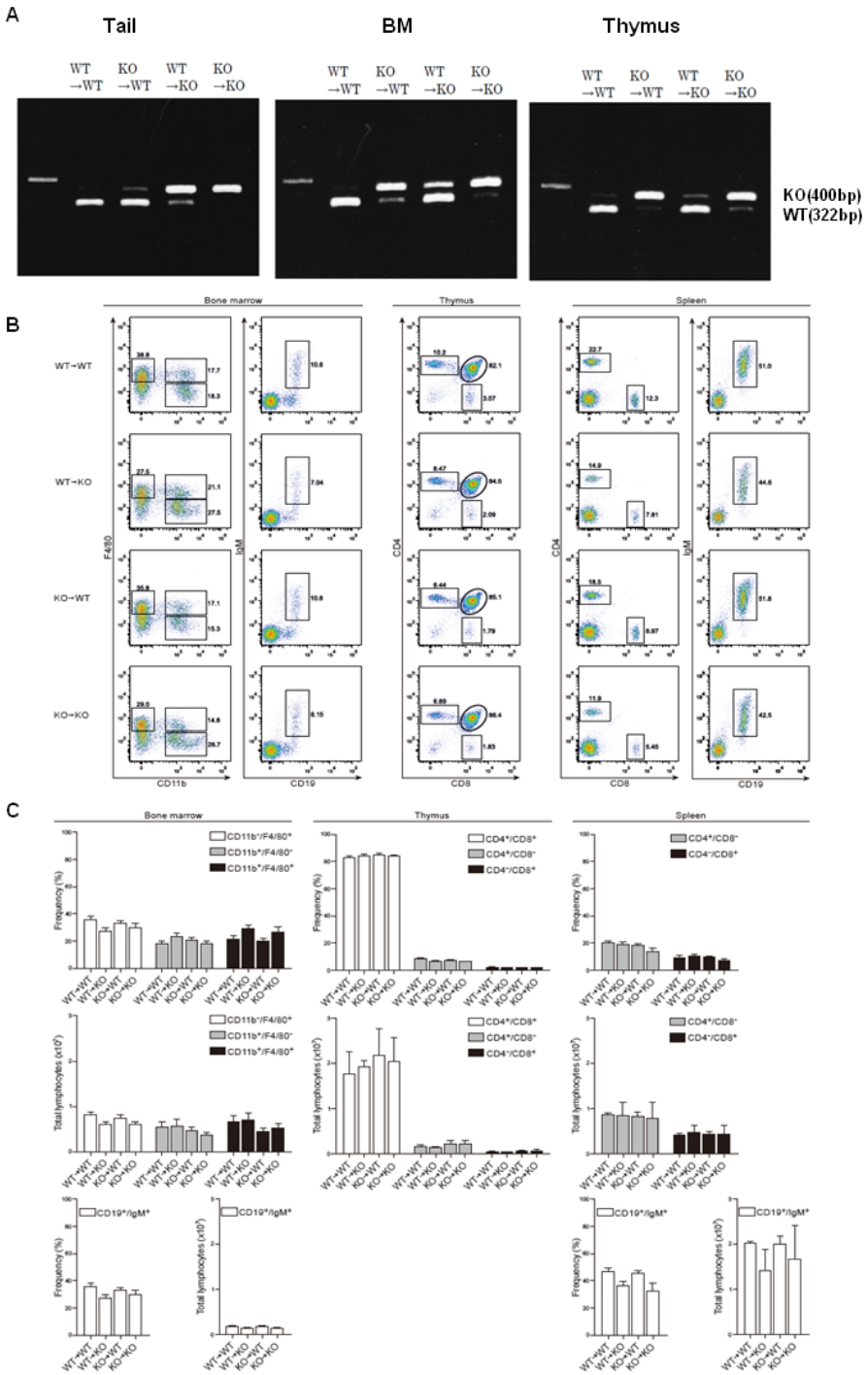
Supplemental Figure 1. Characterization of *Lrig1* WT and KO (3 months) corneas. (A) Histological and morphological examination of *Lrig1* WT and KO corneas using HE staining and transmission electron microscopy (TEM). (B) BrdU labeling of *Lrig1* WT and KO cultured corneal epithelium (3 months). Nuclei are counterstained with DAPI (blue). The dashed line indicates the basal side of cultured epithelium. Scale bar, 100μm.



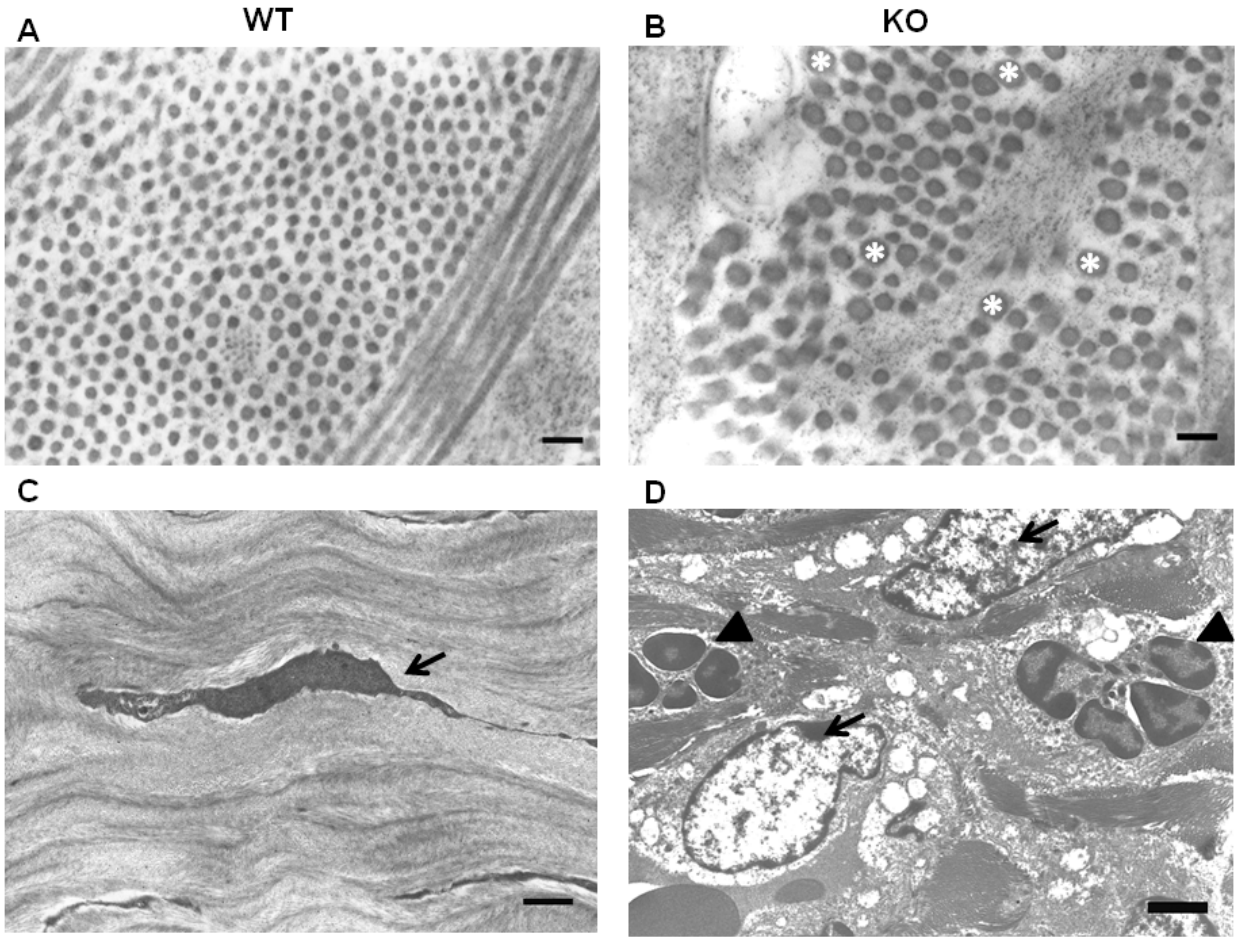
Supplemental Figure 2. Expression of keratin 12 in *Lrig1* WT and KO corneas (3, 8 and 12 months). Keratin 12 is expressed in the *Lrig1* WT corneal epithelium (3, 8 and 12 months). It is also expressed in the *Lrig1* KO corneal epithelium (3 months), but as the corneal tissues show the abnormal phenotype, its expression is gradually decreased (8 and 12 months). Scale bar, 100μm.



Supplemental Figure 3. Images showing no obvious change in the expression of known signal pathways in *Lrig1* WT (3 months) and KO corneas (phenotype (-) 3 months, phenotype (+) 12 months). Immunostaining for EGFR, pEGFR, c-Met, β-catenin, and Notch1 (green) in *Lrig1* WT and KO (phenotype(+)(-)) corneas. Nuclei are counterstained with PI (red). Scale bar, 100μm.



Supplemental Figure 4. Validation of hematopoietic reconstitution after BM chimera generation. (A) Genotyping of a BM chimera *Lrig1* WT/KO mouse using tail, total BM, and thymus by PCR. (B) Representative flow cytometric analyses of WT (*Lrig1*+/+) and KO (*Lrig1*–/–) mice reconstituted with littermate control indicated as WT→WT, WT→KO, KO→WT, and KO→KO chimeric mice. The numbers represent the percentages of monocytes and macrophages (F4/80+/CD11b-, F4/80+/CD11b+, and F4/80-/CD11b+) in the BM, immature, and mature B cells (CD19+/IgM+) in the BM and spleen, and CD4 and CD8 double- and single-positive T cells in the thymus and spleen. (C) Frequencies and total numbers of myeloid and lymphoid populations in the BM, thymus, and spleen are shown. Each bar represents the mean ±SEM (error bars) of 3-5 chimeric mice.



Supplemental Figure 5. The remodeling of the corneal stroma (12 months) examined by transmission electron microscopy (TEM). (A) TEM micrographs of WT basal stroma showing normal diameter collagen fibrils. Scale bar, 100nm. (B) TEM micrographs of *Lrig1* KO of the corneal stroma showing wide variation in the diameter of the collagen fibrils. Some of the fibrils are over 90nm in size (*), over twice the diameter of normal fibrils. Scale bar, 100nm. (C) TEM micrographs of central corneal stroma from WT eyes. The micrograph shows a normal keratocyte (arrow). The collagen fibrils and lamella in the corneal stroma also appear normal. Scale bar, 1μm. (D) TEM micrograph of *Lrig1* KO of the remodelled anterior stroma. Disrupted lamellae are present together with numerous inflammatory cells (arrowheads). Abnormal keratocytes (arrows) are present, with enlarged nuclei and disrupted cytoplasm. Scale bar, 2 μm.