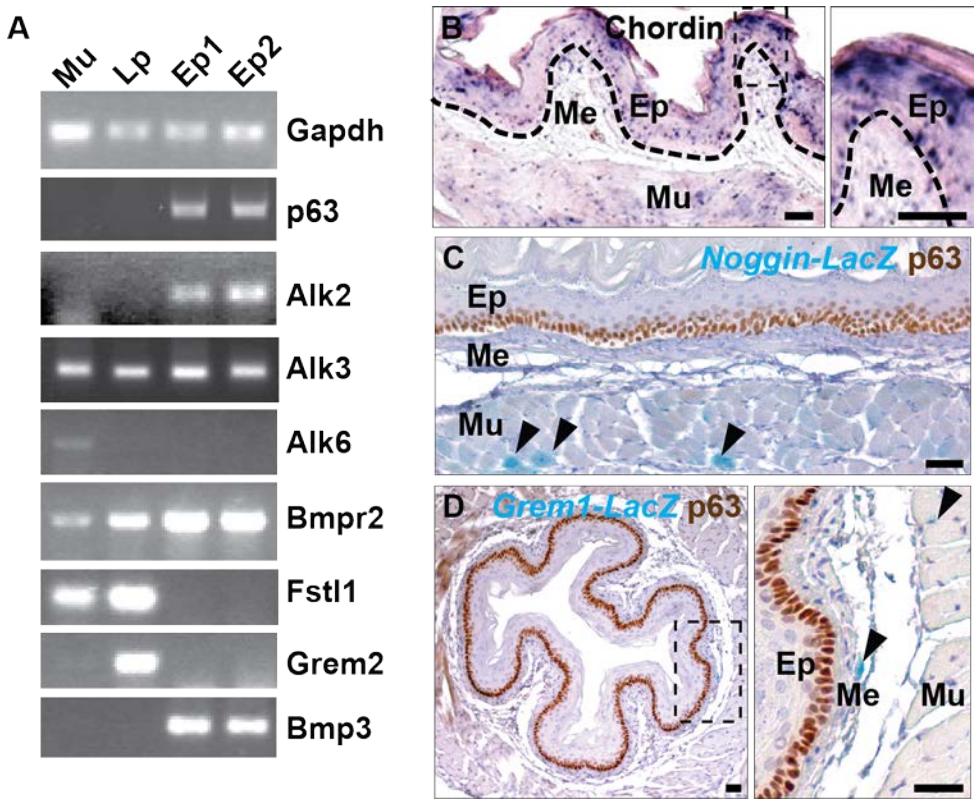
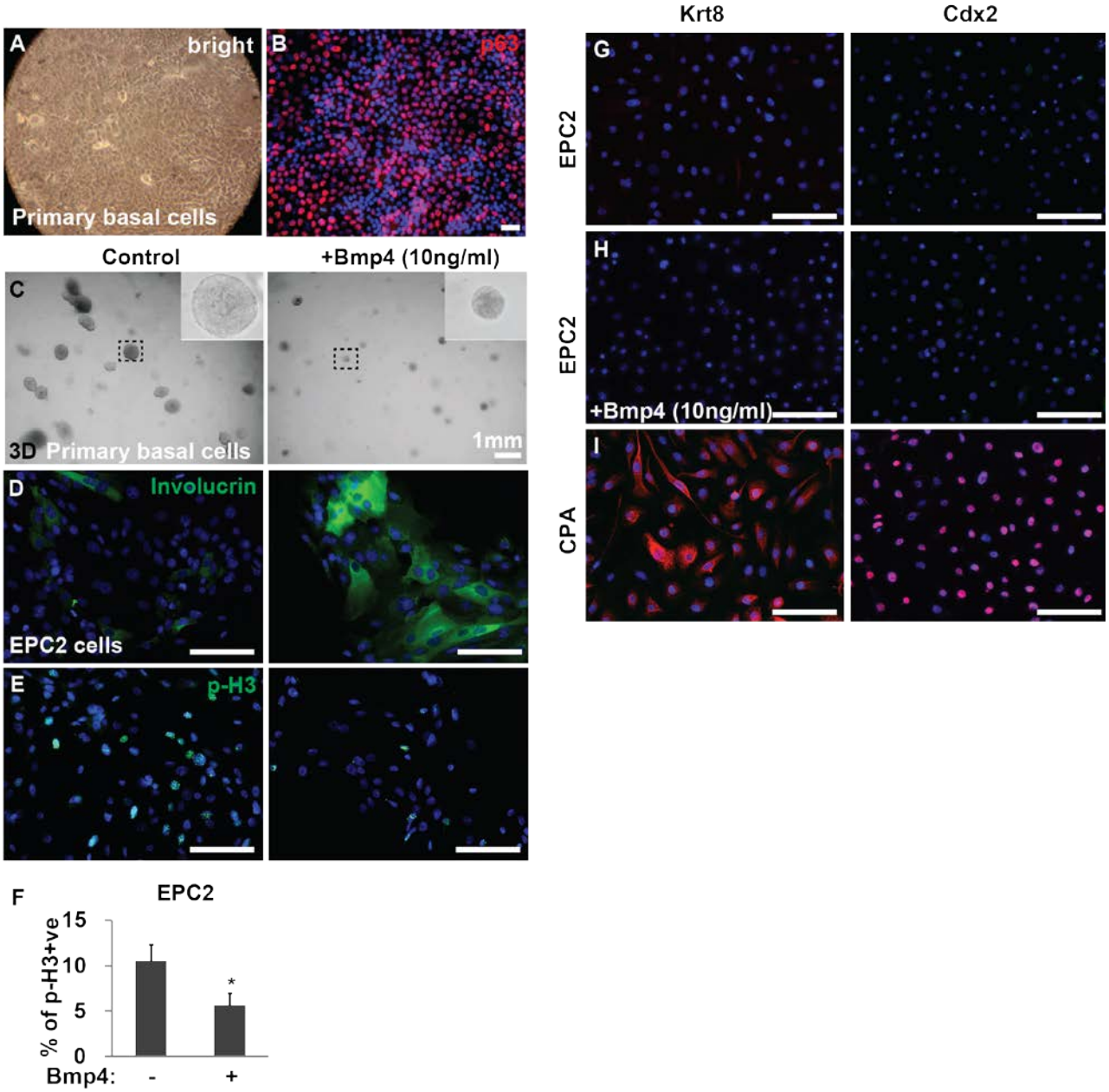
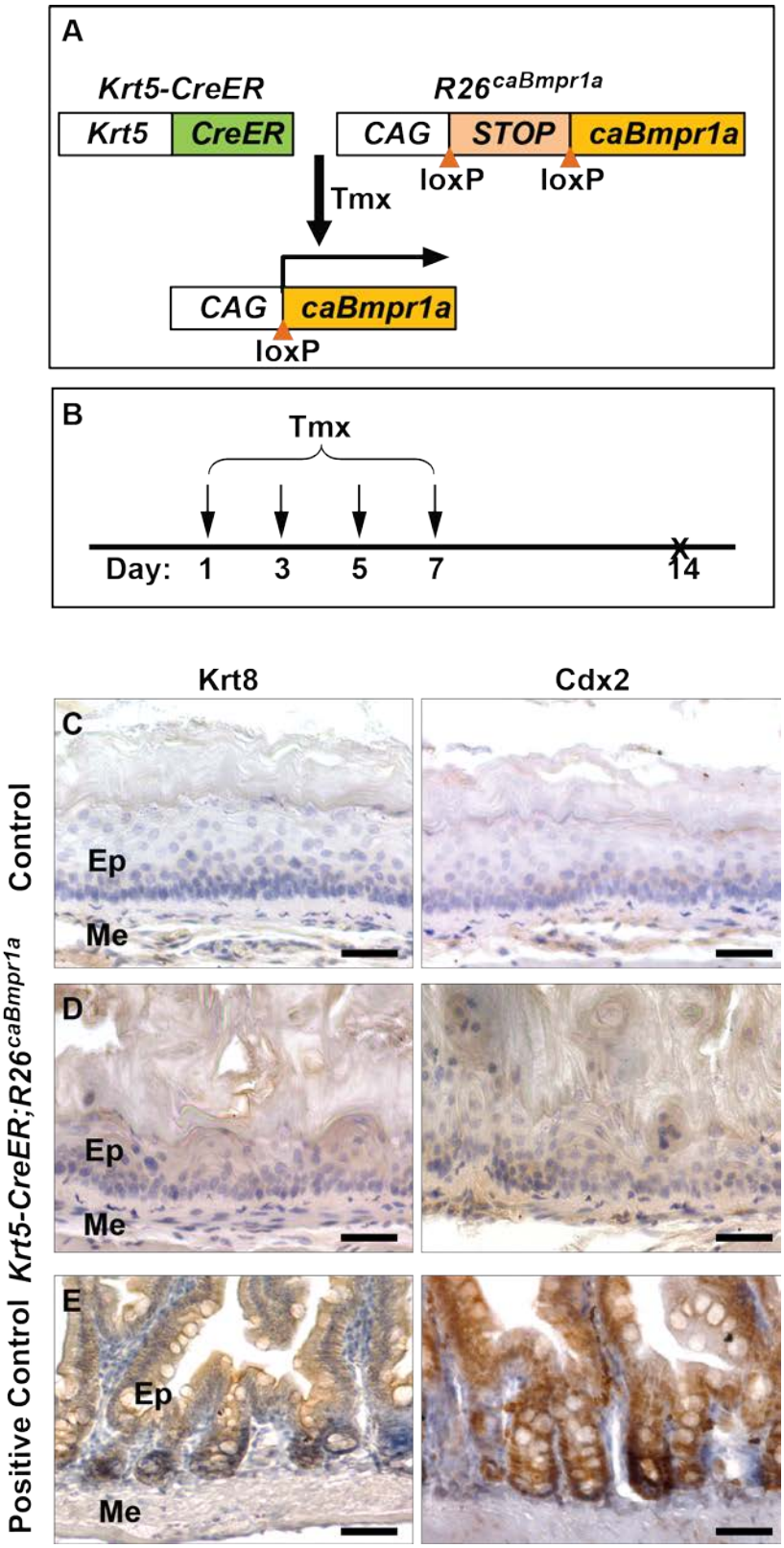


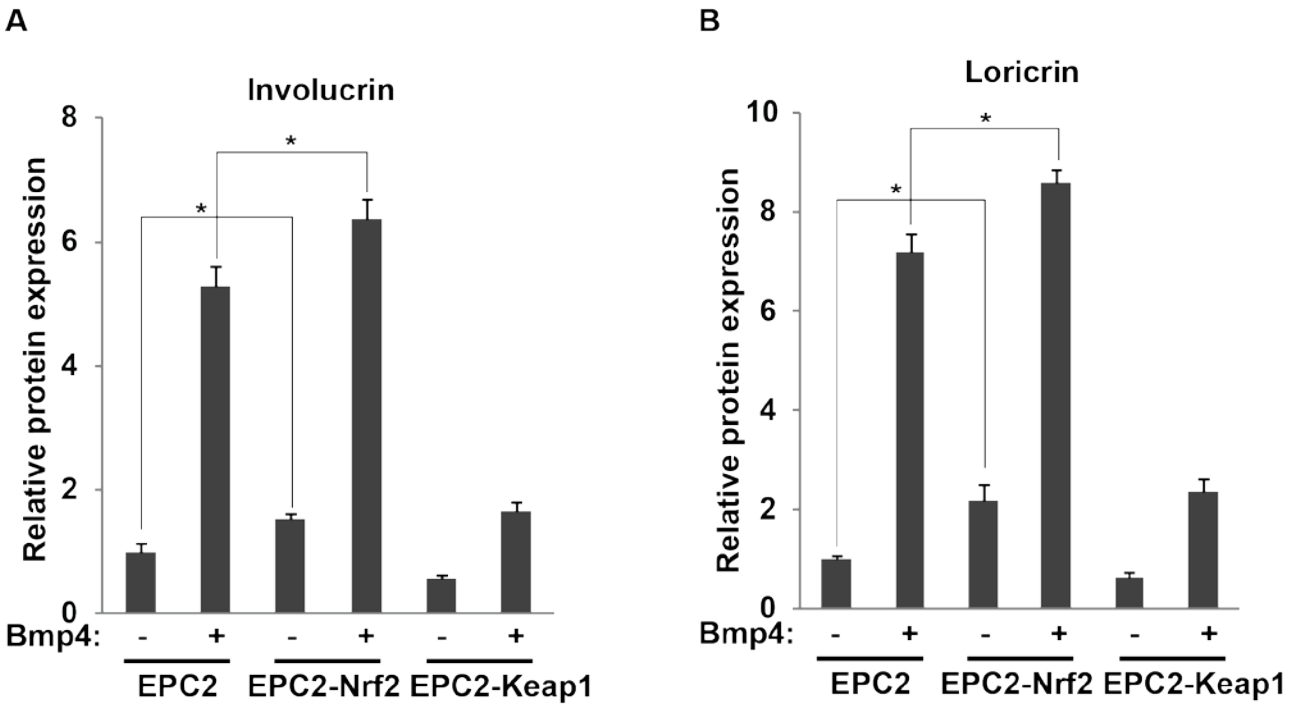
Supplemental Fig. 1. **Expression of the components of the BMP signaling pathway in the adult mouse esophagus.** (A) Expression of the transcripts for Bmps, receptors and inhibitors in different compartments of the adult esophagus. Note that p63 is used as an epithelial marker. (B) The Bmp inhibitor Chordin is enriched in the top most layers of differentiated epithelium as detected by in situ hybridization. The boxed region is shown enlarged at right. (C) *Noggin-lacZ* is expressed in a subpopulation of muscle cells (arrows). (D) *Grem1-lacZ* is expressed in a minor population of mesenchymal cells in the lamina propria and muscle cells (arrows). The boxed region is shown enlarged at right. Abbreviations: Mu, muscle; LP, lamina propria; Ep1, epithelium batch 1; Ep2, epithelium batch 2; Ep, epithelium; Me, mesenchyme. Scale bar: 50μm.



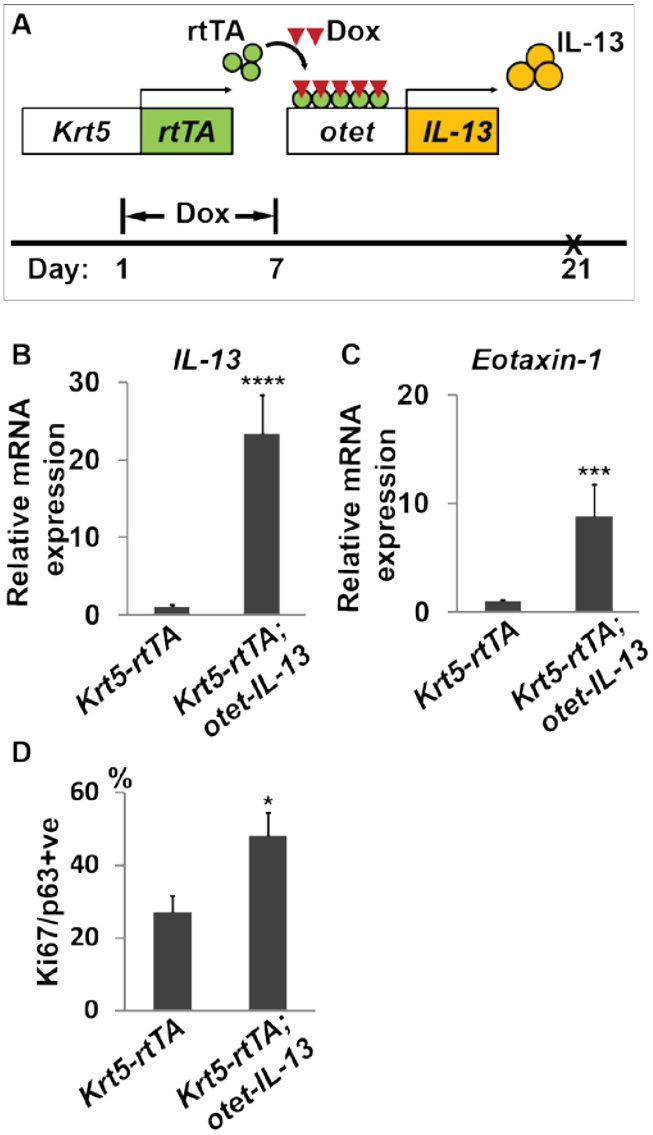
Supplemental Fig. 2. Bmp4-treatment inhibits the proliferation and promotes the squamous differentiation of the esophageal epithelial progenitor cells. (A-B) Primary mouse basal progenitor cells expand in vitro and maintain undifferentiated state (p63+ve). (C) Spheres formed from single mouse basal progenitor cells are smaller in the presence of Bmp4 than in PBS control. (D) Bmp4 treatment promotes the squamous differentiation of human basal cell-like EPC2 cells. (E-F) Bmp4 treatment inhibits the proliferation of EPC2 cells (n=3). (G-I) Bmp4 treatment does not promote the columnar differentiation of EPC2 cells. Note that CPA cells stained with Krt8 and Cdx2 were used as positive controls. Data are represented as mean ± SEM. *P<0.05 by Student's t test. Scale bar: 50μm.



Supplemental Fig. 3. Activation of BMP signaling does not promote the columnar differentiation of the mouse esophageal epithelium. (A-B) Schematic illustration for conditional overexpression of constitutively active *Bmpr1a* (*caBmpr1a*). Four tamoxifen injections were performed every other day and the animals were examined one week after the final injection. (C-E) Activation of BMP signaling does not promote the columnar differentiation of the esophageal epithelium as shown by Krt8 and Cdx2 staining. Intestinal epithelial sections stained with Krt8 and Cdx2 were used as positive controls. Scale bar: 50μm.



Supplemental Fig. 4. Quantification of protein levels of Involucrin and Loricrin in response to Nrf2 or Keap1 overexpression in the presence or absence of 10ng/ml Bmp4. Nrf2 overexpression significantly increases the protein levels of Involucrin (A) and Loricrin (B) in human EPC2 cells. In contrast, overexpression of Keap1, the inhibitor of Nrf2 maintains low levels of Involucrin (A) and Loricrin (B) in the presence of Bmp4. The quantification results were generated from three individual experiments. Data are represented as mean ± SEM. *P<0.05 by 2-way ANOVA.



Supplemental Fig. 5. Examination of basal cell hyperplasia in a mouse model of EoE and human EoE biopsy. (A) Scheme for generating *Krt5-rtTA; otet-IL-13* mutants in which IL-13 is specifically expressed in basal cells upon feeding doxycycline water. (B) The transcript levels of IL-13 are increased in *Krt5-rtTA; otet-IL-13* mutants (n=5). (C) The transcript levels of Eotaxin-1, a downstream mediator of IL-13 are significantly increased in *Krt5-rtTA; otet-IL-13* mutants (n=5). (D) Proliferation of basal cells is significantly increased upon IL-13 overexpression indicated by increased Ki67+ cells (n=5). Data are represented as mean ± SEM. **P*<0.05, ****P*<0.001, *****P*<0.0001 by Student's t test.

Supplemental Table 1

Fold changes in the activity of 45 signaling pathways included in the Cignal Finder 45-pathway Reporter Array.

Signaling pathway	Transcription factor	Fold change (Log_2)
Vitamin D	VDR	3.57*
KLF4	KLF4	3.41*
SP1	SP1	2.11*
Antioxidant response	NRF2	1.88*
MEF2	MEF2	1.75*
Amino Acid Deprivation	ATF2/3/4	1.64*
Retinoic Acid	RAR	1.28*
Type Interferon	STAT1/2	1.20*
NOTCH	RBP-Jk	1.18*
MAPK/ERK	SRF/Elk-1	1.14*
Interferon Regulation	IRF1	1.13*
Glucocorticoid	GR	0.91*
HNF4	HNF4	0.58
STAT3	STAT3	0.56
GATA	GATA	0.39
ER Stress	CBF/NF-Y/YY1	0.35
Myc	c-Myc	0.35
Wnt	TCF/LEF	0.33
NFkB	NFkB	0.24
Sox2	Sox2	0.21
Retinoid X	RXR	0.09
Cell Cycle	E2F	0.09
Pax6	Pax6	0.01
ATF6	ATF6	0.01
Heavy Metal	MTF-1	-0.01
Liver X	LXR	-0.05
cAMP/PKA	CREB	-0.05
Androgen	AR	-0.12
Heat Shock	HSF-1	-0.16
Interferon Gamma	STAT1	-0.18
MAPK/Jnk	AP-1	-0.28
TGFbeta	SMAD2/3/4	-0.30
Xenobiotic	AhR	-0.42
EGR1	EGR1	-0.75*
DNA Damage	p53	-0.82*
Hypoxia	HIF-1a	-1.06*
PI3K/Akt	FOXO	-1.12*
PKC/Ca++	NFAT	-1.12*
Estrogen	ER	-1.22*
Nanog	Nanog	-1.26*

PPAR	PPAR	-1.38*
Oct4	Oct4	-1.40*
C/EBP	C/EBP	-1.45*
Progesterone	PR	-1.54*
Hedgehog	Gli	-1.72*

*Statistically significant: $P < 0.05$, n=3.

Supplemental Table 2

Primer sets used for regular and real-time RT-PCR.

Reverse Transcriptional PCR Primers:	
Mouse p63 Forward	GTCAGCCACCTGGACGTATT
Mouse p63 Reverse	ACCTGTGGTGGCTCATAAGG
Mouse Alk2 Forward	CCAGAGGAACAAAGGAGCTG
Mouse Alk2 Reverse	AGCTGTACCTTCTCCCAGCA
Mouse Alk3 Forward	AGGTCAAAGCTGTTCGGAGA
Mouse Alk3 Reverse	CTGTACACGGCCCTTTGAAT
Mouse Alk6 Forward	GTACTGCAGGGCCACAATTT
Mouse Alk6 Reverse	TCTTCCAGGCTCAGGTGACT
Mouse Bmpr2 Forward	GGGAGCACGTGTTATGGTCT
Mouse Bmpr2 Reverse	CAGAAACTGATGCCAAAGCA
Mouse Bmp3 Forward	TGCTGTGGCTCTATGACAGG
Mouse Bmp3 Reverse	CTCTGAGTGTGATGGGAGCA
Mouse Fstl1 Forward	CCTGTGTGTGGCAGTAATGG
Mouse Fstl1 Reverse	TGGTGATGTTGATGGCTGTT
Mouse Grem2 Forward	CCTGTCATTCACAGAGAGGA
Mouse Grem2 Reverse	CATTCGAGCTCTACGATGAC
Mouse Gapdh Forward	TGTTCCTACCCCCAATGTGT
Mouse Gapdh Reverse	TGTGAGGGAGATGCTCAGTG
Real-Time PCR Primers:	
Human NRF2 Forward	CAAAAGGAGCAAGAGAAAGCC
Human NRF2 Reverse	TCTGATTTGGGAATGTGGGC
Human NQO1 Forward	TCACCGAGAGCCTAGTTCC
Human NQO1 Reverse	TCATGGCATAGTTGAAGGACG
Human Involucrin Forward	TCCAAGACATTCAACCAGCC
Human Involucrin Reverse	CTTGTATGAGACGATCTGAGGG
Human β-Actin Forward	GCTCGTCGTCGACAACGGCTC
Human β-Actin Reverse	CAAACATGATCTGGGTCATCTTCTC
Human IL-13 Forward	CATTGCTCTCACTTGCCTTG
Human IL-13 Reverse	TGATGCTCCATACCATGCTG
Human Eotaxin-3 Forward	GAGTGACATATCCAAGACCTGC
Human Eotaxin-3 Reverse	GGGTACAGACTTTCTTGCCTC
Human Follistatin Forward	GAAGTCCAGTACCAAGGCAG
Human Follistatin Reverse	TGGGCAAATCCGATTACAGG
Human NOX2 Forward	CCAGTGAAGATGTGTTCAGCT
Human NOX2 Reverse	GCACAGCCAGTAGAAGTAGAT
Human NOX4 Forward	TCACAGAAGGTTCCAAGCAG
Human NOX4 Reverse	ACTGAGAAGTTGAGGGCATTC
Human NOX5 Forward	TGTTCATCTGCTCCAGTTCC
Human NOX5 Reverse	ACAAGATTCCAGGCACCAG
Human GCLC Forward	GGCACAAGGACGTTCTCAAGT
Human GCLC Reverse	CAGACAGGACCAACCGGAC

Human GSTP1 Forward	TGCTAGAGATGACTCGGAAGG
Human GSTP1 Reverse	TGCTAGAGATGACTCGGAAGG
Mouse IL-13 Forward	CAGCTCCCTGGTTCTCTCAC
Mouse IL-13 Reverse	CCACACTCCATACCATGCTG
Mouse Eotaxin-1 Forward	CCCAACACACTACTGAAGAGCTACAA
Mouse Eotaxin-1 Reverse	TTTGCCCAACCTGGTCTTG
Mouse Follistatin Forward	AGAGGTCGCTGCTCTCTCTG
Mouse Follistatin Reverse	AGCTTCCTTCATGGCACACT
Mouse Nrf2 Forward	TCCCATTTGTAGATGACCATGAG
Mouse Nrf2 Reverse	CCATGTCCTGCTCTATGCTG
Mouse Nqo1 Forward	AGGATGGGAGGTACTCGAATC
Mouse Nqo1 Reverse	TGCTAGAGATGACTCGGAAGG
Mouse Involucrin Forward	AATTGGAGAACCGGACACAG
Mouse Involucrin Reverse	GTTTTGGCTTCACTGCACTTC
Mouse Loricrin Forward	ACATCAGCATCACCTCCTTC
Mouse Loricrin Reverse	TCTTTCCACAACCCACAGG
Mouse Gclc Forward	CTACCACGCAGTCAAGGACC
Mouse Gclc Reverse	CCTCCATTCAGTAACAACTGGAC
Mouse Gstp1 Forward	ATGCCACCATACACCATTGTC
Mouse Gstp1 Reverse	GGGAGCTGCCCATACAGAC