Appendix File

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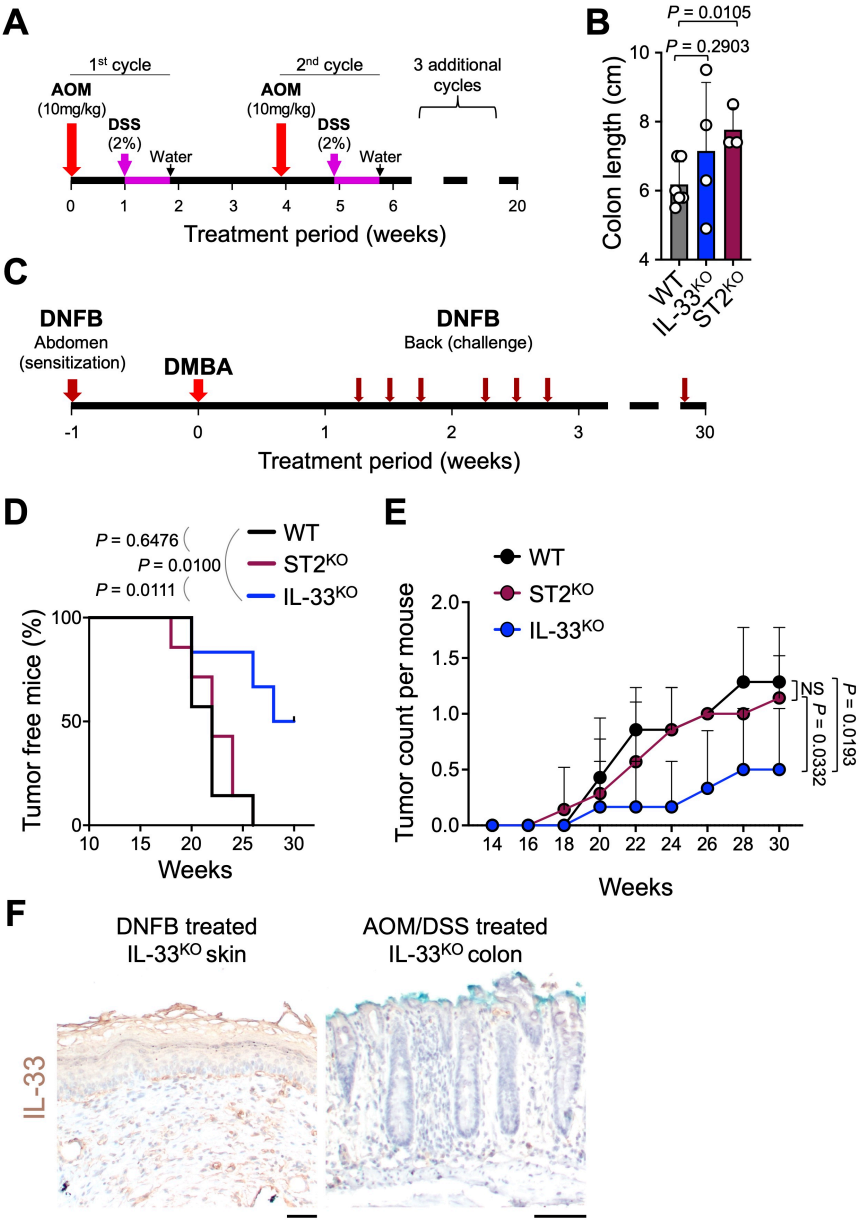
Appendix Figures



Appendix Fig S1. IL-33/ST2 impact on colorectal and skin carcinogenesis in chronic inflammation.

(**A**) Schematic diagram of colitis-induced colorectal carcinogenesis protocol in mice, consisting of five AOM/DSS treatment cycles over 20 weeks.

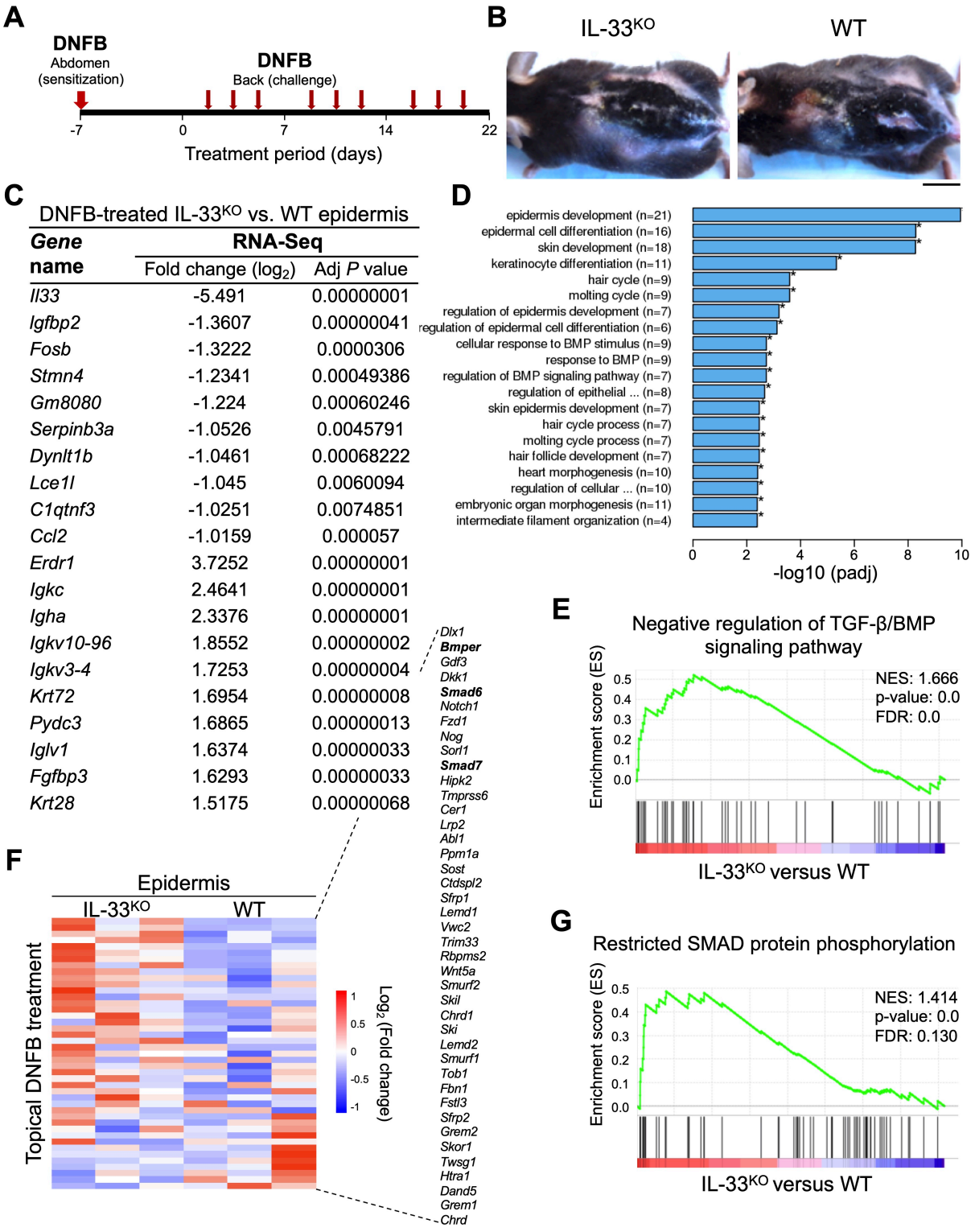
(**B**) Colon length measurement, from cecum to rectum, in WT (n=6), IL-33^{KO} (n=4) and ST2^{KO} (n=3) mice at the completion of the AOM/DSS carcinogenesis protocol.

(**C**) Experimental design for chronic inflammation-induced skin carcinogenesis consisting of an initial sensitization to DNFB allergen on the abdomen followed by treatment with a single dose of DMBA followed by DNFB challenges on the back skin three times a week for 29 weeks.

(**D** and **E**) Skin tumor outcome in WT (n=7), ST2^{KO} (n=7) and IL-33^{KO} (n=6) mice treated with DMBA/DNFB carcinogenesis protocol. (D) Time to tumor onset (log-rank test) and (E) the number of skin tumors over time.

(**F**) Representative images of IL-33 immunostained DNFB-treated skin and AOM/DSS-treated colon tissues from IL-33^{KO} mice (scale bars: 100 μm).

Data information: Graphs show mean + SD, NS: not significant, unpaired *t*-test.



Appendix Fig S2. RNA-Seq analysis to identify IL-33 nuclear function.

(**A**) The experimental design used to induce chronic skin inflammation with repeated topical DNFB treatment. At the completion of the 22-day treatment period, epidermis samples were collected for RNA-Seq.

(**B**) Representative images of IL-33^{KO} and WT mice after 22-day DNFB back skin treatment (scale bar: 1 cm).

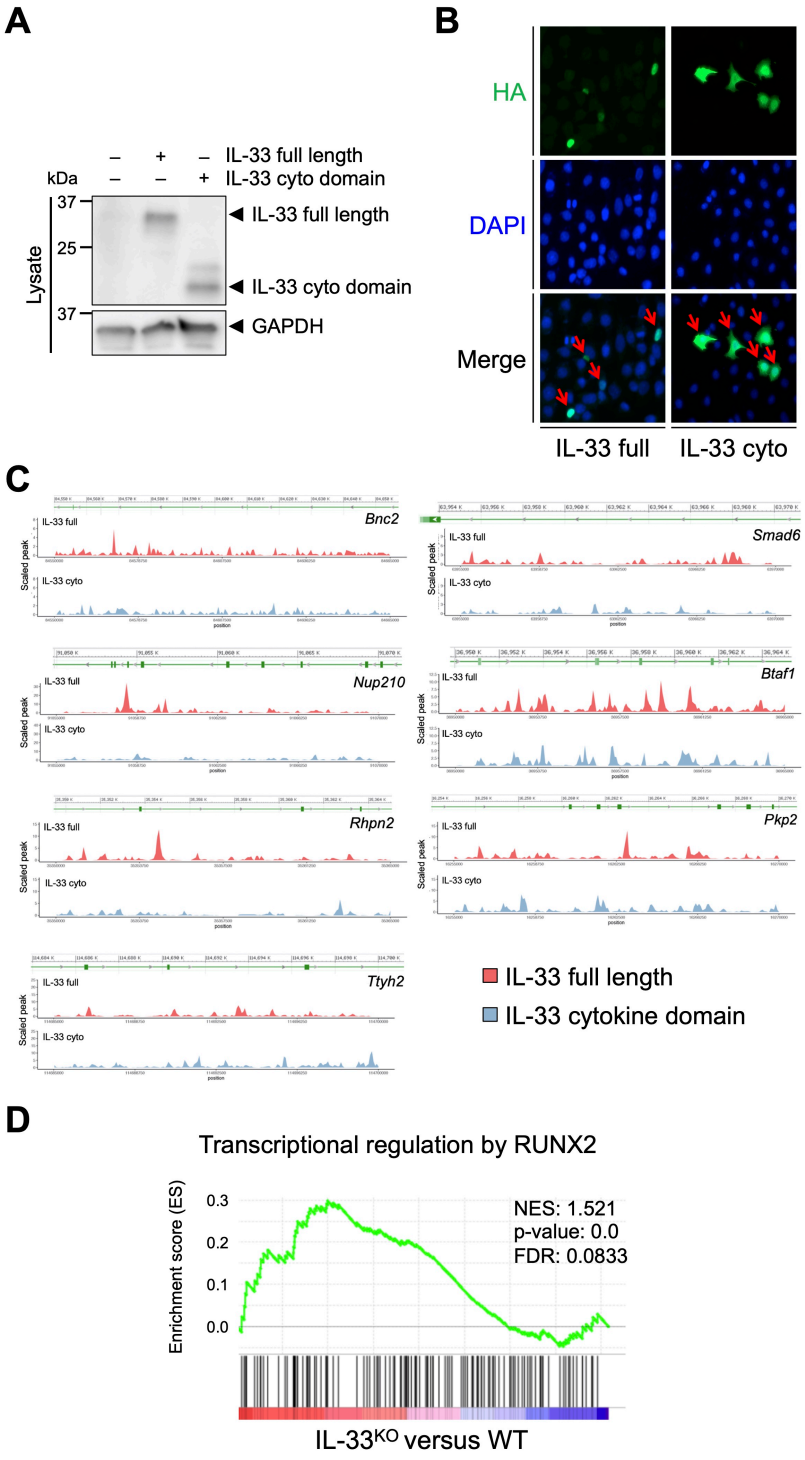
(**C**) Top 20 differentially expressed genes (DEGs) in DNFB-treated IL-33^{KO} compared with WT epidermis from RNA-Seq.

(**D**) Biological pathways highlighted by DEGs from RNA-Seq.

(**E**) The enrichment plot of negative regulation of BMP signaling pathway gene set in IL-33^{KO} compared with WT epidermis treated with DNFB.

(**F**) Heatmap of negative regulation of TGF-β/BMP signaling pathway gene set in IL-33^{KO} versus WT epidermis after topical treatment with DNFB. This gene list contains several genes (highlighted) that are shared between BMP and TGF-β signaling pathways.

(**G**) The enrichment plot of a restricted SMAD protein phosphorylation gene set in IL-33^{KO} compared with WT epidermis treated with DNFB.



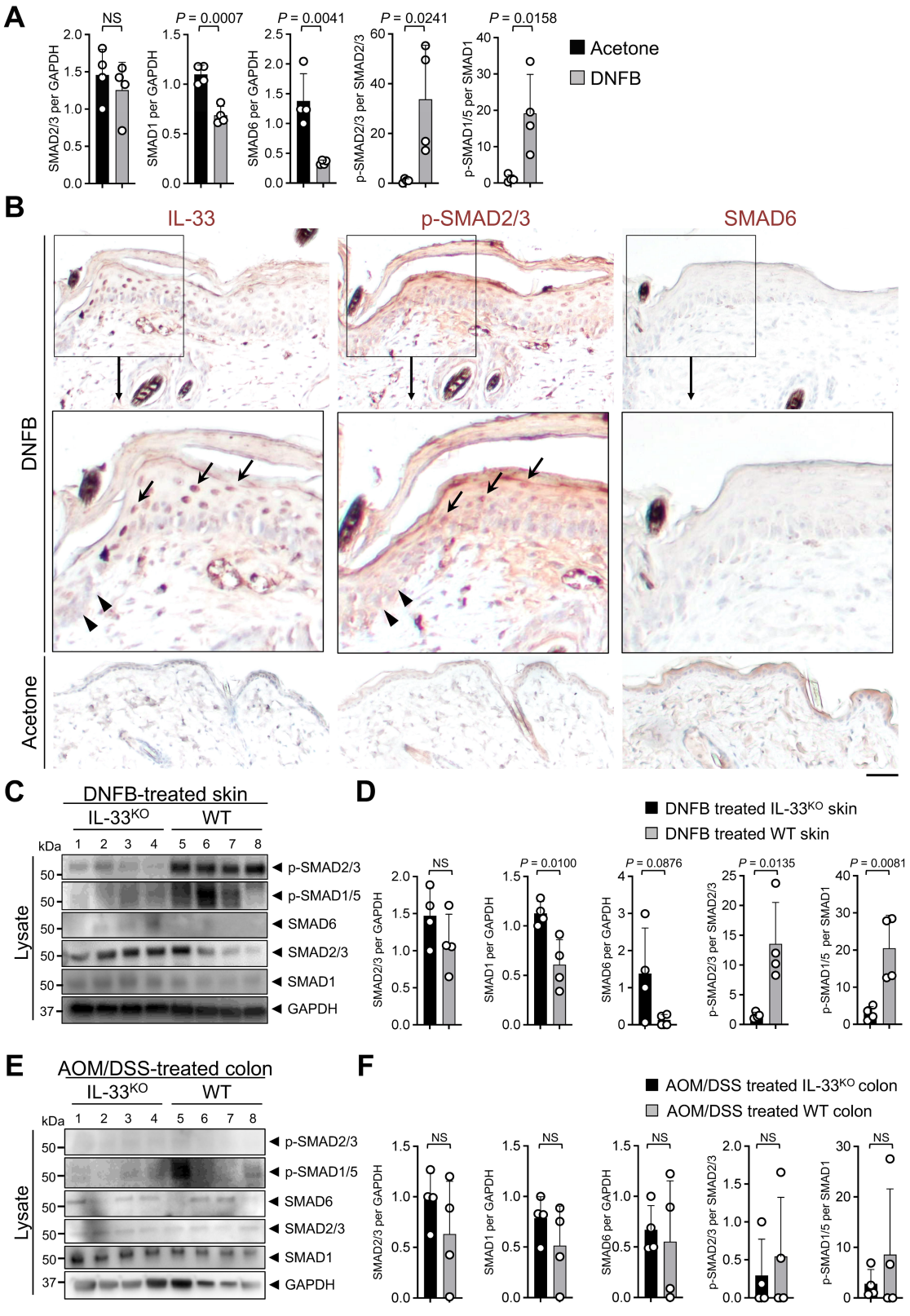
Appendix Fig S3. Integrative analysis of RNA-Seq and ChIP-Seq results.

(**A**) Expression of IL-33 full length and IL-33 cytokine domain in Pam212 cells. GAPDH is used as the control housekeeping protein.

(**B**) Representative images for localization of IL-33 expression constructs. Anti-HA antibody marks the IL-33 constructs. Red arrows point to the IL-33-positive cells.

(**C**) Peak calling analysis of genes identified from the integrative analysis of RNA-Seq and ChIP-Seq results. Genome-browser views of IL-33 full length (full) and IL-33 cytokine domain (cyto) ChIP-Seq signals for *Bnc2*, *Nup210*, *Rhpn2*, *Ttyh2*, *Smad6*, *Btaf1* and *Pkp2* genes.

(**D**) The enrichment plot of transcriptional regulation by RUNX2 gene set in IL-33^{KO} compared with WT epidermis treated with DNFB from RNA-Seq analysis.



Appendix Fig S4. IL-33 regulates SMAD signaling in inflamed skin but not the colon.

(**A**) Quantification of protein bands shown in Figure 3A.

(**B**) Representative images of IL-33, p-SMAD2/3 and SMAD6 IHC on the adjacent sections of DNFB versus acetone-treated mouse skin. Arrows in the insets point to nuclear IL-33 and p-SMAD2/3 stains in the epidermis and arrowheads highlight keratinocytes nuclei that are negative for both IL-33 and p-SMAD2/3 (scale bar: 100 μm).

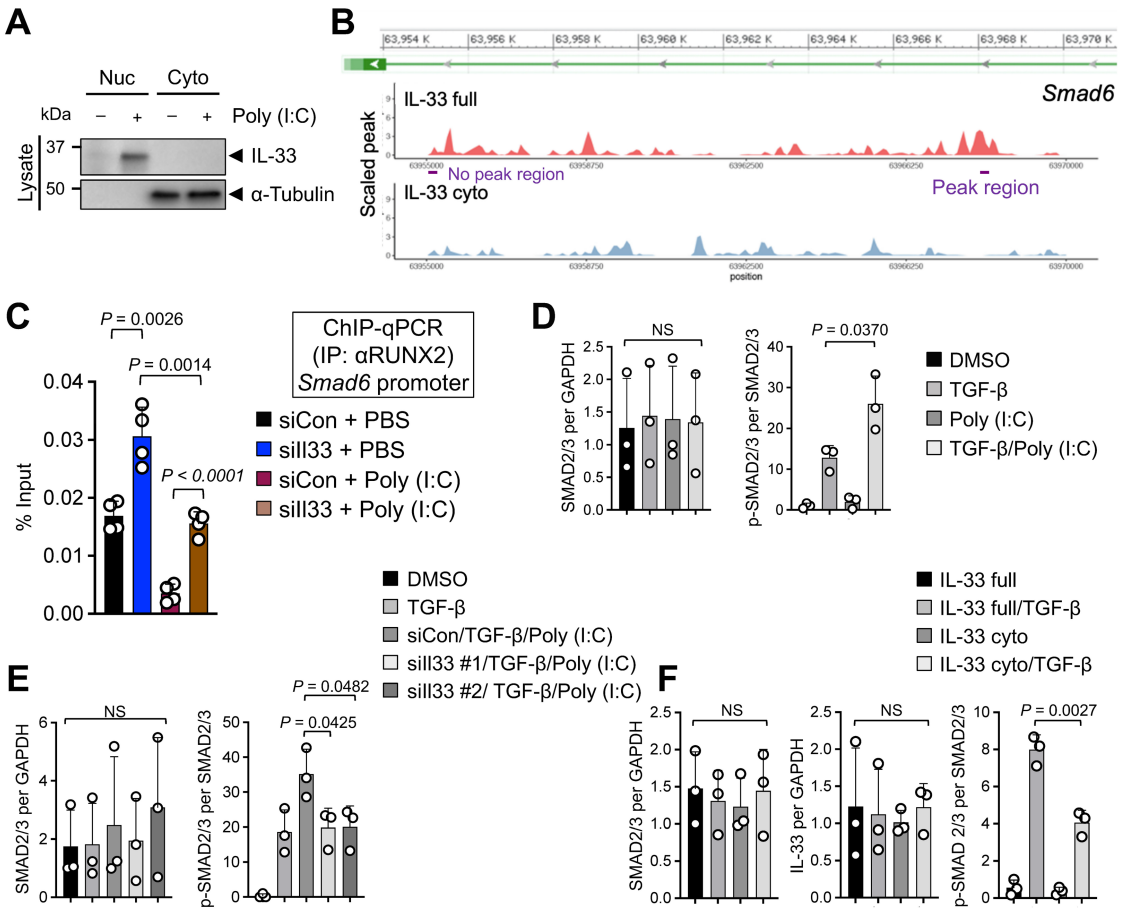
(**C**) Immunoblots for p-SMAD2/3, p-SMAD1/5, SMAD6, SMAD2/3 and SMAD1 proteins in IL-33^{KO} and WT skin after DNFB treatment.

(**D**) Quantification of protein bands shown in S4C.

(**E**) Immunoblots for p-SMAD2/3, p-SMAD1/5, SMAD6, SMAD2/3 and SMAD1 proteins in IL-33^{KO} and WT colon after AOM/DSS treatment.

(**F**) Quantification of protein bands shown in S4E.

Data information: GAPDH is used as the control housekeeping protein, graphs show mean + SD, NS: not significant, unpaired *t*-test.



Appendix Fig S5. Nuclear IL-33 induced by poly (I:C) binds to the *Smad6* regulatory region.

(**A**) IL-33 protein levels in nuclear (Nuc) and cytoplasmic (Cyto) fractions of Pam212 cells treated with poly (I:C). Each fraction's lysate was subjected to immunoblot with anti-IL-33 and anti-α-tubulin antibodies.

(**B**) Peak and no peak regions of *Smad6* regulatory region amplified in ChIP-qPCR assay using an anti-IL-33 antibody.

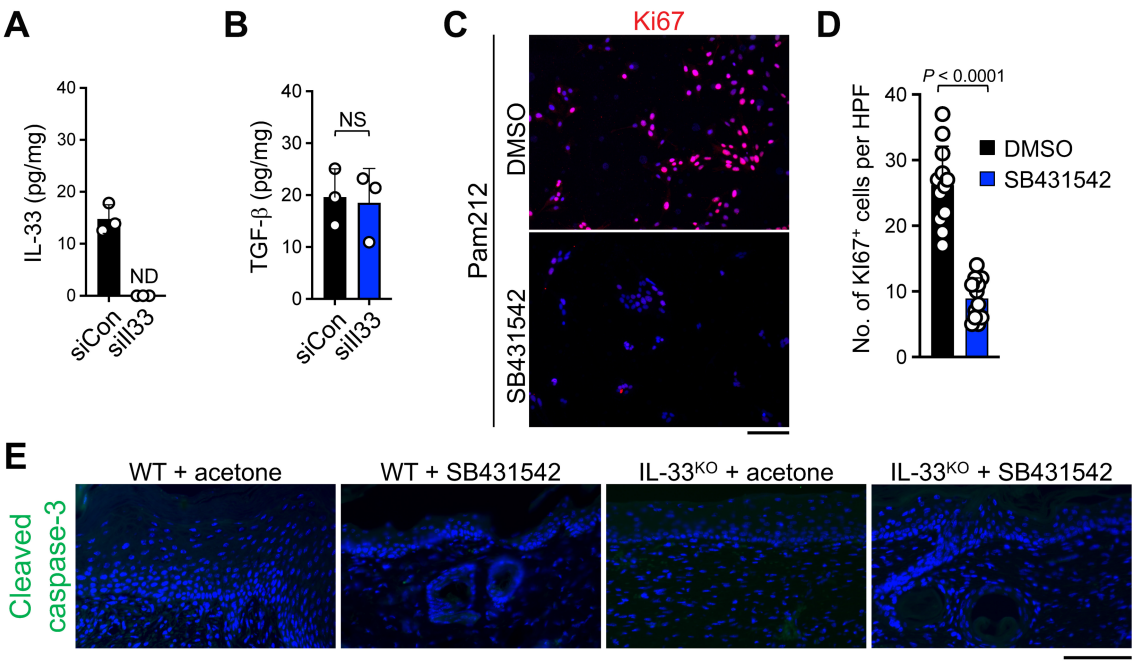
(**C**) ChIP-qPCR assay for *Smad6* promoter upon induction of endogenous IL-33 with or without siIl33 using an anti-RUNX2 antibody. After transfection with siIl33 #1 or control siRNA (siCon) for 24 hours, Pam212 cells were treated with poly (I:C) or PBS (carrier control). Cell lysates were subjected to chromatin-immunoprecipitation with anti-RUNX2 antibody and eluted RUNX2-bound chromatin was used for qPCR with *Smad6* promoter primers.

(**D**) Quantification of protein bands shown in Figure 3D.

(**E**) Quantification of protein bands shown in Figure 3E.

(**F**) Quantification of protein bands shown in Figure 3F.

Data information: Graphs show mean + SD, NS: not significant, unpaired *t*-test.



Appendix Fig S6. SB431542 blocks keratinocyte proliferation but does not induce apoptosis.

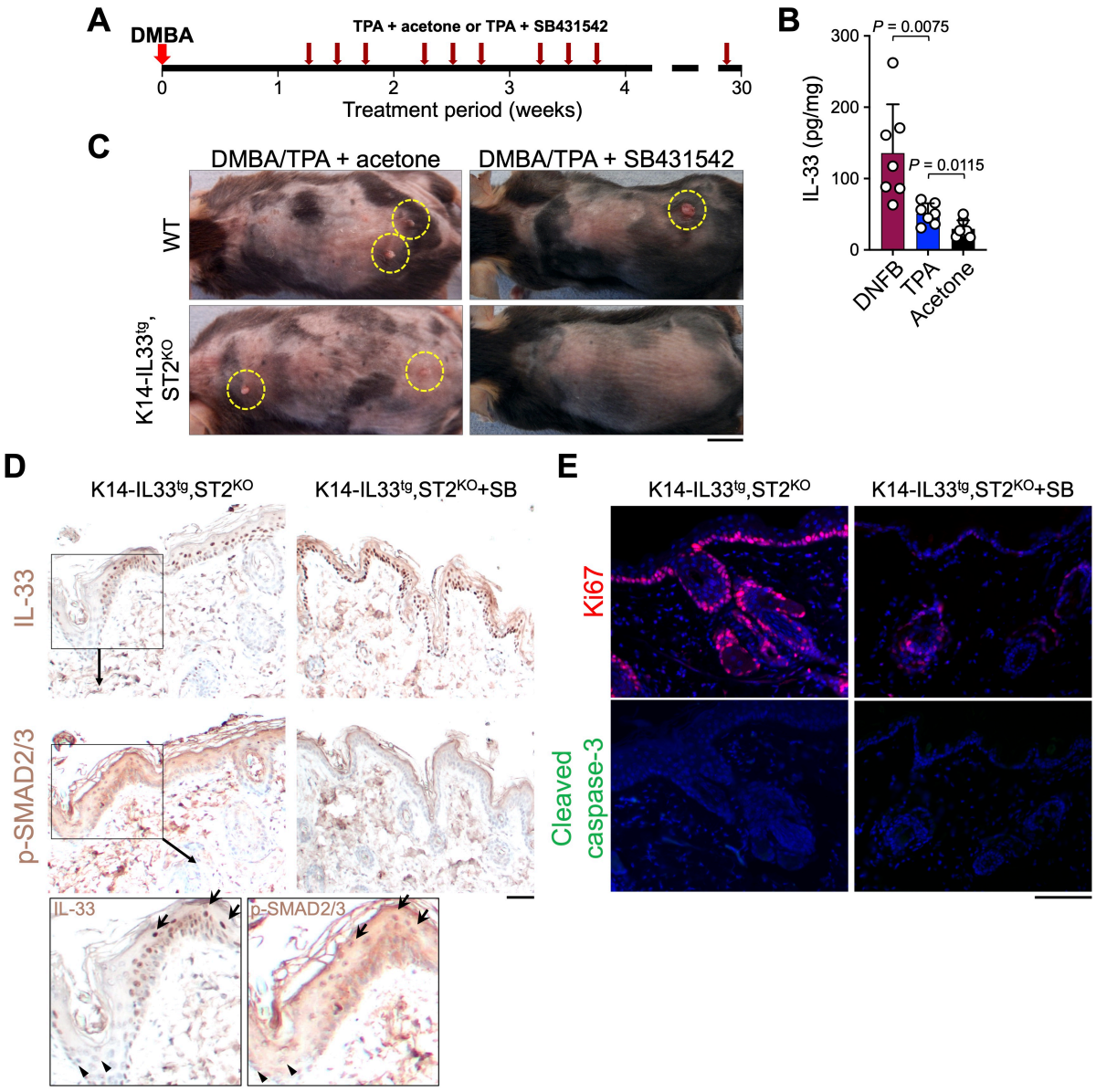
(**A** and **B**) Endogenous (A) IL-33 and (B) TGF-β protein levels in Pam212 cell lysate after treatment with sill33 versus siCon. ND: not detected, NS: not significant.

(**C**) Representative images of Ki67-stained Pam212 cells treated with SB431542 or DMSO (carrier control) for 24 hours.

(**D**) Quantification of Ki67$^+$ Pam212 cells treated with SB431542 versus DMSO (unpaired *t*-test).

(**E**) Representative images of cleaved caspase-3 immunofluorescence-stained skin tissues shown in Figure 3I.

Data information: Scale bars: 100 μm.



Appendix Fig S7. Blocking TGF-β/SMAD signaling attenuates nuclear IL-33 induced skin cancer development.

(**A**) Experimental design for DMBA/TPA skin carcinogenesis protocol in combination with TGF-β/SMAD inhibitor, SB431542, treatment.

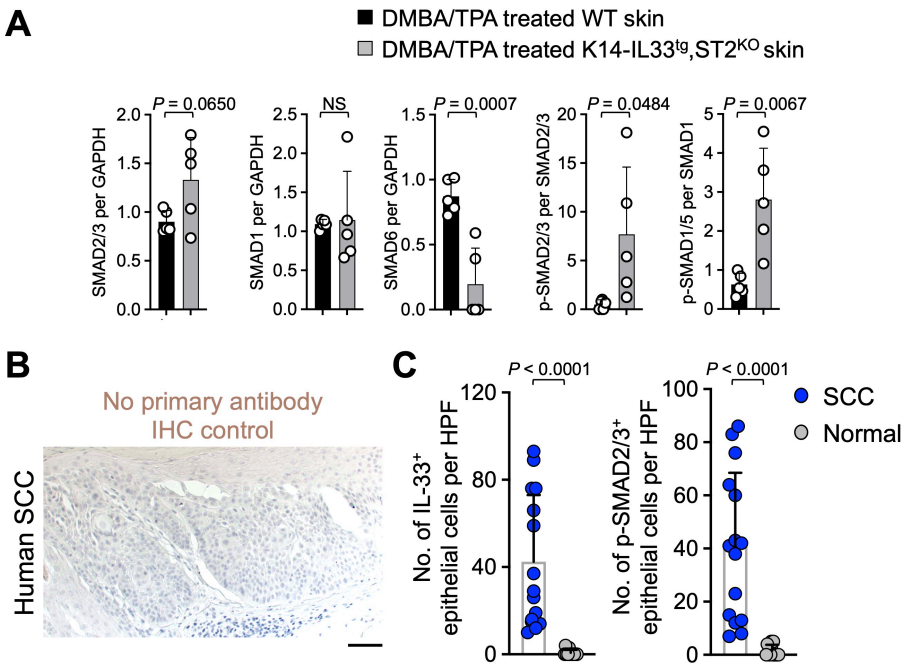
(**B**) IL-33 protein levels in TPA- and DNFB-treated skin compared with acetone (carrier)-treated controls (n=7 in each group, graph shows mean + SD, unpaired *t*-test).

(**C**) Representative images of WT and K14-IL33^{tg},ST2^{KO} mice treated with SB431542 or acetone (carrier control) at the completion of DMBA/TPA carcinogenesis protocol (yellow circles highlight the skin tumors).

(**D**) Representative images of IL-33 and p-SMAD2/3 immunostained adjacent skin sections from SB431542 and acetone-treated K14-IL33^{tg},ST2^{KO} mice that completed DMBA/TPA carcinogenesis protocol. Arrows point to IL-33^{+} and p-SMAD2/3^{+} epidermal keratinocytes. Arrowheads highlight keratinocytes that lack both IL-33 and p-SMAD2/3.

(**E**) Representative images of Ki67 and cleaved caspase-3 immunofluorescence staining on the adjacent sections of SB431542 and acetone-treated K14-IL33tg,ST2^{KO} skin that underwent DMBA/TPA carcinogenesis protocol.

Data information: Scale bars: mouse 1cm, tissue 100 μm.



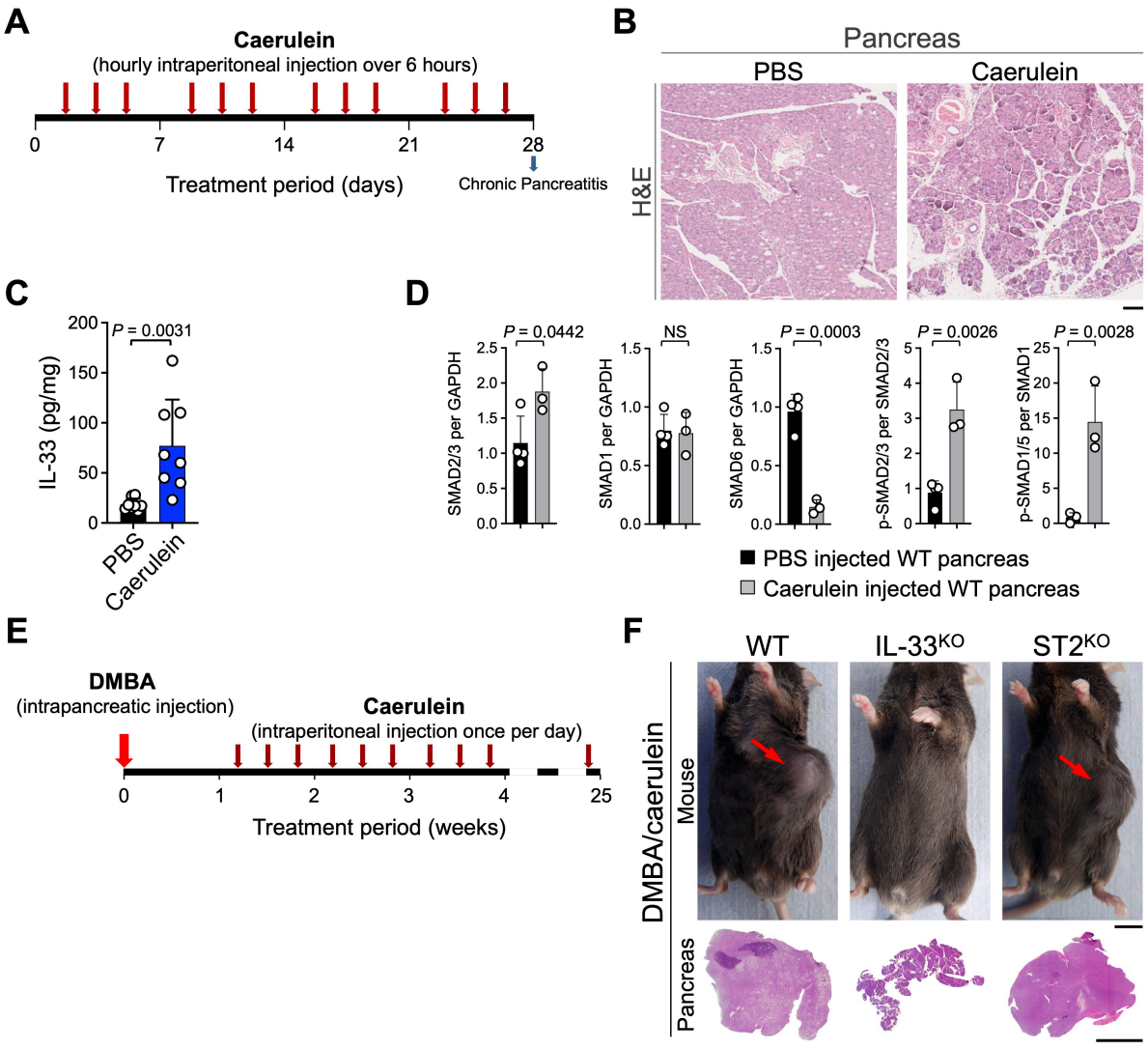
Appendix Fig S8. IL-33 and p-SMAD2/3 are highly expressed in human SCC.

(**A**) Quantification of protein bands shown in Figure 4I.

(**B**) Representative image of negative control (no primary antibody) immunostaining on the adjacent tissue section of the human SCC sample shown in Figure 4J (scale bar: 100 μm).

(**C**) Quantification of nuclear IL-33$^+$ and p-SMAD2/3$^+$ epithelial cells per HPF in SCC versus normal human skin. Dots represent cell counts in three randomly selected HPF images per sample across 5 SCC and 5 normal skin samples.

Data information: Graphs show mean + SD, NS: not significant, unpaired *t*-test.



Appendix Fig S9. Nuclear IL-33 promotes pancreatic cancer development in chronic pancreatitis.

(**A**) Experimental design for the induction of chronic pancreatitis in mice.

(**B**) Representative images of H&E-stained pancreas of WT mice treated with caerulein versus PBS (carrier control) for 4 weeks (scale bar: 100 μm).

(**C**) IL-33 protein levels in caerulein- compared with PBS-treated pancreas.

(**D**) Quantification of protein bands shown in Figure 5C.

(**E**) Experimental design for DMBA/caerulein-induced pancreatic cancer including an intrapancreatic injection with DMBA followed by intraperitoneal caerulein injections once per day, three times a week for 24 weeks.

(**F**) Representative images of DMBA/caerulein-treated WT, IL-33^{KO} and ST2^{KO} mice and H&E-stained pancreas of WT, IL-33^{KO} and ST2^{KO}. Red arrows point to pancreatic tumor mass under the skin of WT and ST2^{KO} mice. Note the replacement of pancreas with large fibrotic tumors in WT and ST2^{KO} mice (scale bar: 1 cm).

Data information: Graphs show mean + SD, NS: not significant, unpaired *t*-test.

Appendix Tables

Appendix Table S1. List of 203 DEGs from RNA-Seq analysis of IL-33^{KO} versus WT epidermis treated with DNFB.

Gene ID	Gene Name	Gene Description
ENSMUSG00000000184	Ccnd2	cyclin_D2
ENSMUSG00000001510	Dlx3	distal-less_homeobox_3
ENSMUSG00000001655	Hoxc13	homeobox_C13
ENSMUSG00000002057	Foxn1	forkhead_box_N1
ENSMUSG00000003418	St8sia6	ST8_alpha-N-acetyl-neuraminide_alpha-28-sialyltransferase_6
ENSMUSG00000003545	Fosb	FBJ_osteosarcoma_oncogene_B
ENSMUSG00000004552	Ctse	cathepsin_E
ENSMUSG00000005262	Ufd1l	ubiquitin_fusion_degradation_1_like
ENSMUSG00000006345	Ggt1	gamma-glutamyltransferase_1
ENSMUSG00000014846	Tppp3	tubulin_polymerization-promoting_protein_family_member_3
ENSMUSG00000015441	Gzmf	granzyme_F
ENSMUSG00000015619	Gata3	GATA_binding_protein_3
ENSMUSG00000015957	Wnt11	wingless-type_MMTV_integration_site_family_member_11
ENSMUSG00000017588	Krt27	keratin_27
ENSMUSG00000018983	E2f2	E2F_transcription_factor_2
ENSMUSG00000019564	Arid3a	AT_rich_interactive_domain_3A_(BRIGHT-like)
ENSMUSG00000020099	Unc5b	unc-5_homolog_B_(C._elegans)
ENSMUSG00000020216	Jsrp1	junctional_sarcoplasmic_reticulum_protein_1
ENSMUSG00000020473	Aebp1	AE_binding_protein_1
ENSMUSG00000020723	Cacng4	calcium_channel_voltage-dependent_gamma_subunit_4
ENSMUSG00000020732	Rab37	RAB37_member_RAS_oncogene_family
ENSMUSG00000020871	Dlx4	distal-less_homeobox_4
ENSMUSG00000020891	Alox8	arachidonate_8-lipoxygenase
ENSMUSG00000020916	Krt36	keratin_36
ENSMUSG00000021061	Sptb	spectrin_beta_erythrocytic
ENSMUSG00000021250	Fos	FBJ_osteosarcoma_oncogene
ENSMUSG00000021469	Msx2	msh_homeobox_2
ENSMUSG00000022044	Stmn4	stathmin-like_4
ENSMUSG00000022243	Slc45a2	solute_carrier_family_45_member_2
ENSMUSG00000022415	Syngr1	synaptogyrin_1
ENSMUSG00000022658	Tagln3	transgelin_3
ENSMUSG00000022871	Fetub	fetuin_beta
ENSMUSG00000022986	Krt75	keratin_75
ENSMUSG00000023034	Nr4a1	nuclear_receptor_subfamily_4_group_A_member_1

ENSMUSG00000023387	Kcnk16	potassium_channel_subfamily_K_member_16
ENSMUSG00000023391	Dlx2	distal-less_homeobox_2
ENSMUSG00000024059	Clip4	CAP-GLY_domain_containing_linker_protein_family_member_4
ENSMUSG00000024190	Dusp1	dual_specificity_phosphatase_1
ENSMUSG00000024232	Bambi	BMP_and_activin_membrane-bound_inhibitor
ENSMUSG00000024353	Mzb1	marginal_zone_B_and_B1_cell-specific_protein_1
ENSMUSG00000024409	Psors1c2	psoriasis_susceptibility_1_candidate_2_(human)
ENSMUSG00000024471	Myot	myotilin
ENSMUSG00000024538	Ppic	peptidylprolyl_isomerase_C
ENSMUSG00000024806	Mlana	melan-A
ENSMUSG00000024810	Il33	interleukin_33
ENSMUSG00000024975	Pdcd4	programmed_cell_death_4
ENSMUSG00000025328	Padi3	peptidyl_arginine_deiminase_type_III
ENSMUSG00000025329	Padi1	peptidyl_arginine_deiminase_type_I
ENSMUSG00000025359	Pmel	premelanosome_protein
ENSMUSG00000025407	Gli1	GLI-Kruppel_family_member_GLI1
ENSMUSG00000025453	Nnt	nicotinamide_nucleotide_transhydrogenase
ENSMUSG00000025461	Cd163l1	CD163_molecule-like_1
ENSMUSG00000026407	Cacna1s	calcium_channel_voltage-dependent_L_type_alpha_1S_subunit
ENSMUSG00000026420	Il24	interleukin_24
ENSMUSG00000026489	Adck3	aarF_domain_containing_kinase_3
ENSMUSG00000026950	Neb	nebulin
ENSMUSG00000027015	Cybrd1	cytochrome_b_reductase_1
ENSMUSG00000027403	Tgm6	transglutaminase_6
ENSMUSG00000027470	Mylk2	myosin_light_polypeptide_kinase_2_skeletal_muscle
ENSMUSG00000027487	Cdk5rap1	CDK5_regulatory_subunit_associated_protein_1
ENSMUSG00000027800	Tm4sf1	transmembrane_4_superfamily_member_1
ENSMUSG00000028111	Ctsk	cathepsin_K
ENSMUSG00000028195	Cyr61	cysteine_rich_protein_61
ENSMUSG00000028358	Zfp618	zinc_finger_protein_618
ENSMUSG00000028487	Bnc2	basonuclin_2
ENSMUSG00000028654	Mycl	v-myc_myelocytomatosis_viral_oncogene_homolog_lung_carcinoma_derived_(avian)
ENSMUSG00000028681	Ptch2	patched_homolog_2
ENSMUSG00000028698	Pik3r3	phosphatidylinositol_3_kinase_regulatory_subunit_polypeptide_3_(p55)
ENSMUSG00000028940	Hes2	hairy_and_enhancer_of_split_2_(Drosophila)
ENSMUSG00000029070	Mxra8	matrix-remodelling_associated_8
ENSMUSG00000029095	Ablim2	actin-binding_LIM_protein_2
ENSMUSG00000029337	Fgf5	fibroblast_growth_factor_5
ENSMUSG00000029380	Cxcl1	chemokine_(C-X-C_motif)_ligand_1

ENSMUSG00000029641	Rasl11a	RAS-like_family_11_member_A
ENSMUSG00000029705	Cux1	cut-like_homeobox_1
ENSMUSG00000030091	Nup210	nucleoporin_210
ENSMUSG00000030108	Slc6a13	solute_carrier_family_6_(neurotransmitter_transporter_GABA)_member_13
ENSMUSG00000030205	Gprc5d	G_protein-coupled_receptor_family_C_group_5_member_D
ENSMUSG00000030409	Dmpk	dystrophia_myotonica-protein_kinase
ENSMUSG00000030494	Rhpn2	rhophilin_Rho_GTPase_binding_protein_2
ENSMUSG00000030523	Trpm1	transient_receptor_potential_cation_channel_subfamily_M_member_1
ENSMUSG00000030592	Ryr1	ryanodine_receptor_1_skeletal_muscle
ENSMUSG00000030717	Nupr1	nuclear_protein_transcription_regulator_1
ENSMUSG00000030739	Myh14	myosin_heavy_polypeptide_14
ENSMUSG00000030905	Crym	crystallin_mu
ENSMUSG00000031963	Bmper	BMP-binding_endothelial_regulator
ENSMUSG00000031995	St14	suppression_of_tumorigenicity_14_(colon_carcinoma)
ENSMUSG00000032053	Pou2af1	POU_domain_class_2_associating_factor_1
ENSMUSG00000032327	Stra6	stimulated_by_retinoic_acid_gene_6
ENSMUSG00000032368	Zic1	zinc_finger_protein_of_the_cerebellum_1
ENSMUSG00000032500	Dclk3	doublecortin-like_kinase_3
ENSMUSG00000032648	Pygm	muscle_glycogen_phosphorylase
ENSMUSG00000032841	Prr5l	proline_rich_5_like
ENSMUSG00000034714	Ttyh2	tweety_homolog_2_(Drosophila)
ENSMUSG00000035385	Ccl2	chemokine_(C-C_motif)_ligand_2
ENSMUSG00000035831	Krt25	keratin_25
ENSMUSG00000036306	Lzts1	leucine_zipper_putative_tumor_suppressor_1
ENSMUSG00000036867	Smad6	SMAD_family_member_6
ENSMUSG00000036923	Stox1	storkhead_box_1
ENSMUSG00000037169	Mycn	v-myc_myelocytomatosis_viral_related_oncogene_neuroblastoma_derived_(avian)
ENSMUSG00000037434	Slc30a1	solute_carrier_family_30_(zinc_transporter)_member_1
ENSMUSG00000037846	Rtkn2	rhotekin_2
ENSMUSG00000037977	6430571L13Rik	RIKEN_cDNA_6430571L13_gene
ENSMUSG00000038580	Sct	secretin
ENSMUSG00000038599	Capn8	calpain_8
ENSMUSG00000039217	Il18	interleukin_18
ENSMUSG00000039323	Igfbp2	insulin-like_growth_factor_binding_protein_2
ENSMUSG00000040565	Btaf1	BTAF1_RNA_polymerase_II_B-TFIID_transcription_factor-associated_(Mot1_homolog_S._cerevisiae)
ENSMUSG00000041120	Nbl1	neuroblastoma_suppression_of_tumorigenicity_1
ENSMUSG00000041911	Dlx1	distal-less_homeobox_1
ENSMUSG00000041957	Pkp2	plakophilin_2

ENSMUSG00000042092	Lce1c	late_cornified_envelope_1C
ENSMUSG00000042109	Csdc2	cold_shock_domain_containing_C2_RNA_binding
ENSMUSG00000042532	Golga7b	golgi_autoantigen_golgin_subfamily_a_7B
ENSMUSG00000043461	Sptssb	serine_palmitoyltransferase_small_subunit_B
ENSMUSG00000044243	Bhlha9	basic_helix-loop-helix_family_member_a9
ENSMUSG00000044430	Klk12	kallikrein_related-peptidase_12
ENSMUSG00000044594	Serpinb3a	serine_(or_cysteine)_peptidase_inhibitor_clade_B _(ovalbumin)_member_3A
ENSMUSG00000045005	Fzd5	frizzled_homolog_5_(Drosophila)
ENSMUSG00000046676	Lce1l	late_cornified_envelope_1L
ENSMUSG00000046997	Spsb4	splA/ryanodine_receptor_domain_and_SOCS_box_containing_4
ENSMUSG00000047419	Cmya5	cardiomyopathy_associated_5
ENSMUSG00000047420	Fam180a	family_with_sequence_similarity_180_member_A
ENSMUSG00000047632	Fgfbp3	fibroblast_growth_factor_binding_protein_3
ENSMUSG00000048450	Msx1	msh_homeobox_1
ENSMUSG00000048582	Gja3	gap_junction_protein_alpha_3
ENSMUSG00000051586	Mical3	microtubule_associated_monooxygenase_calponin_and_ LIM_domain_containing_3
ENSMUSG00000051879	Krt71	keratin_71
ENSMUSG00000052302	Tbc1d30	TBC1_domain_family_member_30
ENSMUSG00000052415	Tchh	trichohyalin
ENSMUSG00000052512	Nav2	neuron_navigator_2
ENSMUSG00000053414	Hunk	hormonally_upregulated_Neu-associated_kinase
ENSMUSG00000053897	Slc39a8	solute_carrier_family_39_(metal_ion_transporter)_member_8
ENSMUSG00000054083	Capn12	calpain_12
ENSMUSG00000054196	Cthrc1	collagen_triple_helix_repeat_containing_1
ENSMUSG00000055194	Actbl2	actin_beta-like_2
ENSMUSG00000055632	Hmcn2	hemicentin_2
ENSMUSG00000055937	Krt28	keratin_28
ENSMUSG00000056270	Prr9	proline_rich_9
ENSMUSG00000056605	Krt72	keratin_72
ENSMUSG00000057137	Tmem140	transmembrane_protein_140
ENSMUSG00000058914	C1qtnf3	C1q_and_tumor_necrosis_factor_related_protein_3
ENSMUSG00000059493	Nhs	Nance-Horan_syndrome_(human)
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ENSMUSG00000074037	Mc1r	melanocortin_1_receptor
ENSMUSG00000074093	Svip	small_VCP/p97-interacting_protein
ENSMUSG00000074206	Adh6b	alcohol_dehydrogenase_6B_(class_V)
ENSMUSG00000074445	Sprr2a3	small_proline-rich_protein_2A3
ENSMUSG00000075570	Krt26	keratin_26
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ENSMUSG00000076523	Igkv15-103	immunoglobulin_kappa_chain_variable_15-103
ENSMUSG00000076526	Igkv12-98	immunoglobulin_kappa_variable_12-98
ENSMUSG00000076563	Igkv5-48	immunoglobulin_kappa_variable_5-48
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ENSMUSG00000076569	Igkv5-39	immunoglobulin_kappa_variable_5-39
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ENSMUSG00000076609	Igkc	immunoglobulin_kappa_constant
ENSMUSG00000076613	Ighg2b	immunoglobulin_heavy_constant_gamma_2B
ENSMUSG00000076672	Ighv3-6	immunoglobulin_heavy_variable_3-6
ENSMUSG00000076674	Ighv3-8	immunoglobulin_heavy_variable_V3-8
ENSMUSG00000076934	Iglv1	immunoglobulin_lambda_variable_1
ENSMUSG00000076937	Iglc2	immunoglobulin_lambda_constant_2
ENSMUSG00000078657	Crnn	cornulin
ENSMUSG00000084228	Gm8080	predicted_gene_8080
ENSMUSG00000085645	Hoxb5os	homeobox_B5_and_homeobox_B6_opposite_strand
ENSMUSG00000092341	Malat1	metastasis_associated_lung_adenocarcinoma_transcript_1_(non-coding_RNA)
ENSMUSG00000092572	Serpinb10	serine_(or_cysteine)_peptidase_inhibitor_clade_B_(ovalbumin)_member_10
ENSMUSG00000093861	Igkv1-110	immunoglobulin_kappa_variable_1-110
ENSMUSG00000094335	Igkv1-117	immunoglobulin_kappa_variable_1-117
ENSMUSG00000094420	Igkv10-96	immunoglobulin_kappa_variable_10-96
ENSMUSG00000094546	Ighv1-26	immunoglobulin_heavy_variable_1-26
ENSMUSG00000094724	Rnaset2b	ribonuclease_T2B
ENSMUSG00000094797	Igkv6-15	immunoglobulin_kappa_variable_6-15
ENSMUSG00000094930	Igkv6-25	immunoglobulin_kappa_chain_variable_6-25
ENSMUSG00000095079	Igha	immunoglobulin_heavy_constant_alpha
ENSMUSG00000095351	Igkv3-2	immunoglobulin_kappa_variable_3-2
ENSMUSG00000095571	Ighv5-17	immunoglobulin_heavy_variable_5-17
ENSMUSG00000095630	Igkv6-23	immunoglobulin_kappa_variable_6-23

ENSMUSG00000095687	Rnaset2a	ribonuclease_T2A
ENSMUSG00000095700	Ighv10-3	immunoglobulin_heavy_variable_V10-3
ENSMUSG00000095870	Lce1k	late_cornified_envelope_1K
ENSMUSG00000095930	Nim1k	NIM1_serine/threonine_protein_kinase
ENSMUSG00000096255	Dynlt1b	dynein_light_chain_Tctex-type_1B
ENSMUSG00000096336	Igkv1-135	immunoglobulin_kappa_variable_1-135
ENSMUSG00000096422	Igkv12-44	immunoglobulin_kappa_variable_12-44
ENSMUSG00000096459	Ighv9-3	immunoglobulin_heavy_variable_V9-3
ENSMUSG00000096715	Igkv3-4	immunoglobulin_kappa_variable_3-4
ENSMUSG00000096768	Erdr1	erythroid_differentiation_regulator_1
ENSMUSG00000096780	Tmem181b-ps	transmembrane_protein_181B_pseudogene
ENSMUSG00000096862	Gm13301	predicted_gene_13301
ENSMUSG00000097296	Gm26532	predicted_gene_26532
ENSMUSG00000101026	RP23-230O9.7	RIKEN_cDNA_D730001G18_gene

Appendix Table S2. Antibodies, staining kits and primers information.

Western blotting Antibodies	**Clone**	**Company**
Primary antibodies		
p-SMAD2/3	D27F4	Cell Signaling Technology, Danvers, MA
p-SMAD1/5	41D10	Cell Signaling Technology
RUNX2	D1L7F	Cell Signaling Technology
GAPDH	D16H11	Cell Signaling Technology
Anti-mouse IL-33	Polyclonal	R&D Systems, Minneapolis, MN
SMAD2/3	Polyclonal	R&D Systems
SMAD6	Polyclonal	NOVUS biologicals, Centennial, CO
SMAD1	EP565Y	Abcam, Cambridge, UK
HA	16B12	Biolegend, San Diego, CA

Secondary antibodies	**Cat #**	**Company**
Peroxidase Goat Anti-Mouse IgG	115-035-003	Jackson ImmunoResearch, West Grove, PA
Peroxidase Goat Anti-Rabbit IgG	111-035-003	Jackson ImmunoResearch
Peroxidase Bovine Anti-Goat IgG	805-035-180	Jackson ImmunoResearch

siRNA	**Cat #**	**Company**
siIl33 #1	SI00870443	QIAGEN, Hilden, Germany
siIl33 #2	SI00870450	QIAGEN
siCon	1022076	QIAGEN

Immunostaining antibodies	**Clone**	**Company**
IL-33 (mouse)	Nessy-1	ENZO, Farmingdale, NY
IL-33 (human)	Polyclonal	Sigma, St. Louis, MO
p-SMAD2/3 (mouse and human)	D27F4	Cell Signaling Technology

Staining kits	**Cat #**	**Company**
Antigen unmasking solution	H3300	Vector Laboratories, Burlingame, CA
VECTASTAIN Elite ABC universal Kit	PK6200	Vector Laboratories
ImmPACT DAB chromogen staining kit	SK-4105	Vector Laboratories

Immunofluorescence staining Antibodies	**Clone**	**Company**
Ki67	Polyclonal	Abcam
Cleaved caspase-3 (Asp 175)	5A1E	Cell Signaling Technology

Secondary antibodies	**Cat #**	**Company**
Goat anti-Mouse IgG, Alexa Fluor 488 conjugate	A32723	Thermo Fisher Scientific, Waltham, MA
Goat anti-Rabbit IgG, Alexa Fluor 647 conjugate	A32733	Thermo Fisher Scientific

qPCR primers	**Cat #**	**Company**
Taqman		
Il33	Mm.PT.58.12022572	Integrated DNA Technologies, Coralville, Iowa
Gapdh	Mm.PT.39a.1	Integrated DNA Technologies

SYBR green	
Smad6	forward: GCAACCCCTACCACTTCAGC reverse: GTGGCTTGTACTGGTCAGGAG
Gapdh	forward: AATGTGTCCGTCGTGGATCTGA reverse: GATGCCTGCTTCACCACCTTCT
Smad6 promoter	forward: GGACTGACTCTAAAGTGCTATGCGC reverse: ACAGTGCCCGCGACTCACTCTCAAG
Smad6 no peak	forward: GTTCAGATGATGTGGCAGAA reverse: CTTTCTAAGCCCTGGGACCCT
Smad6 peak	forward: CTTGGCAATCCTCAGAGAAG reverse: ATGAGTGGATTACATAGTCAG

PCR primers for mouse genotyping

Gene name	
IL-33	forward: GAGAGATCAAATGAGGCC forward mutant: GGTCGCTACCATTACCAG reverse: GCTGGAGACCAGACTTGT
ST2	forward wild-type: GAAGAGGGCTTCACTCTGTATC reverse wild-type: GGAGGAGGAGGAGTTGTTAAAG forward mutant: GATCTCCTGTCATCTCACCTTG reverse mutant: GCCAACGCTATGTCCTGATA
K14-IL33	forward: GGAGGGGGCAAAGTTTTCAGGGTG reverse: TTTGCAAGGCGGGACCAGGG