

Supplementary information

Pharmacological and genetic reappraisals of protease and oxidative stress pathways in a mouse model of obstructive lung diseases

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Fig. S1

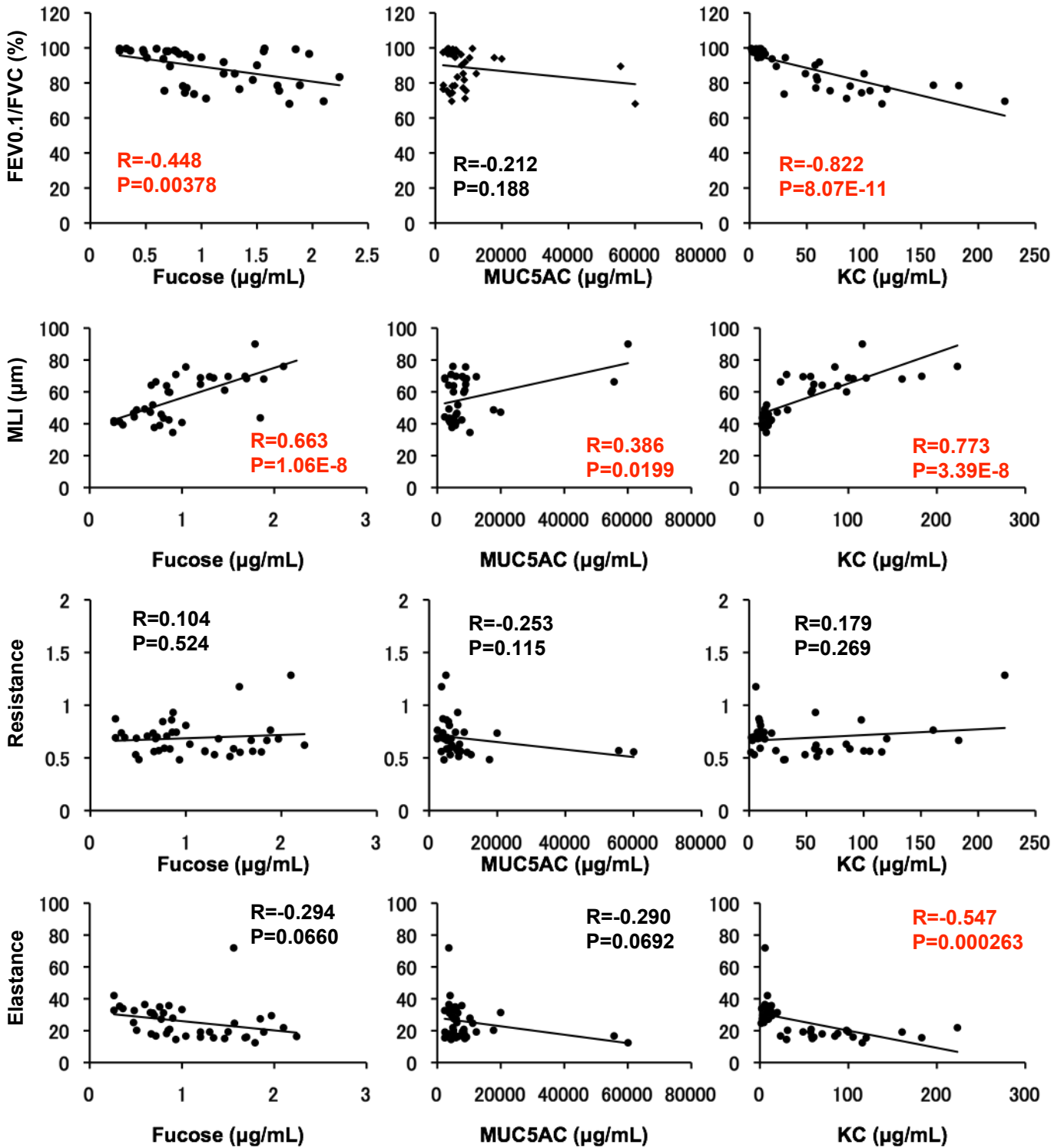


Fig. S1. Correlation analysis of parameters. Analysis between pulmonary parameters and biochemical parameters in BALF in WT and C57/BL6J- $\beta\text{ENaC-Tg}$ mice ($n=36-41$) and correlation scatter plots were shown.

Fig. S2

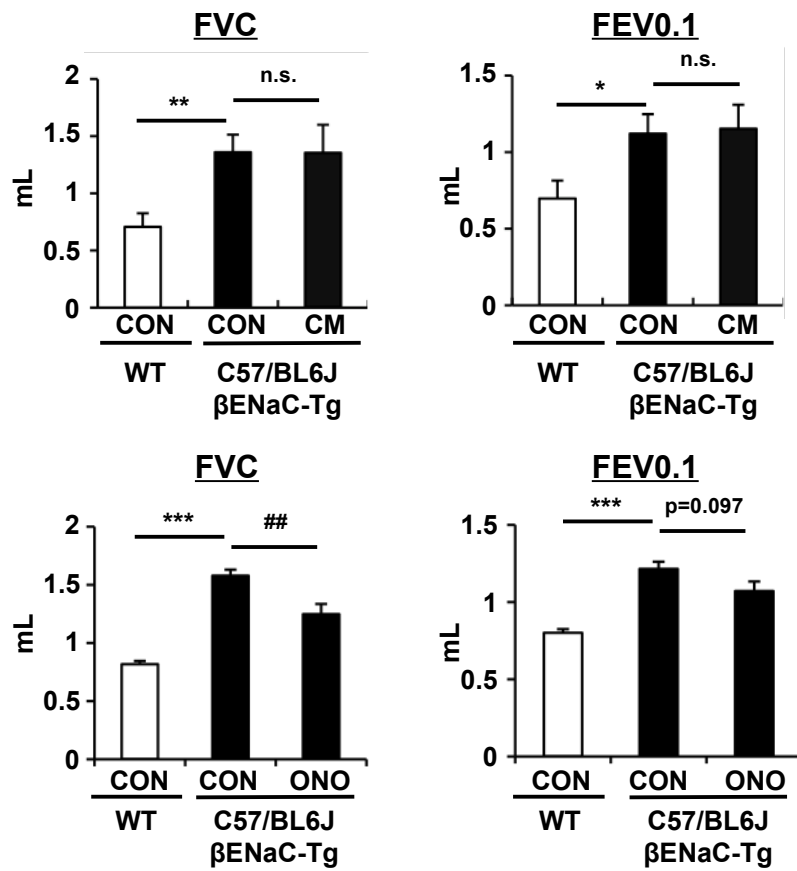


Fig. S2. Effect of protease inhibitors on FVC and FEV0.1 in C57/BL6J-βENaC-Tg mice. Pulmonary phenotypes (FVC and FEV0.1) were evaluated in oral camostat methylate (CM)- or ONO3403-treated C57/BL6J-βENaC-Tg mice. Age-matched C57/BL6J mice (WT) were used as healthy controls. n=4-7 and n=7-8 for CM and ONO3403 treatments, respectively. *p < 0.05, **p < 0.01, ***p < 0.001, versus WT mice; ##p < 0.01, versus vehicle-treated C57/BL6J-βENaC-Tg mice; Student's t test.

Fig. S3

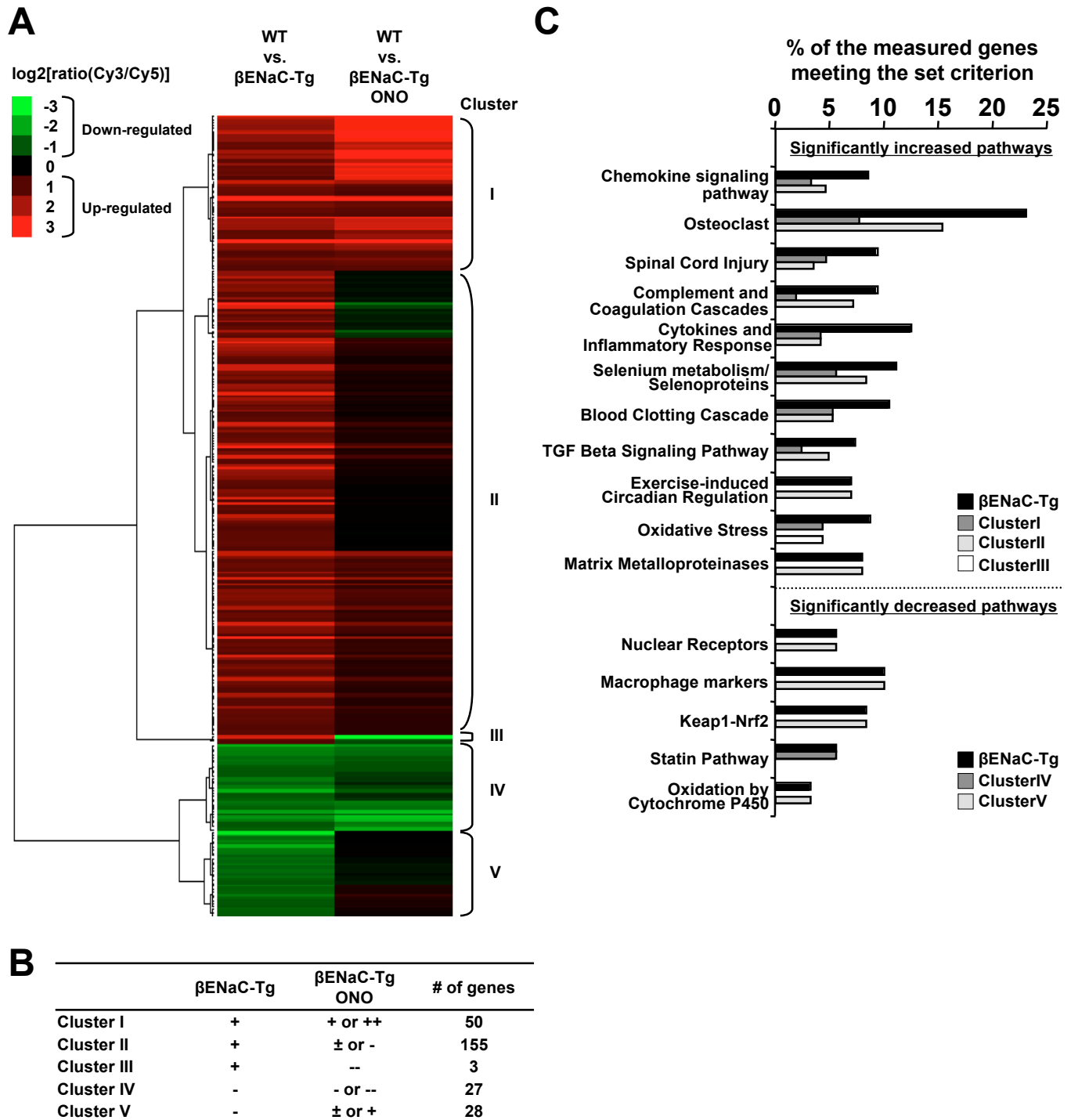


Fig. S3. Microarray and cluster analyses of ONO3403-treated C57/BL6J- β ENaC-Tg mice. (A) A heatmap representing the cluster analysis of gene alteration based on the microarray in lung tissue of ONO-3403-treated and -untreated C57BL/6J- β ENaC-Tg mice compared to WT mice. Patterns of five cluster sets were indicated in (B). +, up-regulated; ++, highly up-regulated; \pm , not altered; -, down-regulated; --, highly down-regulated: versus WT mice. (C) Comparison of pathway analysis of ONO-3403-treated and -untreated C57BL/6J- β ENaC-Tg mice compared to WT mice.

Fig. S4

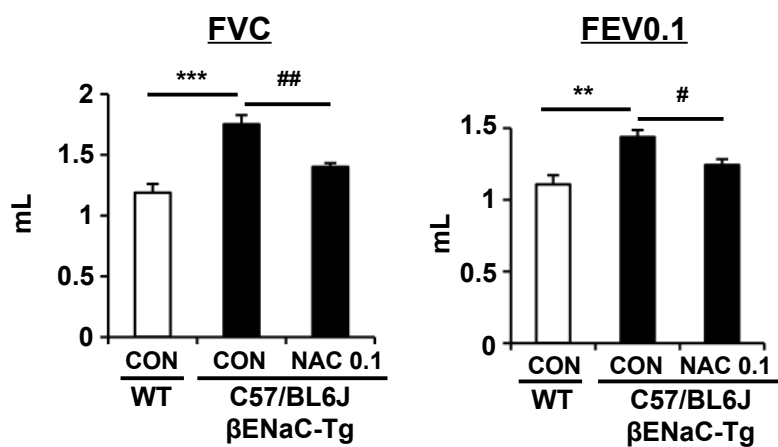


Fig. S4. Effect of NAC on FVC and FEV0.1 in C57/BL6J-βENaC-Tg mice. Pulmonary phenotypes (FVC and FEV0.1) were evaluated intratracheal N-acetylcysteine (NAC)-treated C57/BL6J-βENaC-Tg mice. Age-matched C57/BL6J mice (WT) were used as healthy controls. n=4-5 mice/group. **p < 0.01, ***p < 0.001, versus WT mice; Student's t test. #p < 0.05, ##p < 0.01, versus vehicle-treated C57/BL6J-βENaC-Tg mice; Dunnett's test.

Fig. S5

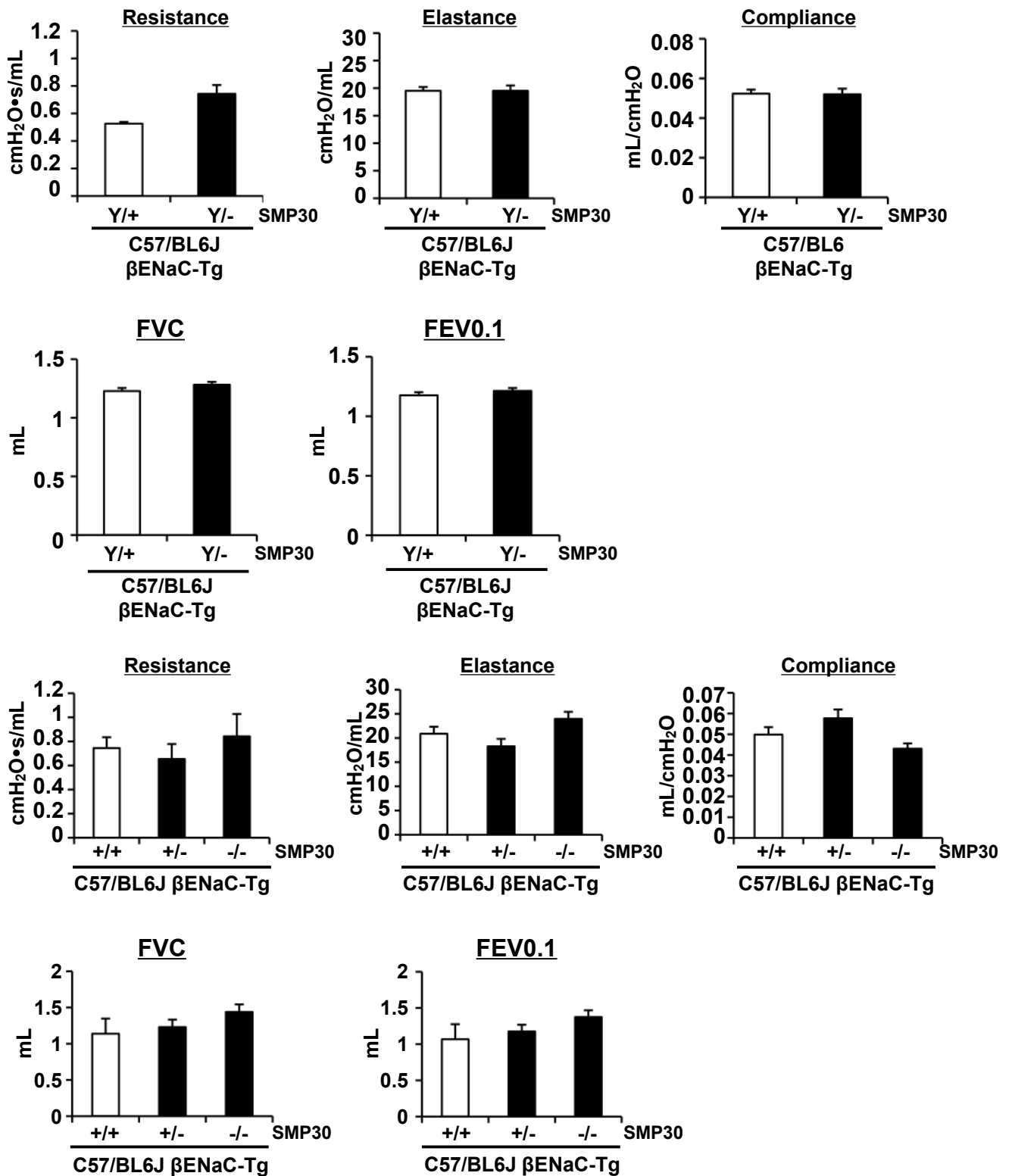


Fig. S5. Effect of SMP30 deficiency on Pulmonary mechanics, FVC and FEV0.1 in C57/BL6J-βENaC-Tg mice. Pulmonary phenotypes (Resistance, Compliance, Elastance, FVC and FEV0.1) were evaluated in male (Y/+ and Y/-) and female (+/+, +/- and -/-) C57/BL6J-βENaC-Tg and C57/BL6J-βENaC-Tg-SMP KO mice. n=6 mice/group.

Fig. S6

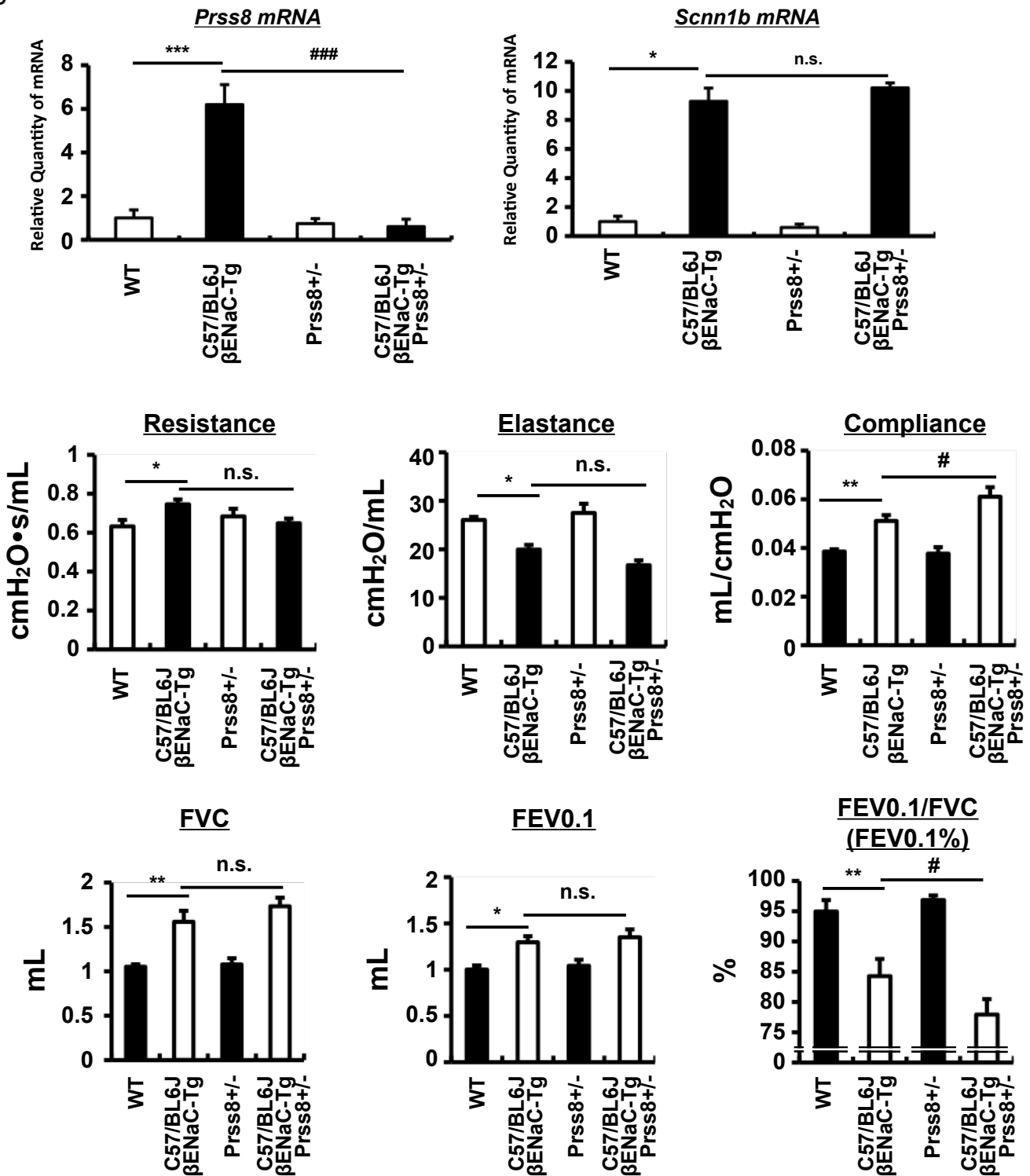


Fig. S6. Effect of heterozygous deletion of Prss8 on genes expression, Pulmonary mechanics, FVC and FEV0.1 in C57/BL6J-βENaC-Tg mice. Gene expression levels of Prss8 and Scnn1b (βENaC) and pulmonary phenotypes (Resistance, Compliance, Elastance, FVC, FEV0.1 and FEV0.1%) were evaluated in WT, Prss8+/-, C57/BL6J-βENaC-Tg and double mutant Prss8+/- C57/BL6J-βENaC-Tg mice. n=3 mice/group. *p < 0.05, **p < 0.01, ***p < 0.001, versus WT mice; #p < 0.05, ###p < 0.001 versus C57/BL6J-βENaC-Tg mice; Student's t test. n.s. not significant.

Table. S1. Genes Increased in the lung tissue of ENaC-Tg mice (2-fold \leq , Cy3 \geq 20)

(1/3)

RefSeq_id	Enterz_id	symbol	description	Cy5 (WT)	Cy3 (ENaC-Tg)	Cy3/Cy5 (fold)
NM_178241	227288	Il8ra	interleukin 8 receptor, alpha	8.63	203.36	23.58
NM_025989	67133	Gp2	glycoprotein 2 (zymogen granule membrane)	4.73	74.91	15.83
NM_009141	100044702	Cxcl5	chemokine (C-X-C motif) ligand 5	10.22	133.71	13.08
NM_053113	93726	Ear11	eosinophil-associated, ribonuclease A family, member 11	5.13	66.09	12.88
NM_016960	20297	Ccl20	chemokine (C-C motif) ligand 20	10.75	127.40	11.85
NM_011315	20210	Saa3	serum amyloid A 3	58.11	652.21	11.22
XM_139051	214922	Slc39a2	solute carrier family 39 (zinc transporter), member 2	24.60	246.27	10.01
NM_008176	14825	Cxcl1	chemokine (C-X-C motif) ligand 1	19.67	182.34	9.27
NM_028946	74446	Slc9b1	RIKEN cDNA 4933425K02 gene	6.20	49.25	7.95
NM_010584	16429	Itlna	intelectin a	4.98	38.90	7.82
NM_053110	93695	Gpnmb	glycoprotein (transmembrane) nmb	175.11	1214.87	6.94
NM_206535	271375	Cd200r2	Cd200 receptor 2	8.32	57.10	6.86
NM_133245	51327	Ahsp	alpha hemoglobin stabilizing protein (Ahsp)	78.35	515.11	6.57
NM_010766	17167	Marco	macrophage receptor with collagenous structure	164.80	1060.77	6.44
-	668389	IGHV2-4	Immunoglobulin heavy chain V gene segment	12.01	74.99	6.25
NM_145126	104183	Chi3l4	chitinase 3-like 4	405.04	2506.70	6.19
NM_007802	13038	Ctsk	cathepsin K	171.24	1055.24	6.16
-	667859	IGKV8-18	Immunoglobulin Kappa light chain V gene segment	4.41	26.89	6.10
NM_020498	57248	Ly6i	lymphocyte antigen 6 complex, locus I	45.00	265.66	5.90
NM_017474	23844	Clca3	chloride channel calcium activated 3	6.90	40.25	5.83
NM_145594	234199	Fgl1	fibrinogen-like protein 1	4.18	23.88	5.71
XM_138376	238448	Ighv1-62-2	Immunoglobulin heavy chain V gene segment	30.20	165.25	5.47
NM_008046	14313	Fst	follistatin	13.49	73.68	5.46
NM_183249	66107	1100001G20Rik	RIKEN cDNA 1100001G20 gene	167.03	897.54	5.37
-	780799	IGHV7-1	Immunoglobulin heavy chain V gene segment	21.46	110.41	5.15
NM_008694	18054	Ngp	neutrophilic granule protein	8.77	45.09	5.14
XM_357633	620017	IGKV5-39	Immunoglobulin Kappa light chain V gene segment	48.60	247.10	5.08
NM_133862	99571	Fgg	fibrinogen, gamma polypeptide	16.64	83.81	5.04
NM_010479	193740	Hspa1a	heat shock protein 1A	198.37	978.64	4.93
NM_009892	12655	Chi3l3	chitinase 3-like 3	7566.47	36918.29	4.88
NM_009140	20311	Cxcl5	chemokine (C-X-C motif) ligand 5	11.88	57.36	4.83
NM_011867	23985	Slc26a4	solute carrier family 26, member 4	12.92	60.72	4.70
-	619833	IGHV1-69	Immunoglobulin heavy chain V gene segment	31.21	145.42	4.66
NM_001286493	546038	Spag11b	predicted gene, EG546038	33.02	153.78	4.66
XM_138377	382695	IGHV1-56	Immunoglobulin heavy chain V gene segment	131.01	606.10	4.63
NM_009921	12796	Camp	cathelicidin antimicrobial peptide	10.06	45.37	4.51
-	384411	IGKV12-89	Immunoglobulin Kappa light chain V gene segment	6.95	30.26	4.35
NM_007739	12837	Col8a1	procollagen, type VIII, alpha 1	13.14	54.98	4.18
XM_357683	384514	IGKV4-57-1	Immunoglobulin Kappa light chain V gene segment	148.30	618.50	4.17
NM_145603	234671	Ces2	carboxylesterase 2	5.04	20.81	4.13
NM_011337	20302	Ccl3	chemokine (C-C motif) ligand 3	51.54	209.59	4.07
NM_207281	403183	4832428D23Rik	RIKEN cDNA 4832428D23 gene	11.22	45.44	4.05
NM_007739	12837	COL8A1	collagen, type VIII, alpha 1	58.40	232.72	3.98
M34982	-	IGHV1S52	Immunoglobulin heavy chain V gene segment	126.99	503.93	3.97
XM_111360	28453	IGHV3-6	Immunoglobulin heavy chain V gene segment	64.83	254.06	3.92
NM_174998	170638	Hpcal4	hippocalcin-like 4	7.73	30.23	3.91
NM_031254	83433	Trem2	triggering receptor expressed on myeloid cells 2	71.80	277.93	3.87
XM_129391	71884	Chit1	chitinase 1 (chitotriosidase)	20.45	78.33	3.83
NM_009890	12642	Ch25h	cholesterol 25-hydroxylase	86.57	327.90	3.79
NM_145227	246728	Oas2	2'-5' oligoadenylate synthetase 2	17.47	65.10	3.73
XM_203589	640979	IGHV1S5	Immunoglobulin heavy chain V gene segment	71.73	266.36	3.71
NM_008920	19074	Prg2	proteoglycan 2, bone marrow	8.21	30.41	3.70
-	-	IGHV1S7	Immunoglobulin heavy chain V gene segment	101.05	372.95	3.69
NM_207244	271375	Cd200r2	Cd200 receptor 2	65.26	236.67	3.63
NM_133362	170942	Erd1	erythroid differentiation regulator 1	847.02	3062.68	3.62
NM_009139	20305	Ccl6	chemokine (C-C motif) ligand 6	882.07	3166.88	3.59
XM_283962	74152	Stra6l	RIKEN cDNA 1300002K09 gene	7.38	26.37	3.57
NM_007739	12837	Col8a1	procollagen, type VIII, alpha 1	39.83	140.77	3.53
XM_355832	-	IGKV4-58	Immunoglobulin Kappa light chain V gene segment	53.35	187.89	3.52
NM_134160	171166	Mcoln3	mucoilin 3	38.25	134.68	3.52
-	-	IGHV1-55	Immunoglobulin Kappa light chain V gene segment	152.19	529.14	3.48
XM_356629	-	IGHV1-56	Immunoglobulin Kappa light chain V gene segment	47.55	163.18	3.43
NM_013532	14728	Lilrb4	leukocyte immunoglobulin-like receptor, subfamily B, member 4	177.68	590.79	3.32
XM_127186	-	IGHV1-11	Immunoglobulin heavy chain V gene segment	164.27	545.79	3.32
NM_177836	23792	Adam23	a disintegrin and metallopeptidase domain 23	7.46	24.63	3.30
XM_138324	-	IGHV6S4	Immunoglobulin heavy chain V gene segment	8.20	27.02	3.30
-	-	-	unknown	324.36	1056.43	3.26
-	-	-	unknown	277.82	901.17	3.24
NM_027552	70789	Kynu	kynureninase (L-kynurenine hydrolase)	21.85	70.26	3.22
NM_008605	17381	Mmp12	matrix metallopeptidase 12	32.21	102.88	3.19
NM_013532	14728	Lilrb4	leukocyte immunoglobulin-like receptor, subfamily B, member 4	253.48	807.33	3.18
NM_198164	78334	Cdc2l6	cell division cycle 2-like 6 (CDK8-like)	172.64	547.61	3.17
XM_487248	-	IGHV1S125	Immunoglobulin heavy chain V gene segment	193.91	614.75	3.17
NM_172814	239393	Lrp12	low density lipoprotein-related protein 12	87.12	275.37	3.16
NM_021364	23845	Clec5a	C-type lectin domain family 5, member a	15.90	50.06	3.15
NM_145222	227327	B3gnt7	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 7	60.91	187.42	3.08
NM_013655	20315	Cxcl12	chemokine (C-X-C motif) ligand 12	1194.92	3675.63	3.08
XM_487240	634100	IGHV1-31	Immunoglobulin heavy chain V gene segment	12.85	39.19	3.05

Table. S1. Genes Increased in the lung tissue of ENaC-Tg mice (2-fold \leq , Cy3 \geq 20)

(2/3)

RefSeq_id	Enterz_id	symbol	description	Cy5 (WT)	Cy3 (ENaC-Tg)	Cy3/Cy5 (fold)
NM_009969	12981	Csf2	colony stimulating factor 2 (granulocyte-macrophage)	23.02	69.99	3.04
NM_020509	57262	Retnla	resistin like alpha	841.60	2554.65	3.04
XM_138364	-	IGHV1S6	Immunoglobulin heavy chain V gene segment	89.15	269.52	3.02
NM_007388	11433	Acp5	acid phosphatase 5, tartrate resistant	174.80	527.97	3.02
NM_011819	23886	Gdf15	growth differentiation factor 15	41.00	123.06	3.00
NM_029931	70122	Mlt3	myeloid/lymphoid or mixed lineage-leukemia translocation to 3 homolog (Drosophila)	10.77	32.17	2.99
NM_008611	17394	Mmp8	matrix metalloproteinase 8	108.36	322.88	2.98
NM_001168304	78334	Cdk19	cyclin-dependent kinase 19	15.90	47.15	2.97
NM_021325	57781	Cd200r1	CD200 receptor 1	32.47	95.75	2.95
NM_008491	16819	Lcn2	lipocalin 2	1671.51	4922.58	2.94
010512;NM_184	16000	Igf1	insulin-like growth factor 1	90.28	263.33	2.92
NM_013559	-	Hsp110	heat shock protein 110	108.81	314.37	2.89
-	-	-	unknown	7.22	20.77	2.88
NM_018746	16427	Itih4	inter alpha-trypsin inhibitor, heavy chain 4	446.02	1280.97	2.87
XM_138378	636126	IGHV1S53	Immunoglobulin heavy chain V gene segment	69.27	198.40	2.86
NM_025844	66917	Chordc1	cysteine and histidine-rich domain (CHORD)-containing, zinc-binding protein 1	103.19	295.25	2.86
NM_021334	16411	Itgax	integrin alpha X	234.95	664.11	2.83
NM_013559	15505	Hsph1	predicted gene, ENSMUSG00000053750	30.14	84.55	2.80
NM_010934	18166	Npy1r	neuropeptide Y receptor Y1	26.03	72.78	2.80
NM_145515	226778	Mark1	MAP/microtubule affinity regulating kinase 1	51.07	142.36	2.79
NM_133775	77125	Il33	interleukin 33	732.03	2035.04	2.78
NM_011331	20293	Ccl12	chemokine (C-C motif) ligand 12	41.75	115.79	2.77
NM_019911	56720	Tdo2	tryptophan 2,3-dioxygenase	20.83	57.65	2.77
NM_010634	16592	Fabp5	fatty acid binding protein 5, epidermal	110.57	300.43	2.72
-	-	IGKV4-54	Immunoglobulin Kappa light chain V gene segment	48.96	132.32	2.70
-	-	IGKV4-72	Immunoglobulin Kappa light chain V gene segment	197.99	533.35	2.69
XM_135414	-	IGKV4-57	Immunoglobulin Kappa light chain V gene segment	62.65	167.72	2.68
XM_888439	623924	Gm6462	predicted gene 6462	238.41	632.52	2.65
NM_027836	109225	Ms4a7	membrane-spanning 4-domains, subfamily A, member 7	101.80	264.19	2.60
NM_009853	12514	Cd68	CD68 antigen	429.97	1100.12	2.56
-	-	IGKV4-91	Immunoglobulin Kappa light chain V gene segment	71.44	180.81	2.53
XM_131683	76574	Mfsd2	major facilitator superfamily domain containing 2	66.74	168.30	2.52
NM_145467	223272	Itgbl1	integrin, beta-like 1	65.44	164.62	2.52
NM_008768	18405	Orm1	orosomucoid 1	12.69	31.86	2.51
NM_023655	72169	Trim29	tripartite motif protein 29	9.05	22.57	2.50
NM_010104	13614	Edn1	endothelin 1	572.74	1427.75	2.49
NM_175406	242341	Atp6v0d2	ATPase, H ⁺ transporting, lysosomal V0 subunit D2	435.61	1083.13	2.49
NM_008590	17294	Mest	mesoderm specific transcript	21.18	52.54	2.48
XM_111360	-	IGHV3-5	Immunoglobulin heavy chain V gene segment	15.68	38.85	2.48
NM_031198	21426	Tcfec	transcription factor EC	35.02	86.51	2.47
XM_111361	100045791	IGHV9-3	Immunoglobulin heavy chain V gene segment	36.09	89.02	2.47
NM_016737	20867	Stip1	stress-induced phosphoprotein 1	304.89	749.13	2.46
XM_356617	-	IGHV1S99	Immunoglobulin heavy chain V gene segment	149.99	367.62	2.45
NM_011031	18452	P4ha2	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha II polypeptide	109.06	265.16	2.43
NM_010819	17474	Clec4d	C-type lectin domain family 4, member d	183.45	444.30	2.42
NM_007969	14038	Wfdc18	WAP four-disulfide core domain 18	12.08	29.11	2.41
NM_144943	246278	Cd207	CD 207 antigen	14.00	33.60	2.40
-	-	IGKV4-71	Immunoglobulin Kappa light chain V gene segment	150.94	361.66	2.40
NM_016812	53325	Banp	Btg3 associated nuclear protein	318.07	759.85	2.39
NM_001004174	433470	AA467197	expressed sequence AA467197	46.79	111.67	2.39
XM_134720	235130	Adams15	a disintegrin-like and metalloproteinase (repolysin type) with thrombospondin type 1 motif, 15	209.73	498.76	2.38
NM_172589	218454	Lhfp12	lipoma HMGIC fusion partner-like 2	75.25	178.66	2.37
-	-	IGHV1-20	Immunoglobulin heavy chain V gene segment	278.87	661.36	2.37
NM_031999	83924	Gpr137b	G protein-coupled receptor 137B	196.67	465.96	2.37
-	-	IGKV4-55	Immunoglobulin Kappa light chain V gene segment	141.82	334.75	2.36
-	-	-	unknown	108.64	256.19	2.36
NM_011260	19695	Reg3g	regenerating islet-derived 3 gamma	337.37	792.49	2.35
XM_129166	77836	Mlana	melan-A	20.62	48.08	2.33
-	108857	Ankhd1	ankyrin repeat and KH domain containing 1	9.52	22.16	2.33
NM_009303	20972	Syng1	synaptogyrin 1	132.86	309.26	2.33
NM_009983	13033	Ctsd	cathepsin D	5658.60	13154.38	2.32
NM_010188	14131	Fcgr3	Fc receptor, IgG, low affinity III	297.07	689.81	2.32
NM_144559	246256	Fcgr3a	Fc fragment of IgG, low affinity IIIa, receptor	106.69	247.35	2.32
NR_073011	381715	4930572O03Rik	RIKEN cDNA 4930572O03 gene	29.32	67.95	2.32
-	-	IGHV1S55	Immunoglobulin heavy chain V gene segment	180.68	417.02	2.31
NM_025759	360220	Spee4d	spermatogenesis associated glutamate (E)-rich protein 4d	23.23	53.59	2.31
NM_029796	76905	Lrg1	leucine-rich alpha-2-glycoprotein 1	876.17	2020.68	2.31
NM_001039562	654824	Ankrd37	ankyrin repeat domain 37	26.03	59.71	2.29
NM_008599	17329	Cxcl9	chemokine (C-X-C motif) ligand 9	15.97	36.60	2.29
NM_027988	71893	Noxo1	NADPH oxidase organizer 1	30.73	70.28	2.29
NM_008522	17002	Ltf	lactotransferrin	65.12	148.89	2.29
NM_011612	21942	Tnfrsf9	tumor necrosis factor receptor superfamily, member 9	10.54	23.81	2.26
NM_008083	14432	Gap43	growth associated protein 43	288.38	649.71	2.25
NM_010234	14281	Fos	FBJ osteosarcoma oncogene	387.03	870.57	2.25
NM_029103	74840	Armet	arginine-rich, mutated in early stage tumors	843.37	1894.12	2.25
NM_153101	235712	Mrgpra2	MAS-related GPR, member A2	11.67	26.17	2.24
NM_008298	100048597	Dnaja1	DnaJ (Hsp40) homolog, subfamily A, member 1	913.76	2039.89	2.23
NM_145144	108897	2810003C17Rik	RIKEN cDNA 2810003C17 gene	42.13	93.73	2.23

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(3/3)

RefSeq_id	Enterz_id	symbol	description	Cy5 (WT)	Cy3 (ENaC-Tg)	Cy3/Cy5 (fold)
NM_010442	15368	Hmox1	heme oxygenase (decycling) 1	232.62	514.46	2.21
NM_011146	19016	Pparg	peroxisome proliferator activated receptor gamma	112.58	248.45	2.21
NR_040420	625253	Dnajb9	DnaJ (Hsp40) homolog, subfamily B, member 9	125.21	276.27	2.21
XM_142364	100047132	IGKV6-20	Immunoglobulin Kappa light chain V gene segment	44.87	98.96	2.21
NM_013825	17076	Ly75	lymphocyte antigen 75	67.24	148.26	2.20
XM_138237	238393	Serpina3f	serine (or cysteine) peptidase inhibitor, clade A, member 3F	35.81	78.95	2.20
NM_007752	12870	Cp	ceruloplasminprovided	1156.31	2548.47	2.20
NM_183187	268709	Fam107a	cDNA sequence BC055107	9.83	21.65	2.20
NM_007469	11812	Apoc1	apolipoprotein C-I	320.78	706.74	2.20
NM_029639	76509	Plet1	RIKEN cDNA 1600029D21 gene	944.37	2071.43	2.19
-	-	IGKV16-104	Immunoglobulin Kappa light chain V gene segment	337.81	738.27	2.19
NM_013489	12523	Cd84	CD84 antigen	112.41	244.90	2.18
NM_009263	20750	Spp1	secreted phosphoprotein 1	974.98	2122.61	2.18
NM_007913	13653	Egr1	early growth response	466.30	1013.73	2.17
NM_011020	18415	Hspa4l	heat shock protein 4 like	132.69	287.63	2.17
NM_007408	11520	Adfp	adipose differentiation related protein	771.95	1665.59	2.16
NM_011539	21391	Tbxas1	thromboxane A synthase 1, platelet	127.89	275.39	2.15
NM_008620	76074	Gbp8	cDNA sequence BC057170	117.61	252.98	2.15
NM_010762	17153	Mal	myelin and lymphocyte protein, T-cell differentiation protein	269.36	579.20	2.15
NM_145953	107869	Cth	cystathionase (cystathionine gamma-lyase)	41.12	88.40	2.15
NM_010172	14068	F7	coagulation factor VII	102.04	217.17	2.13
NM_022430	64381	Ms4a8a	membrane-spanning 4-domains, subfamily A, member 8A	212.00	449.74	2.12
NM_024406	11770	Fabp4	fatty acid binding protein 4, adipocyte	453.38	960.71	2.12
NM_009251	20715	Serpina3g	serine (or cysteine) peptidase inhibitor, clade A, member 3G	63.60	134.50	2.11
NM_026931	69068	1810011O10Rik	RIKEN cDNA 1810011O10 gene	399.48	844.01	2.11
XM_485781	-	IGKV5-48	Immunoglobulin Kappa light chain V gene segment	59.80	126.28	2.11
NM_009779	12267	C3ar1	complement component 3a receptor 1	27.48	57.97	2.11
NM_011780	23792	Adam23	a disintegrin and metallopeptidase domain 23	14.44	30.44	2.11
-	791346	Gm10118	predicted gene, ENSMUSG00000062561	141.45	297.62	2.10
NM_011414	20568	Slpi	secretory leukocyte peptidase inhibitor	460.54	968.53	2.10
NM_144520	67815	Sec14l2	SEC14-like 2 (S. cerevisiae)	209.53	438.33	2.09
-	675749	Gm10693	predicted pseudogene 10693	37.19	77.70	2.09
NM_028808	74191	P2ry13	purinergic receptor P2Y, G-protein coupled 13 [Source:MarkerSymbol;Acc:MGI:1921441]	42.63	88.95	2.09
NM_008147	14727	Gp49a	leukocyte immunoglobulin-like receptor, subfamily B, member 4B	118.97	247.46	2.08
NM_013650	20201	S100a8	S100 calcium binding protein A8 (calgranulin A)	3273.25	6803.14	2.08
NM_008198	14962	Cfb	complement factor B	423.72	879.13	2.07
NM_145434	217166	Nr1d1	nuclear receptor subfamily 1, group D, member 1	32.52	67.03	2.06
NM_172542	77739	Adamts1	ADAMTS-like 1	20.41	42.01	2.06
NM_010588	16450	Jag2	jagged 2	28.74	59.15	2.06
NM_008223	15160	Serpind1	serine (or cysteine) peptidase inhibitor, clade D, member 1	14.48	29.78	2.06
NM_013560	15507	Hspb1	heat shock protein 1	2177.34	4477.24	2.06
NM_024495	71934	Car13	carbonic anhydrase 13	12.43	25.54	2.05
022431;NM_026	68774	Ms4a6d	membrane-spanning 4-domains, subfamily A, member 6D	196.16	402.93	2.05
NM_011333	20296	Ccl2	chemokine (C-C motif) ligand 2	49.33	101.25	2.05
NM_031165	15481	Hspa8	heat shock protein 8	3990.34	8174.50	2.05
NM_011407	20555	Ap2b1	adaptor-related protein complex 2, beta 1 subunit	33.92	69.46	2.05
NM_009786	12301	Cacybp	calcyclin binding protein	1466.62	3002.36	2.05
-	-	IGKV19-93	Immunoglobulin Kappa light chain V gene segment	158.38	321.86	2.03
NM_172679	229227	4932438A13Rik	RIKEN cDNA 4932438A13 gene	59.01	119.87	2.03
NM_007444	11702	Amd1	S-adenosylmethionine decarboxylase 1	110.90	224.82	2.03
NM_016704	12274	C6	complement component 6	189.96	384.12	2.02
NM_177084	110895	Slc9a4	solute carrier family 9 (sodium/hydrogen exchanger), member 4	10.17	20.51	2.02
NM_024435	67405	Nts	neurotensin	11.97	24.10	2.01
NM_007675	26366	Ceacam10	carcinoembryonic antigen-related cell adhesion molecule 10	18.97	38.17	2.01
NM_010554	16175	Il1a	interleukin 1 alpha	18.41	37.00	2.01
NM_009912	12768	Ccr1	chemokine (C-C motif) receptor 1	24.01	48.17	2.01
NM_008303	628438	Hspe1-rs1	heat shock protein 1 (chaperonin 10), related sequence 1	1125.36	2257.46	2.01
NM_011124	100042493	Ccl21b	chemokine (C-C motif) ligand 21b	2142.49	4290.31	2.00

Table. S2. Genes Decreased in the lung tissue of ENaC-Tg mice (0.5-fold \geq , Cy5 \geq 20)

RefSeq_id	Enterz_id	symbol	description	Cy5 (WT)	Cy3 (ENaC-Tg)	Cy3/Cy5 (fold)
NM_016771	53315	Sult1d1	sulfotransferase family 1D, member 1	78.64	11.86	0.15
NM_198028	241197	Serp1b10	serine (or cysteine) peptidase inhibitor, clade B (ovalbumin), member 10	60.06	12.38	0.21
NM_011681	22287	Scgb1a1	secretoglobin, family 1A, member 1 (uteroglobin)	65031.42	14646.36	0.23
NM_023612	71690	Esm1	endothelial cell-specific molecule 1	314.03	70.78	0.23
NM_010444	15370	Nr4a1	nuclear receptor subfamily 4, group A, member 1	1038.59	239.47	0.23
NM_011126	18843	Plunc	palate, lung, and nasal epithelium carcinoma associated	676.45	179.30	0.27
NM_008343	16009	Igf3	insulin-like growth factor binding protein 3	327.73	92.32	0.28
NM_001278161	15129	Hbb-b1	hemoglobin, beta adult major chain	62517.42	18607.36	0.30
NM_009695	11813	Apoc2	apolipoprotein C-II	117.04	38.80	0.33
NM_175012	225642	Grp	gastrin releasing peptide	82.67	28.09	0.34
NM_008218	110257	Hba-a1	hemoglobin alpha, adult chain 1	57378.42	20249.72	0.35
NM_007621	12409	Cbr2	carbonyl reductase 2	38360.42	13576.28	0.35
XM_144122	242805	Ankrd65	ankyrin repeat domain 65	36.87	13.24	0.36
-	-	-	unknown	35.73	12.83	0.36
NM_009714	11889	Asgr1	asialoglycoprotein receptor 1	46.34	16.74	0.36
NM_011784	23796	Agtr1	angiotensin receptor-like 1	454.59	165.64	0.36
-	-	-	unknown	34.77	12.69	0.36
NM_173052	282663	Serp1b1b	serine (or cysteine) peptidase inhibitor, clade B, member 1b	22.68	8.28	0.37
XM_110691	75863	Clec4g	C-type lectin domain family 4, member g	25.61	9.70	0.38
XM_287054	68874	1190002J23Rik	RIKEN cDNA 1190002J23 gene	32.18	12.25	0.38
NM_028848	74717	Spata17	spermatogenesis associated 17	24.18	9.45	0.39
NM_008311	15559	Htr2b	5-hydroxytryptamine (serotonin) receptor 2B	27.92	11.29	0.40
XM_133956	213002	Ifit6	interferon induced transmembrane protein 6	289.45	118.27	0.41
XM_129390	69169	Faim3	Fas apoptotic inhibitory molecule 3	506.40	208.34	0.41
NM_019487	56016	Hebp2	heme binding protein 2	23.47	9.69	0.41
NM_054038	117158	Scgb3a2	secretoglobin, family 3A, member 2	20687.05	8603.05	0.42
NM_009234	20666	Sox11	SRY (sex determining region Y)-box 11	79.25	32.99	0.42
NM_009922	12797	Cnn1	calponin 1	595.95	248.24	0.42
NM_007817	13107	Cyp2f2	cytochrome P450, family 2, subfamily f, polypeptide 2	16658.78	6961.71	0.42
XM_131840	230899	Nppa	natriuretic peptide precursor type A	95.54	40.39	0.42
NM_013613	18227	Nr4a2	nuclear receptor subfamily 4, group A, member 2	147.89	62.91	0.43
XM_128291	68311	Lypd2	Ly6/Plaur domain containing 2	508.95	224.07	0.44
NM_001033170	73813	Fam83e	RIKEN cDNA 4930403C10 gene	27.43	12.09	0.44
NM_009749	12069	Bex2	brain expressed X-linked 2	654.07	290.15	0.44
NM_007719	12775	Ccr7	chemokine (C-C motif) receptor 7	166.16	73.72	0.44
NM_023597	71354	Wdr31	WD repeat domain 31	57.65	25.73	0.45
NM_011620	21957	Tnnt3	troponin T3, skeletal, fast	35.65	15.95	0.45
XM_134806	70989	4931429I11Rik	RIKEN cDNA 4931429I11 gene	25.07	11.28	0.45
NM_029064	74711	Ttl9	tubulin tyrosine ligase-like family, member 9	25.84	11.66	0.45
NM_029627	76486	Ly6k	lymphocyte antigen 6 complex, locus K	35.48	16.05	0.45
NM_017372	17105	Lyzs	lysozyme	56345.42	25566.51	0.45
NM_021278	100047211	Tmsb4x	thymosin, beta 4, X chromosome	49135.42	22309.22	0.45
NM_001081977	108089	Rnf144	ring finger protein 144 [Source:MarkerSymbol;Acc:MGI:1344401]	20.25	9.25	0.46
NM_177876	330192	Vps37b	vacuolar protein sorting 37B (yeast)	22.50	10.35	0.46
NM_183094	667387	Xlr4b	X-linked lymphocyte-regulated 4B	26.62	12.55	0.47
XM_485890	72383	Cnfn	cornifelin	142.03	67.15	0.47
NM_011580	640441	Thbs1	thrombospondin 1	67.46	31.93	0.47
XM_489730	71236	Rtdr1	rhabdoid tumor deletion region gene 1	39.11	18.55	0.47
NM_007641	12482	Ms4a1	membrane-spanning 4-domains, subfamily A, member 1	561.05	268.25	0.48
NM_172050	217306	Cd300e	CD300e antigen	61.22	29.40	0.48
NM_008182	14858	Gsta2	glutathione S-transferase, alpha 2 (Yc2)	81.64	39.36	0.48
NM_153391	213081	Wdr19	WD repeat domain 19	51.80	25.13	0.49
NM_138949	192651	Zfp286	zinc finger protein 286 [Source:MarkerSymbol;Acc:MGI:2384758]	27.74	13.60	0.49
NM_009189	20471	Six1	sine oculis-related homeobox 1 homolog (Drosophila)	37.64	18.53	0.49
NM_138652	192113	Atp12a	ATPase, H ⁺ /K ⁺ transporting, nongastric, alpha polypeptide	21.97	10.83	0.49
NM_007549	12143	Blk	B lymphoid kinase	46.11	22.82	0.49
-	-	-	unknown	25.90	12.84	0.50
NM_007812	-	Cyp2a5	cytochrome P450, family 2, subfamily a, polypeptide 5	116.43	57.76	0.50