Disease	Genetic Modification	Type of Mouse Engineered	Phenotype/Biology
COPD (Reviewed in 13,24, 99,135,158): cigarette smoke inhalation model	Matrix Metalloproteinases (MMP): Collagenase-1 (MMP-1)	MMP1: TG overexpression of human MMP-1 with lung specificity in some lines, driven by haptoglobulin promoter	MMP-1 TG mice: Airspace enlargement: challenged elastase-antielastase hypothesis and raised importance of collagen deposition in COPD (27)
	MMP-12 (macrophage elastase)	MMP-12 KO mice	MMP-12 KO mice: Protected from cigarette smoke (CS)-induced emphysema and smoke-induced macrophage accumulation in the lung (69)
	Serine proteinases Neutrophil elastase (NE)	NE KO mice	NE KO mice: Protected from cigarette smoke-induced lung inflammation (PMN and monocytes) and airspace enlargement (135)
	Proteinase inhibitors Tissue inhibitor of metalloproteinase-3 (TIMP3)	TIMP-3 KO mice	TIMP-3 KO mice: Spontaneous airspace enlargement evident by 2 weeks; don't regularly survive beyond 13 months; increased MMP activity without increased inflammation (88)
	Cytokines: Interleukin (IL)-13 (Th2-cytokine)	IL-13: Doxycycline (Dox)-inducible, conditional transgene (CC10 rtTA)	IL-13 TG: Airway remodeling, goblet cell hypertrophy, subepithelial collagen deposition; Development of inflammation and lung destruction that was MMP-9, MMP-12, and cysteine proteinase-dependent; supports "dutch hypothesis" that asthma and COPD emanate from similar underlying mechanisms (181)
	Interferon (IFN)-γ (Th1-cytokine)	Interferon-γ: Dox-inducible, conditional transgene (CC10 rtTA)	IFN-γ TG: Inflammation and proteinase-dependent emphysema with prominent apoptosis and no airway involvement (162)
	Interleukin-18 Receptor-α	IL-18Rα KO mice	IL18Rα KO: Attenuated inflammation and emphysema following cigarette smoke exposure; increased IL-18 in mice and humans exposed to cigarette smoke and humans with COPD (80)
	TNF-α	TNFR KO mice	TNF-α signaling is required for smoke-induced PMN recruitment to the lung, extracellular matrix (ECM) destruction, and airspace enlargement (25)

	Developmental abnormalities resembling emphysema: Tight skin (Tsk)	Tsk+/- natural mutants	Tsk mutants: Mutation in fibrillin-1 (matrix protein that is an important component of elastic fibers) (60); abnormal lung development with sequestration of TGF-β in the matrix (117)
	Fibroblast growth factor family (FGF)	FGF-3/4 KO	FGF-3/4 KO: Impaired alveologenesis and increased collagen synthesis (163)
	Platelet-derived growth factor-A (PDGF-A)	PDGF-A KO	PDGFA KO: Deficient alveolar septation as a result of myofibroblast deficiency→deficient tropoelastin (16,95)
	Elastin	Elastin +/-	Elastin heterozygote: Abnormal lung development (KO mice die within 48h of birth and also have abnormal lung development) (164)
	Klotho (KL): single-pass membrane protein; sequence similarity with beta-glucosidase enzymes	KL KO	KL KO: Development of emphysema at 4 wks of age in conjunction with other signs of early aging including arteriosclerosis, osteoporosis, and skin atrophy (86,146)
	Inflammation: β-6 integrin	αvβ6 KO	αvβ6 KO: Exhibit normal alveolar development but develop spontaneous emphysema with age; develop macrophage-rich inflammation and excess MMP-12 production via failure to activate latent TGF-β (113)
	Host Defense: Surfactant Protein D (SPD)	SPD KO mice	SPD KO: Spontaneous emphysema evident by 3 weeks; increased NF-κB and MMP activity (177)
	Autophagy: Microtubule associated-protein 1 light chain 3B (LC3B)	LC3B KO mice	LC3B KO: Resistant to apoptosis and emphysema following prolonged cigarette smoke exposure (22)
	Oxidants/anti-oxidants	Nrf2 KO mice	Nrf2 reduces lung inflammation, increased lung proteinase levels, and airspace enlargement induced by cigarette smoke (77)
	Superoxide dismutase (SOD)	CuZn SOD transgenic mice	Over-expression of CuZn SOD prevented smoke-induced lung inflammation and airspace enlargement (44)

Asthma (focus on inflammation; Reviewed in 37,38,68); variety of models	Cytokines: Interleukin-13 (IL-13)	IL-13 TG Dox-inducible, driven by CCSP	IL-13 TG: Mucus metaplasia, accumulation of eosinophils in airway, subepithelial fibrosis and supports important role for IL-13 in airway remodeling (183); IL-11Rα plays an important role in IL-13 mediated pathogenesis of airway inflammation and remodeling (20,184); With prolonged IL-13 overexpression, subepithelial fibrosis spreads to parenchyma, thus suggesting role for IL-13 in interstitial lung disease, as well (see IPF section, TGFβ1 entry) (183)
	Interleukin-9 (IL-9)	IL-9 TG driven by CCSP	IL-9 TG: Airway inflammation (eosinophils, lymphocytes), mast cell hyperplasia, bronchial hyperresponsiveness, increased subepithelial collagen deposition (151)
	Interleukin-4 (IL-4)	IL-4 TG driven by CCSP	IL-4 TG: Mixed mononuclear and eosinophilic, mucus metaplasia, mild fibrotic airway response (126)
	Interleukin-5 (IL-5)	IL-5 TG driven by CCSP	IL-5 TG: Tissue eosinophilia, mucus metaplasia, subepithelial fibrosis, airway hyperresponsiveness (93)
	Th2 locus control region (LCR)	CD4-specific Th2 LCR-deficient (KO) mice using Cre-LoxP	LCR KO mouse: Th2 cytokine genes on mouse chr 11 regulated by Th2 LCR; deletion resulted in depressed Th2 cytokines and reduction in OVA-induced eosinophils, lymphocytes, IgE, lung airway inflammation, airway mucus production, AHR; LCR important in regulation of Th2 cytokines, chromatin remodeling of Th2 cytokine locus (84)
	Transcription Factors: T-bet	T-bet KO	T-bet KO: Spontaneous AHR, airway inflammation, elevation BAL Th2 cytokines, subepithelial collagen deposition, myofibroblast deposition—mediated by IL-13 (42)
	GATA-3	T-cell over-expression of DN-GATA-3	GATA-3 is important in IL-4, IL-5, IL-13-mediated airway eosinophilia, mucus secretion, IgE production (180)
	Growth Factors: Vascular endothelial growth	VEGF TG: dox-inducible, driven by CCSP (VEGF	VEGF TG: Inflammation, parenchymal/vascular remodeling, edema, mucus metaplasia, myocyte hyperplasia,

	factor (VEGF)	constitutive overexpression lethal in fetal development)	airway responsiveness; enhances respiratory Ag sensitization (92); Via IL-13 dependent and independent pathways
	Allergen mediation/ enzymes: Chitinase	BRP-39 KO mice; YKL-40 (human analogue) Dox-inducible TG mice driven by CCSP with tetracycline-controlled transcriptional repressor (CC10-rtTA-tTS-YKL-40); BRP-39 KO mice with epithelial-specific expression of YKL-40	Chitinases: Play important roles in aeroallergen-induced Th2 inflammation and IL-13 effector responses; important regulators of allergen sensitization and Th2 cytokine effector responses that augment IgE production, DC accumulation and activation and alternative macrophage activation (91)
	Proteinases: Matrix Metalloproteinase (MMP)-9	MMP-9 KO mice	MMP9 limits airway eosinophilia and reduced airway Th2 cytokine levels (103)
	MMP-8	MMP-8 KO mice	MMP-8 limits allergic airway inflammation (AAI) by increasing granulocyte apoptosis (122)
Pneumonia (Bacterial, reviewed. in 5,96,111)	Chemokines and Chemokine Receptors: CXCL5	CXCL-5 KO	CXCL5 KO: Important role in regulating availability of CXCL1 and 2 and in recruitment of neutrophils to the lung (85,104)
	Keratinoycte Chemoattractant (KC)	KC TG: CC10-driven	KC TG protected from *E. Coli* pneumonia; associated with increased neutrophil recruitment and enhanced bacterial clearance (156)
	CXCL15 (Lungkine)	CXCL15 KO	CXCL15 KO more susceptible to *K. pneumoniae,* and CXCL15 important for neutrophil migration (21)
	CXCR2	CXCR2 KO	CXCR2 KO mice more susceptible to *S. pneumoniae* with perturbed lung macrophage and neutrophil recruitment (70)
	Pathogen Recognition, Toll-Like Receptors: TLR 2, 4, 5, 9, and TLR Adaptor molecules	TLR 2 and TLR 4 KO	Inflammatory response to pneumococcal infection (pneumolysin) dependent upon both TLR2 and TLR4 signaling with TLR2 more classically recognizing Gram Positive (GP) infection signaling and TLR4 recognizing LPS and Gram Negative (GN) signaling (though not exclusively) (31)

		TLR 5 KO	TLR5 recognizes GN flagellated bacteria (*P. Aeruginosa* pneumonia) and cooperates with TLR4 in antibacterial effect (41)
		TLR9 KO mice	TLR9 KO mice more susceptible to pneumococcal pneumonia—TLR9 recognizes prokaryotic unmethylated CpG dinucleotides and plays role in early host defense GN and GP organisms (5)
		TLR adaptors (Reviewed in 9): TRIF KO, MyD88 KO, TIRAP KO	TRIF: control of GN infections MyD88: control of GN infections TIRAP: control of *E. Coli, K. Pneumoniae*
	Pathogen Recognition, NOD-like Receptors (NLR) and MARCO: NALP3	NALP3 KO mice	NALP3: Sense intracellular pathogens and protective in *K. pneumoniae* (169)
		MARCO (Macrophage Receptor with Collagenous Structure) KO	MARCO is important in host defense against pneumococcal pneumonia (7)
	Cytokines: IL-17	IL17R (interleukin-17 receptor) KO	IL-17R-deficient mice: higher mortality with *K. pneumoniae* (KP) with delay in alveolar neutrophil recruitment and greater bacterial dissemination; reduced steady-state levels of GCSF and MIP-2; IL-17R signaling important for GCSF and MIP-2 and control of KP infection (175)
	Transcription Factors: NF-κB	NF-κB p50 KO	p50 protective during *E. Coli* pneumonia (110)
		NF-κB p65 KO (on TNFR1-deficient background)	p65 protective during pneumococcal pneumonia (124)
	Stat-3	Dox-inducible deletion of Stat-3 in alveolar epithelial cells (SP-C driven) mediated by Cre recombinase	Stat-3 promotes neutrophil recruitment and limits lung injury in *E. Coli* pneumonia (139)
	Stat-4	Stat-4 KO mice	Stat-4 important for host defense in Klebsiella pneumonia (30)
	Other Mechanisms: Bacteriostatic─ Lipocalcin	Lipocalcin KO mice	Lipocalcin: Bacteriostatic protein binds siderophore (enterobactin, iron-chelating protein produced by *E. Coli* and required for bacterial growth) and protective

			against *E. Coli* (147) and *K. pneumoniae* (19,172)
	Surfactant disruption─ Atp8b1	Mutant mice with substantially reduced levels of Atp8b1 (single amino acid substitution resulting in defect in cellular import of phosphatidylserine)	Atp8b1 is an alveolar epithelial cardiolipin import pump; deficiency of Atp8b1: increased vulnerability to *E. Coli* via increased alveolar cardiolipin concentrations resulting in inhibition of surfactant activity, disruption of pulmonary architecture and reduced epithelial cell viability (127)
ARDS (focus on Ventilator-Induced Lung Injury (VILI))	<u>Transcription factors</u>: Activating transcription factor (ATF)-3	ATF3 KO	ATF3 KO mice with increased sensitivity to VILI (2); ATF pulled out from micro-array examining regulatory regions of genes activated by cyclic stretch
	Nrf2	Nrf2 KO	Nrf2 regulates levels several anti-oxidant enzymes ; Nrf2 KO mice more injured with VILI and rescued by anti-oxidants (118)
	<u>Metalloproteinases and matrix molecules:</u> MMP 8	MMP8 KO	MMP8 KO mice with attenuated lung injury from VILI, perhaps as a result of lower pro-inflammatory indices when compared with WT mice (3,32)
	MMP 9	MMP9 KO	Lack of MMP9 worsens high TV VILI and correlated with increased neutrophilic inflammation (no change in MMP-8 or TIMP1 levels) (4)
	Hyaluronan synthase-3	Hyaluronan synthase 3 KO	Hyaluronan synthase 3 deficiency protective against pro-inflammatory aspects of lung injury (8)
	<u>Cytokines:</u> IL-6	IL-6 KO mice (and chimeric mice generated by BMT)	Neutrophil-derived IL-6 protective against barrier-function disruption in VILI (170)
	IL1-Receptor 1 (IL1R1)	IL1R1 KO mice	IL1R1 KO mice protected from VILI (and similar effects seen with IL1R antagonist) and associated with decreased inflammation and improved barrier function (45)
	<u>Kinases:</u> MAP kinase activated protein kinase 2 (MK2)	MK2 KO mice	MK2 KO mice resistant to vascular leak in high TV MV; MK2 (downstream of p38 MAP kinase) mediates vascular permeability through regulation of HSP25-phosphorylation and actin

			cytoskeletal remodeling (28)
	Mitogen-activated protein kinase kinase-3 (MKK3) and c-JUN-NH(2)-terminal kinase-1 (jnk1)	MKK3 KO mice; jnk1 KO mice	MKK3 and jnk1 KO mice protected in VILI (32)
	<u>Neutrophil adhesion:</u> Neutrophil elastase	NE KO mice	NE KO mice with worse injury despite fewer neutrophils recruited; NE cleaves ICAM-1 allowing neutrophil egress from endothelium and perhaps in absence of NE, longer neutrophil adhesion and worse permeability from that interaction (82)
	$\alpha_v\beta_6$ integrin	Itgb6 KO mice	Thrombin: agonist of protease-activated receptor (PAR)-1 → $\alpha_v\beta_6$-dependent TGF-β activation→activation of the coagulation cascade → acute lung injury: Itgb6 KO mice protected from VILI-induced edema and protective against lung injury effects of PAR-1 peptide (79)
	<u>Gaseous Molecules:</u> Inducible nitric oxide synthase (NOS)-2; Endothelial nitric oxide synthase (NOS)-3	NOS2 KO mice; eNOS TG mice (bovine eNOS under expression of the preproendothelin-1 promoter thus with over-expression in the endothelium)	iNOS deficiency protective in VILI (119); eNOS overexpression protective in VILI (149)
	Heme-oxygenase-1 (HO-1) pathway (via production of carbon monoxide, CO)	Caveolin (cav)-1 KO mice; Egr-1 KO mice	Caveolin-deficient mice more susceptible to VILI and not rescued by CO as were WT-VILI mice; Cav-1 important for CO-protective effects in VILI (73); CO prevented upregulation of Egr-1 in VILI, and Egr-1 KO mice protected from VILI suggesting inhibition of Egr-1 expression plays a role in protective effects of CO during VILI (72)
	<u>Other mechanisms:</u> Gelsolin	Gsn KO mice	Gelsolin is an actin-binding protein and substrate of caspase-3; gelsolin KO mice protected from VILI perhaps in part mediated by reduction in apoptosis and inflammation (100)
	A2B adenosine receptor	A2BAR KO mice	A2BAR signaling attenuates lung injury via alveolar fluid clearance (34)

	5-Lipoxygenase	5-LO KO mice	5-LO deficiency protective, perhaps via amelioration of hypoxic pulmonary vasoconstriction (see pulmonary hypertension section of Table on 5-LO) (18)
	Pre B-cell Colony Enhancing Factor (PBEF)	Transgenic PBEF +/- mice	TG mice protected from VILI; administered recombinant PBEF neutrophil chemoattractant (74)
Pulmonary Fibrosis (Reviewed in 64,111, 112, 173)	<u>Growth Factors:</u> TGF-β1	Dox-inducible CCSP-driven biologically active TGFβ1 TG containing the tTS (tetracycline-controlled transcriptional silencer that binds and actively suppresses rtTA in the absence of Dox—see text for details)	Complex roles of TGF-β1, with paradigm of "TGF-β-dependent" and "TGF-β-independent" fibrosis; Constitutive over-expression using SPC promoter resulted in fetal lethality (block in branching morphogenesis); low level basal transgenic leak in an inducible system also resulted in fetal lethality prompting use of tTS; increase in TGFβ1→epithelial apoptosis→mononuclear inflammation, fibrosis, myofibroblast and myocyte hyperplasia, septal rupture/ honey-combing (182); IL-13 signaling via TGF-β (184) and EGR-1 critical for TGF-β response (90); Smad signaling important in TGF-β1-driven fibrosis, as Smad3 KO mice resistant to TGFβ1-mediated fibrosis (15), though signaling occurs also via Smad-independent pathways (34)
	TGF-α (ligand for EGFR)	TG Dox-inducible CCSP-selective TGF-α expression; expression in adult lung only	Fibrosis detected within 4d of TGF-α over-expression; fibrotic regions with increased collagen and ECM deposition adjacent to epithelial areas of TGF-α expression; appeared independent of TGF-β (66); TGF-α null mutation TG mice with less bleomycin-induced fibrotic lung injury; no compensatory increase in expression of other EGF family members (98)
	<u>Matrix Proteins:</u> Aortic Carboxypeptidase-like Protein (ACLP)	ACLP KO	ACLP is a collagen-associated protein containing a discoidin-like domain; ACLP-deficient mice protected from bleomycin-induced fibrosis; ACLP mediates lung fibroblast spreading/proliferation on collagen and collagen matrix contraction (134)
	<u>Proteinases and proteinase inhibitors:</u>	NE KO mice	NE activates TGF-β in the lung (23)

	Neutrophil elastase (NE)		
	Matrix metalloproteinase (MMP)-7	MMP7 KO mice	MMP-7 promotes lung fibrosis (185)
	MMP-9	MMP-9 KO mice	MMP-9 promotes bronchiolar alveolarization in response to bleomycin (14)
	Tissue and urokinase type plasminogen activators (tPA, uPA)	u-PA KO, uPAR KO and tPA KO mice	PAs inhibit lung fibrosis by activating plasmin, which degrades the provisional matrix and activates pro-MMPs (147)
	Plasminogen activator inhibitor - 1 (PAI-1)	PAI-1 KO and PAI-1 transgenic mice	PAI-1 promotes lung fibrosis by inhibiting plasmin activation and clearance of the provisional matrix and pro-MMP activation (36)
	<u>Cytokines</u>: Monocyte chemotactic protein (MCP)-1 (CCL2)	MCP1 KO mice	Promotes lung fibrosis by increasing macrophage accumulation in the lung and lung CTGF levels (10)
	Macrophage Colony Stimulating Factor (M-CSF)	M-CSF KO mice	Promotes lung fibrosis by increasing macrophage accumulation in the lung and lung CTGF levels (10)
	Tumor Necrosis Factor (TNF)-α	TNF-α transgenic mice (SPC promoter)	TNF-α protects murine lungs from fibrosis, and this is associated with increased lung levels of PGE2 and reduced expression of TNFR1 (49)
	Interferon-gamma Induced Protein (IP-10) (CXCL10)	IP10 KO mice	IP-10 inhibits lung fibrosis by reducing fibroblast migration (148)
	<u>Lipid mediators</u>: Cysteinyl leukotrienes	5-Lipoxygenase (5-LO) KO mice; Leukotriene C4 (LTC4) synthase KO mice	5-LO and LTC synthase-4 promote lung fibrosis by generating cysteinyl leukotrienes, which activate fibrocytes, fibroblasts, and macrophages (12,157)

	Prostaglandin E2	Cyclooxygenase (COX)-2 KO mice	COX-2 limits lung fibrosis by generating prostaglandin E2, which inhibits fibroblast proliferation and collagen synthesis (83,71)
	<u>Miscellaneous:</u> Surfactant disruption: Surfactant protein-C	SPC KO mice	Develop features consistent with interstitial pneumonitis (thickened alveolar walls that stain positive for α-SM actin; monocytic infiltrates and increased MMP-2 and -9 expression, epithelial cell dysplasia with MUC5A/C expression in conducting airways, accumulation of intracellular lipids) (53); increased susceptibility to bleomycin-induced fibrotic lung injury (87); Also exhibit features some emphysematous features (septal thinning and pulmonary capillary bed loss)
	Tumor suppressor: Phophatase and tensin homolog (PTEN)	PTEN haploinsufficient mice (+/-)	PTEN: tumor-suppressor and negative regulator of PI3K-Akt pathway felt to be active in a number of pathways leading to development of fibrosis; PTEN haploinsufficient mice developed exaggerated fibrotic lung injury in response to bleomycin (36)
Pulmonary Hyper-tension (Reviewed in 17,47,50; chronic hypoxia and monocro-taline models)	<u>Gaseous molecules:</u> e-NOS	e-NOS KO	e-NOS derived NO important for PV-response to hypoxia; 50% expression required for normal pulmonary vascular tone (89); Adenoviral gene transfer protective against hypoxia (78)
	Heme oxygenase-1 (HO-1)	Constitutive lung-specific overexpression HO-1 (SPC-driven expression)	Over expression of HO-1 protected against hypoxia-induced pulmonary inflammation and pHTN (107)
	<u>Arachidonic acid downstream pathways:</u> 5-Lipoxygenase (LO) activating protein (FLAP)	FLAP KO	FLAP KO: Less RVH with chronic hypoxia; role in pulmonary vascular tone (160)
	Cyclo-oxygenase-2 (COX2)	COX2 KO	Hypoxia-induced pHTN and vascular remodeling exacerbated with absence COX2; perhaps via increasing ET-A receptor expression and increased PASMC hypertrophy; rescued by PGE1 or PGE2 (46)

	Prostacyclin synthase (PGIS) and prostacyclin receptor	SP-C driven lung-specific overexpression of PGIS (hypobaric hypoxia chronic exposure); prostacyclin receptor KO mice	PGIS overexpression protective from PH development and modified chronic vascular response to hypoxia (52); prostacyclin receptor KO mice with more severe PH with chronic hypoxia: important modulating role for PGI2 (76); Adenoviral gene transfer protective against hypoxia (51) and monocrotaline (116)
	Bone morphogenic protein and downstream signaling: Bone Morphogenic Protein (BMP) signaling (166)	SM22α-specific expression of dominant negative Bmpr2 (34); SM22α-specific deletion of Bmpr1a in vascular smooth muscle cells and cardiac myocytes with doxycycline withdrawal (37)	SM22α-specific Bmpr2 deficiency: PH but with modest vascular remodeling; SM22α–Bmpr1a deficiency protective against pulmonary vascular remodeling with decreased muscularization of pulmonary vessels (reduced proliferation) and loss of hypoxia-mediated vascular loss (resistance to apoptosis); however Bmpr1a-deficient mice had impaired cardiac contractility
	PPAR-γ	Targeted deletion in arterial SMC (Floxed), driven by SM22-α (SM22-α/Cre/PPAR-γ/Flox/Flox)	Spontaneous development of PAH (63, 108); PPAR/apo E axis downstream of BMP-2 signaling in pulmonary artery smooth muscle cells
	apoE	apoE KO mice	ApoE KO mice: Develop PAH in setting of high fat diet and insulin resistance and can be rescued by PPAR-γ (63)
	Serotonin pathway: Serotonin (5-hydroxytryptamine) transporter (5-HTT)	5-HTT KO mice	5-HTT mediates hypoxia-induced mitogenic activity of serotonin on PSMCs; 5-HTT KO mice protected from development of PHTN and vascular remodeling (35)
	Autophagy: Microtubule associated-protein 1 light chain 3B (LC3B)	LC3B KO mice	LC3B KO mice: Develop exaggerated pulmonary hypertension with hypoxia; LC3B may play a role in the regulation of hypoxic cell proliferation (94)
	Miscellaneous: IL-6	Lung-specific (CC10-driven) IL-6 TG	IL-6 TG: Increased muscularization pulmonary vascular tree exacerbated by hypoxia via pro-proliferative/anti-apoptotic mechanisms (143)
	Vasointestinal peptide (VIP)	VIP KO mice	VIP: Pulmonary vasodilator and inhibitor of VSMC proliferation; VIP KO mice develop moderate spontaneous pulmonary hypertension that is attenuated with VIP administration (131)

	Elafin (serine elastase inhibitor)	TG (pre-proendothelin-1 promoter targets CV system with expression in heart, lungs, arteries)	Elafin overexpression protective against hypoxia-induced pHTN and correlates with suppression of MMP-9 expression (178)

AHR: airway hyperreactivity; pHTN: pulmonary hypertension; TG: transgenic; KO: knockout; Dox: doxycycline; GN: gram negative; GP: gram positive; MMP: matrix metalloproteinase; IL: interleukin; PAH: pulmonary arterial hypertension; PSMCs (pulmonary smooth muscle cells)

TABLE S1: Key genetically modified mice in developing our understanding of lung disease pathophysiology