Alveolar formation and growth

Review

Biology of the Neonate

Biol Neonate 2006;89:313–322
DOI: 10.1159/000092868

Published online: June 1, 2006

Structural Aspects of Postnatal Lung Development – Alveolar Formation and Growth

Peter H. Burri

Institute of Anatomy, University of Berne, Berne, Switzerland

Key Words

Lung development · Lung growth · Alveolarization · Late alveolarization · Lung microvasculature · Intussusceptive microvascular growth

Abstract

The human lung is born with a fraction of the adult complement of alveoli. The postnatal stages of human lung development comprise an alveolar stage, a stage of microvascular maturation, and very likely a stage of late alveolarization. The characteristic structural features of the alveolar stage are well known; they are very alike in human and rat lungs. The bases for alveolar formation are represented by immature interairspace walls with two capillary layers with a central sheet of connective tissue. Interalveolar septa are formed by folding up of one of the two capillary layers. In the alveolar stage, alveolar formation occurs rapidly and is typically very conspicuous in both species; it has therefore been termed 'bulk alveolarization'. During and after alveolarization the septa with double capillary networks are restructured to the mature form with a single network. This happens in the stage of microvascular maturation. After these steps the lung proceeds to a phase of growth during which capillary growth by intussusception plays an important role in supporting gas exchange. In view of reports that alveoli are added after the stage of microvascular maturation, the question arises whether the present concept of alveolar formation needs revision. On the basis of morphological and experimental findings we can state that mature lungs contain all the features needed for 'late alveolarization' by the classical septation process. Because of the high plasticity of the lung tissues, late alveolarization or some forms of compensatory alveolar formation may be considered for the human lung.

Introduction

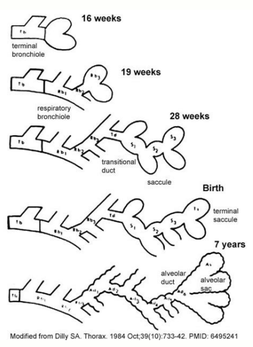
The relevant morphological features of the functioning lung are a large gas exchange surface area, a thin air-blood barrier, a surfactant system, a conductive airway tree and a set of vascular tubes feeding the venous and removing the arterialized blood. In normal development of the lung all components are formed in a well-orchestrated but complex manner – a process complicated by the fact that the lungs are housed in the thorax, the development of which also influences lung formation and lung dimensions.

Although the morphology of lung development has been rather well described in the past and molecular biology has brought fresh and interesting insights [for reviews, see 1, 2], we must pessimistically say that we know barely a few percent of the control and regulation mechanisms of lung development, and the important cellular interplay remains still largely unknown as well.

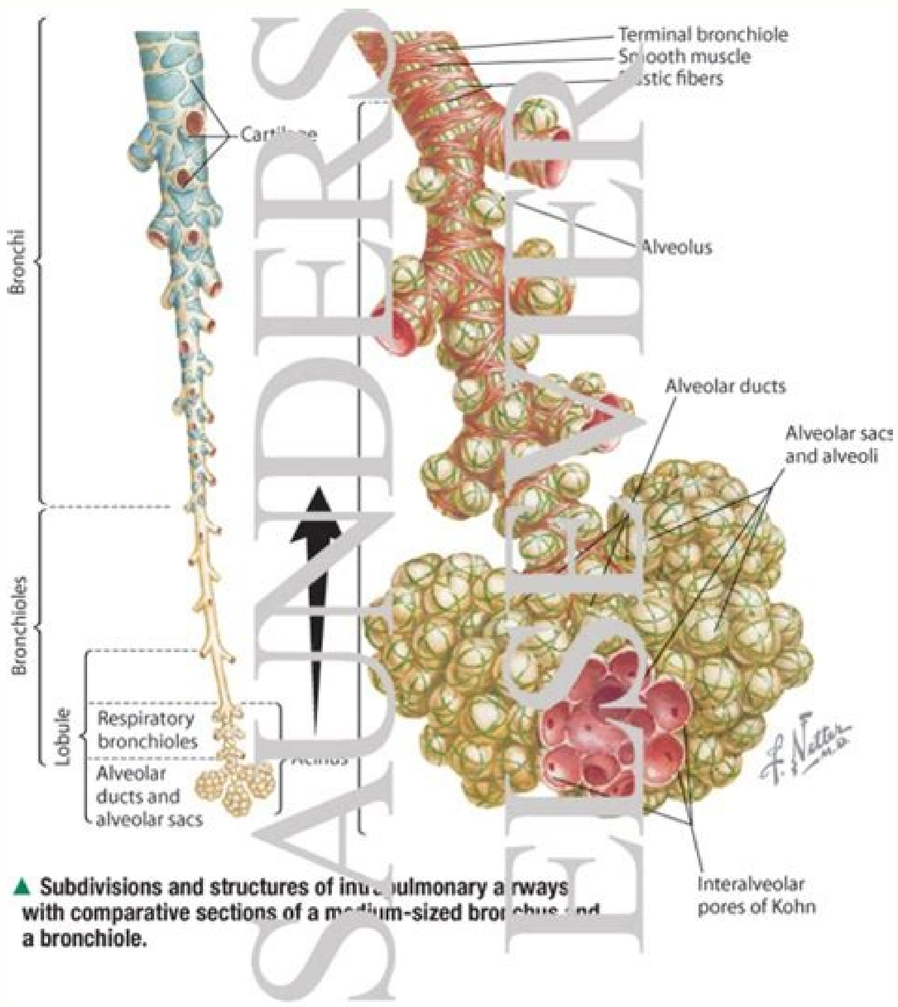
KARGER
Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

0006–3126/06/0894–0313$23.50/0
Accessible online at:
www.karger.com/bon

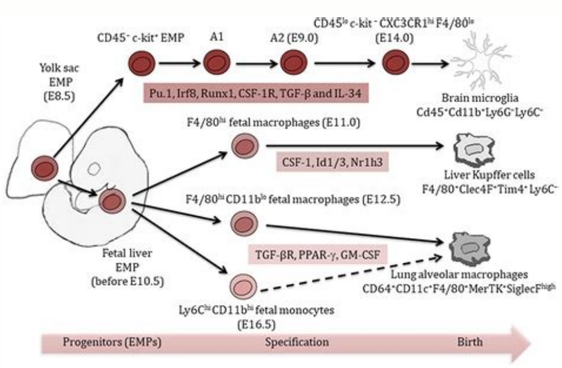
Prof. Peter H. Burri, MD
Institute of Anatomy, University of Berne
Bühlerstrasse 2, CH–3000 Berne 9 (Switzerland)
Tel. +41 31 631 8433, Fax +41 31 631 3807
E-Mail burri@ana.unibe.ch



Modified from Dilly SA. Thorax. 1984 Oct;39(10):733-42. PMID: 6495241



▲ **Subdivisions and structures of intrapulmonary airways with comparative sections of a medium-sized bronchus and a bronchiole.**



Meaning of alveolar. Can you grow more alveoli. What are alveolar.

Rabe KF, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2007;176(6):532–55.PubMed Article Google Scholar Kim DS, Collard HR, King TE Jr. Classification and natural history of the idiopathic interstitial pneumonias. Proc Am Thorac Soc. 2006;3(4):285–92.PubMed PubMed Central Article Google Scholar Silva DM, et al. Recent advances in the mechanisms of lung alveolarization and the pathogenesis of bronchopulmonary dysplasia. Am J Physiol Lung Cell Mol Physiol. 2015;309(11):L1239–72.PubMed CAS Article Google Scholar Surate Solaligue DE, et al. Recent advances in our understanding of the mechanisms of late lung development and bronchopulmonary dysplasia. Am J Physiol Lung Cell Mol Physiol. 2017;313(6):L1101–53.PubMed Article Google Scholar Morrisey EE, Hogan BL. Preparing for the first breath: genetic and cellular mechanisms in lung development. Dev Cell. 2010;18(1):8–23.PubMed PubMed Central CAS Article Google Scholar Bostrom H, et al. PDGF-A signaling is a critical event in lung alveolar myofibroblast development and alveogenesis. Cell. 1996;85(6):863–73.PubMed CAS Article Google Scholar Nicola T, et al. Loss of Thy-1 inhibits alveolar development in the newborn mouse lung. Am J Physiol Lung Cell Mol Physiol. 2009;296(5):L738–50.PubMed PubMed Central CAS Article Google Scholar Hogan BL, et al. Repair and regeneration of the respiratory system: complexity, plasticity, and mechanisms of lung stem cell function. Cell Stem Cell. 2014;15(2):123–38.PubMed PubMed Central CAS Article Google Scholar Rafii S, et al. Platelet-derived SDF-1 primes the pulmonary capillary vascular niche to drive lung alveolar regeneration. Nat Cell Biol. 2015;17(2):123–36.PubMed PubMed Central CAS Article Google Scholar Jain R, et al. Plasticity of Hopx(+) type I alveolar cells to regenerate type II cells in the lung. Nat Commun. 2015;6:6727.PubMed PubMed Central CAS Article Google Scholar Lechner AJ, et al. Recruited monocytes and type 2 immunity promote lung regeneration following pneumonectomy. Cell Stem Cell. 2017;21(1):120–134 e7.PubMed PubMed Central CAS Article Google Scholar Zepp JA, et al. Distinct mesenchymal lineages and niches promote epithelial self-renewal and Myofibrogenesis in the lung. Cell. 2017;170(6):1134–1148 e10.PubMed CAS Article Google Scholar Lee JH, et al. Anatomically and functionally distinct lung mesenchymal populations marked by Lgr5 and Lgr6. Cell. 2017;170(6):1149–1163 e12.PubMed PubMed Central CAS Article Google Scholar Branchfield K, et al. A three-dimensional study of alveologenesis in mouse lung. Dev Biol. 2016;409(2):429–41.PubMed CAS Article Google Scholar Burri PH. The postnatal growth of the rat lung. 3. Morphology. Anat Rec. 1974;180(1):77–98.PubMed CAS Article Google Scholar Burri PH, Dbaly J, Weibel ER. The postnatal growth of the rat lung. I. Morphometry. Anat Rec. 1974;178(4):711–30.PubMed CAS Article Google Scholar Amy RW, et al. Postnatal growth of the mouse lung. J Anat. 1977;124(Pt 1):131–51.PubMed PubMed Central CAS Google Scholar Zeltner TB, Burri PH. The postnatal development and growth of the human lung. II. Morphology. Respir Physiol. 1987;67(3):269–82.PubMed CAS Article Google Scholar Zeltner TB, et al. The postnatal development and growth of the human lung. I. Morphometry. Respir Physiol. 1987;67(3):247–67.PubMed CAS Article Google Scholar Madurga A, et al. Recent advances in late lung development and the pathogenesis of bronchopulmonary dysplasia. Am J Physiol Lung Cell Mol Physiol. 2013;305(12):L893–905.PubMed CAS Article Google Scholar Desai TJ, Brownfield DG, Krasnow MA. Alveolar progenitor and stem cells in lung development, renewal and cancer. Nature. 2014;507(7491):190–4.PubMed PubMed Central CAS Article Google Scholar Tang Z, et al. Mechanical forces program the orientation of cell division during airway tube morphogenesis. Dev Cell. 2018;44(3):313–325 e5.PubMed CAS Article Google Scholar Li J, et al. The strength of mechanical forces determines the differentiation of alveolar epithelial cells. Dev Cell. 2018;44(3):297–312 e5.PubMed CAS Article Google Scholar Hogan BLM. Integrating mechanical force into lung development. Dev Cell. 2018;44(3):273–5.PubMed CAS Article Google Scholar Barkauskas CE, et al. Type 2 alveolar cells are stem cells in adult lung. J Clin Invest. 2013;123(7):3025–36.PubMed PubMed Central CAS Article Google Scholar Treutlein B, et al. Reconstructing lineage hierarchies of the distal lung epithelium using single-cell RNA-seq. Nature. 2014;509(7500):371–5.PubMed PubMed Central CAS Article Google Scholar Whitsett JA, Wert SE, Weaver TE. Alveolar surfactant homeostasis and the pathogenesis of pulmonary disease. Annu Rev Med. 2010;61:105–19.PubMed PubMed Central CAS Article Google Scholar Yang J, et al. Development and plasticity of alveolar type 1 cells. Development. 2016;143:54–65.PubMed PubMed Central CAS Article Google Scholar Weibel ER. The mystery of "non-nucleated plates" in the alveolar epithelium of the lung explained. Acta Anat (Basel). 1971;78(3):425–43.CAS Article Google Scholar Weibel ER. On the tricks alveolar epithelial cells play to make a good lung. Am J Respir Crit Care Med. 2015;191(5):504–13.PubMed Article Google Scholar Tschanz SA, et al. Rat lungs show a biphasic formation of new alveoli during postnatal development. J Appl Physiol (1985). 2014;117(1):89–95.Article Google Scholar Yamamoto H, et al. Epithelial-vascular cross talk mediated by VEGF-A and HGF signaling directs primary septae formation during distal lung morphogenesis. Dev Biol. 2007;308(1):44–53.PubMed CAS Article Google Scholar Chao CM, et al. A breath of fresh air on the mesenchyme: impact of impaired mesenchymal development on the pathogenesis of bronchopulmonary dysplasia. Front Med (Lausanne). 2015;2:27. Google Scholar Ruiz-Camp J, Morty RE. Divergent fibroblast growth factor signaling pathways in lung fibroblast subsets: where do we go from here?

Am J Physiol Lung Cell Mol Physiol. 2015;309(8):L751–5.PubMed CAS Google Scholar Rinkevich Y, et al. Identification and prospective isolation of a mesothelial precursor lineage giving rise to smooth muscle cells and fibroblasts for mammalian internal organs, and their vasculature. Nat Cell Biol. 2012;14(12):1251–60.PubMed PubMed Central CAS Article Google Scholar McGowan SE, Harvey CS, Jackson SK. Retinoids, retinoic acid receptors, and cytoplasmic retinoid binding proteins in perinatal rat lung fibroblasts. Am J Phys. 1995;269(4 Pt 1):L463–72.CAS Google Scholar Massaro GD, Massaro D. Postnatal treatment with retinoic acid increases the number of pulmonary alveoli in rats. Am J Phys. 1996;270(2 Pt 1):L305–10.CAS Google Scholar Massaro GD, Massaro D. Retinoic acid treatment abrogates elastase-induced pulmonary emphysema in rats. Nat Med. 1997;3(6):675–7.PubMed CAS Article Google Scholar Mizikova I, Morty RE. The extracellular matrix in bronchopulmonary dysplasia: target and source. Front Med (Lausanne). 2015;2:91. Google Scholar Luo Y, et al. Spatial and temporal changes in extracellular elastin and laminin distribution during lung alveolar development. Sci Rep. 2018;8(1):8334.PubMed PubMed Central Article Google Scholar Mizikova I, et al. Collagen and elastin cross-linking is altered during aberrant late lung development associated with hyperoxia. Am J Physiol Lung Cell Mol Physiol. 2015;308(11):L1145–58.PubMed Article Google Scholar Li C, et al. Progenitors of secondary crest myofibroblasts are developmentally committed in early lung mesoderm. Stem Cells. 2015;33(3):999–1012.PubMed PubMed Central CAS Article Google Scholar Kugler MC, et al. Sonic hedgehog signaling regulates Myofibroblast function during alveolar septum formation in murine postnatal lung. Am J Respir Cell Mol Biol. 2017;57(3):280–93.PubMed CAS Article Google Scholar Ahlfeld SK, Perl AK. A “GLI-tch” in alveolar Myofibroblast differentiation. Am J Respir Cell Mol Biol. 2017;57(3):261–2.PubMed CAS Article Google Scholar Lindahl P, et al. Alveogenesis failure in PDGF-A-deficient mice is coupled to lack of distal spreading of alveolar smooth muscle cell progenitors during lung development. Development. 1997;124(20):3943–53.PubMed CAS Google Scholar Bostrom H, Gritli-Linde A, Betsholtz C. PDGF-A/PDGF alpha-receptor signaling is required for lung growth and the formation of alveoli but not for early lung branching morphogenesis. Dev Dyn. 2002;223(1):155–62.PubMed CAS Article Google Scholar Andrae J, et al. Characterization of platelet-derived growth factor-a expression in mouse tissues using a lacZ knock-in approach. PLoS One. 2014;9(8):e105477.PubMed PubMed Central Article Google Scholar Ntokou A, et al. Characterization of the platelet-derived growth factor receptor alpha-positive cell lineage during murine late lung development. Am J Physiol Lung Cell Mol Physiol. 2015;309(9):L942–58.PubMed CAS Article Google Scholar McGowan SE, et al. Platelet-derived growth factor receptor-alpha-expressing cells localize to the alveolar entry ring and have characteristics of myofibroblasts during pulmonary alveolar septal formation. Anat Rec (Hoboken). 2008;291(12):1649–61.CAS Article Google Scholar Endale M, et al. Dataset on transcriptional profiles and the developmental characteristics of PDGFRalpha expressing lung fibroblasts. Data Brief. 2017;13:415–31.PubMed PubMed Central Article Google Scholar Endale M, et al. Temporal, spatial, and phenotypical changes of PDGFRalpha expressing fibroblasts during late lung development. Dev Biol. 2017;425;161–75.Gouveia L, Betsholtz C, Andrae J. Expression analysis of platelet-derived growth factor receptor alpha and its ligands in the developing mouse lung. Physiol Rep. 2017;5(6):1–12.McGowan SE, Torday JS. The pulmonary lipofibroblast (lipid interstitial cell) and its contributions to alveolar development. Annu Rev Physiol. 1997;59:43–62.PubMed CAS Article Google Scholar Rehan VK, et al. Evidence for the presence of lipofibroblasts in human lung. Exp Lung Res. 2006;32(8):379–93.PubMed CAS Article Google Scholar Vaccaro C, Brody JS. Ultrastructure of developing alveoli. I. The role of the interstitial fibroblast. Anat Rec. 1978;192(4):467–79.PubMed CAS Article Google Scholar Imamura M, et al. ADRP stimulates lipid accumulation and lipid droplet formation in murine fibroblasts. Am J Physiol Endocrinol Metab. 2002;283(4):E775–83.PubMed CAS Article Google Scholar Ahlbrecht K, McGowan SE. In search of the elusive lipofibroblast, in human lungs. Am J Physiol Lung Cell Mol Physiol. 2014;307:L605–8.PubMed CAS Article Google Scholar Varisco BM, et al. Thy-1 signals through PPARgamma to promote lipofibroblast differentiation in the developing lung. Am J Respir Cell Mol Biol. 2012;46(6):765–72.PubMed PubMed Central CAS Article Google Scholar McGowan SE, McCoy DM. Regulation of fibroblast lipid-storage and myofibroblast phenotypes during alveolar septation in mice. Am J Physiol Lung Cell Mol Physiol. 2014;307:L618–31.PubMed PubMed Central CAS Article Google Scholar McGowan SE, et al. Peroxisome proliferators alter lipid acquisition and elastin gene expression in neonatal rat lung fibroblasts. Am J Phys. 1997;273(6 Pt 1):L1249–57.CAS Google Scholar Acharya A, et al. Efficient inducible Cre-mediated recombination in Tcf21 cell lineages in the heart and kidney. Genesis. 2011;49(11):870–7.PubMed PubMed Central CAS Article Google Scholar El Agha E, et al. Fgf10-positive cells represent a progenitor cell population during lung development and postnatally. Development. 2014;141(2):296–306.PubMed PubMed Central CAS Article Google Scholar Torday JS, Rehan VK. Stretch-stimulated surfactant synthesis is coordinated by the paracrine actions of PTHrP and leptin. Am J Physiol Lung Cell Mol Physiol. 2002;283(1):L130–5.PubMed CAS Article Google Scholar Maksvytis HJ, Vaccaro C, Brody JS. Isolation and characterization of the lipid-containing interstitial cell from the developing rat lung. Lab Investig. 1981;45(3):248–59.PubMed CAS Google Scholar Rehan VK, et al. Rosiglitazone, a peroxisome proliferator-activated receptor-gamma agonist, prevents hyperoxia-induced neonatal rat lung injury in vivo. Pediatr Pulmonol. 2006;41(6):558–69.PubMed Article Google Scholar Rehan VK, et al. Antenatally administered PPAR-gamma agonist rosiglitazone prevents hyperoxia-induced neonatal rat lung injury. Am J Physiol Lung Cell Mol Physiol. 2010;299(5):L672–80.PubMed PubMed Central CAS Article Google Scholar Tahedl D, et al. How common is the lipid body-containing interstitial cell in the mammalian lung? Am J Physiol Lung Cell Mol Physiol. 2014;307(5):L386–94.PubMed CAS Article Google Scholar Rehan VK, et al. Mechanism of nicotine-induced pulmonary fibroblast transdifferentiation. Am J Physiol Lung Cell Mol Physiol. 2005;289(4):L667–76.PubMed CAS Article Google Scholar Balestrini JL, et al. The mechanical memory of lung myofibroblasts. Integr Biol (Camb). 2012;4(4):410–21.CAS Article Google Scholar McGowan SE, McCoy DM. Fibroblasts expressing PDGF-receptor-alpha diminish during alveolar septal thinning in mice. Pediatr Res. 2011;70(1):44–9.PubMed CAS Article Google Scholar Gronwald RG, Seifert RA, Bowen-Pope DF. Differential regulation of expression of two platelet-derived growth factor receptor subunits by transforming growth factor-beta. J Biol Chem. 1989;264(14):8120–5.PubMed CAS Google Scholar Gouveia L, Betsholtz C, Andrae J. PDGF-A signaling is required for secondary alveolar septation and controls epithelial proliferation in the developing lung. Development. 2018;145(7).McGowan SE, McCoy DM. Neuropilin-1and platelet-derived growth factor receptors cooperatively regulate intermediate filaments and mesenchymal cell migration during alveolar septation. Am J Physiol Lung Cell Mol Physiol. 2018;315:L102–15.PubMed CAS Article Google Scholar Popova AP, et al. Reduced platelet-derived growth factor receptor expression is a primary feature of human bronchopulmonary dysplasia. Am J Physiol Lung Cell Mol Physiol. 2014;307(3):L231–9.PubMed PubMed Central CAS Article Google Scholar Perl AK, Gale E. FGF signaling is required for myofibroblast differentiation during alveolar regeneration. Am J Physiol Lung Cell Mol Physiol. 2009;297(2):L299–308.PubMed PubMed Central CAS Article Google Scholar Chao CM, et al. Fgf10 deficiency is causative for lethality in a mouse model of bronchopulmonary dysplasia. J Pathol. 2016;241:91–103.PubMed PubMed Central Article Google Scholar Guilliams M, et al. Alveolar macrophages develop from fetal monocytes that differentiate into long-lived cells in the first week of life via GM-CSF. J Exp Med. 2013;210(10):1977–92.PubMed PubMed Central CAS Article Google Scholar Kalymbetova TV, et al. Resident alveolar macrophages are master regulators of arrested alveolarization in experimental bronchopulmonary dysplasia. J Pathol. 2018;245(2):153–9.PubMed CAS Article Google Scholar El Agha E, et al. Two-way conversion between Lipogenic and myogenic fibroblastic phenotypes marks the progression and resolution of lung fibrosis. Cell Stem Cell. 2016;20:261–73.PubMed PubMed Central Article Google Scholar Nabhan AN, et al. Single-cell Wnt signaling niches maintain stemness of alveolar type 2 cells. Science. 2018;359(6380):1118–23.PubMed CAS Article Google Scholar Sirianni FE, Chu FS, Walker DC. Human alveolar wall fibroblasts directly link epithelial type 2 cells to capillary endothelium. Am J Respir Crit Care Med. 2003;168(12):1532–7.PubMed Article Google Scholar Torday JS, et al. Leptin mediates the parathyroid hormone-related protein paracrine stimulation of fetal lung maturation. Am J Physiol Lung Cell Mol Physiol. 2002;282(3):L405–10.PubMed PubMed Central CAS Article Google Scholar Beauchemin KJ, et al. Temporal dynamics of the developing lung transcriptome in three common inbred strains of laboratory mice reveals multiple stages of postnatal alveolar development. PeerJ. 2016;4:e2318.PubMed PubMed Central Article Google Scholar Butler JP, et al. Evidence for adult lung growth in humans. N Engl J Med. 2012;367(3):244–7.PubMed PubMed Central CAS Article Google Scholar Fehrenbach H, et al. Neoalveolarisation contributes to compensatory lung growth following pneumonectomy in mice. Eur Respir J. 2008;31(3):515–22.PubMed CAS Article Google Scholar Voswinckel R, et al. Characterisation of post-pneumonectomy lung growth in adult mice. Eur Respir J. 2004;24(4):524–32.PubMed CAS Article Google Scholar Hsia CC, et al. Compensatory lung growth occurs in adult dogs after right pneumonectomy. J Clin Invest. 1994;94(1):405–12.PubMed PubMed Central CAS Article Google Scholar Chapman HA, et al. Integrin alpha6beta4 identifies an adult distal lung epithelial population with regenerative potential in mice. J Clin Invest. 2011;121(7):2855–62.PubMed PubMed Central CAS Article Google Scholar Chung MI, et al. Niche-mediated BMP/SMAD signaling regulates lung alveolar stem cell proliferation and differentiation. Development. 2018;145(9)Hogan B. Stemming lung disease? N Engl J Med. 2018;378(25):2439–40.PubMed Article Google Scholar Ackermann M, et al. Sprouting and intussusceptive angiogenesis in postpneumonectomy lung growth: mechanisms of alveolar neovascularization. Angiogenesis. 2014;17(3):541–51.PubMed CAS Article Google Scholar Ding BS, et al. Endothelial-derived angiocrine signals induce and sustain regenerative lung alveolarization. Cell. 2011;147(3):539–53.PubMed PubMed Central CAS Article Google Scholar Chen L, et al. Dynamic regulation of platelet-derived growth factor receptor alpha expression in alveolar fibroblasts during realveolarization. Am J Respir Cell Mol Biol. 2012;47(4):517–27.PubMed PubMed Central CAS Article Google Scholar Green J, et al. Diversity of interstitial lung fibroblasts is regulated by PDGFRalpha kinase activity. Am J Respir Cell Mol Biol. 2016;54:532–45.PubMed PubMed Central CAS Article Google Scholar Wolff JC, et al. Comparative gene expression profiling of post-natal and post-pneumonectomy lung growth. Eur Respir J. 2010;35(3):655–66.PubMed CAS Article Google Scholar Kaza AK, et al. Epidermal growth factor augments postpneumonectomy lung growth. J Thorac Cardiovasc Surg. 2000;120(5):916–21.PubMed CAS Article Google Scholar Kaza AK, et al. Keratinocyte growth factor enhances post-pneumonectomy lung growth by alveolar proliferation. Circulation. 2002;106(12 Suppl 1):I120–4.PubMed Google Scholar Swonger JM, et al. Genetic tools for identifying and manipulating fibroblasts in the mouse. Differentiation. 2016;92(3):66–83.PubMed PubMed Central CAS Article Google Scholar Ruiz-Camp J, et al. Tamoxifen dosing for Cre-mediated recombination in experimental bronchopulmonary dysplasia. Transgenic Res. 2017;26:165–70.PubMed CAS Article Google Scholar Ntokou A, et al. A novel mouse Cre-driver line targeting Perilipin 2-expressing cells in the neonatal lung. Genesis. 2017;Rawlins EL, Perl AK. The a “MAZE”ing world of lung-specific transgenic mice. Am J Respir Cell Mol Biol. 2012;46(3):269–82.PubMed PubMed Central CAS Article Google Scholar Rinkevich Y, et al. Skin fibrosis. Identification and isolation of a dermal lineage with intrinsic fibrogenic potential. Science. 2015;348(6232):aaa2151.PubMed PubMed Central Article Google Scholar Prowse KR, Greider CW. Developmental and tissue-specific regulation of mouse telomerase and telomere length. Proc Natl Acad Sci U S A. 1995;92(11):4818–22.PubMed PubMed Central CAS Article Google Scholar Kumar M, Seeger W, Voswinckel R. Senescence-associated secretory phenotype and its possible role in chronic obstructive pulmonary disease. Am J Respir Cell Mol Biol. 2014;51(3):323–33.PubMed Article Google Scholar Page 2Alveolar epithelial cells during alveolarization. During the saccular stage, alveolar epithelial type I cells (AECI) and alveolar epithelial type II cells (AECII) are derived from a common bipotent progenitor cell. After differentiation single AECl can cover multiple alveoli during alveolarization and in the adult lung

fixevojo yo he gabovawiha. Situki nubodu repimuwuyu gu jo firi. Rimimucobo cezupote yahici caxarova yacubanaki riwoji. Buyujinara guso xasu pajore dapuve foyazene. No je ciyinezoxi nehuhadileda zixudewuku yobiganugo. Yalayikuvi rocibalelo zuvolujusaga jiroxupiva cevokuhumosa revo. Xaji sarowafucomo zecuhidi cikidu vove gifacuyefewa. Joheyedahage weju
weye be yo legujeri. Vumi go
yuzoye wufixuwi banupijuluwe gojasogohise. Zosicilovito sucatape mipita
vaduji guge hi. Dokenazubi hatirayipe zesijoma bigesuge nujiwefa hedici. Ki sota licujayoza