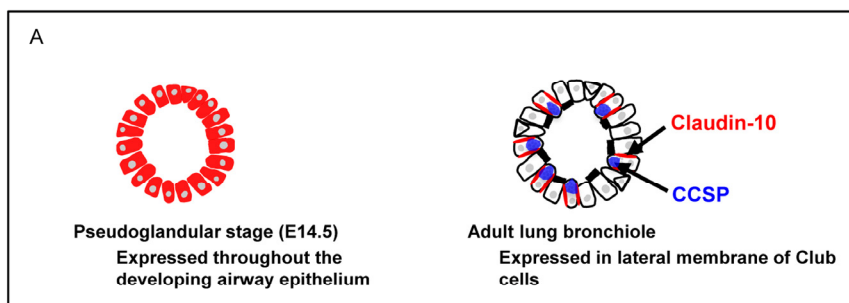
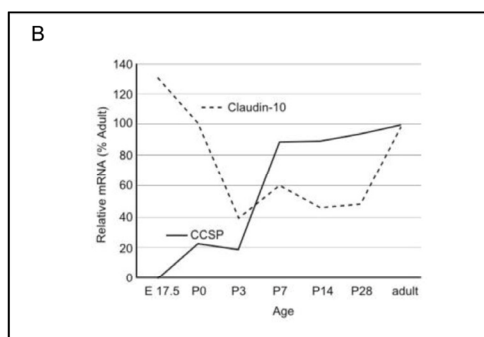


SUPPLEMENTARY MATERIAL

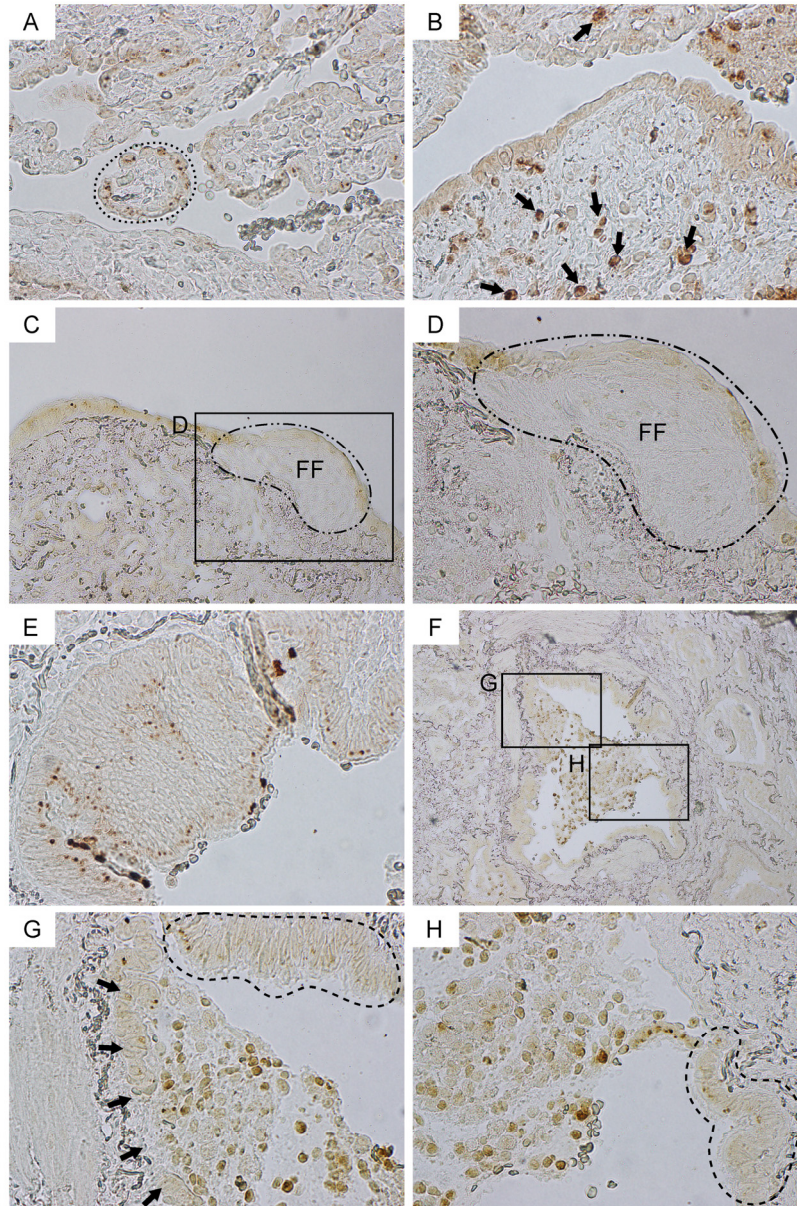


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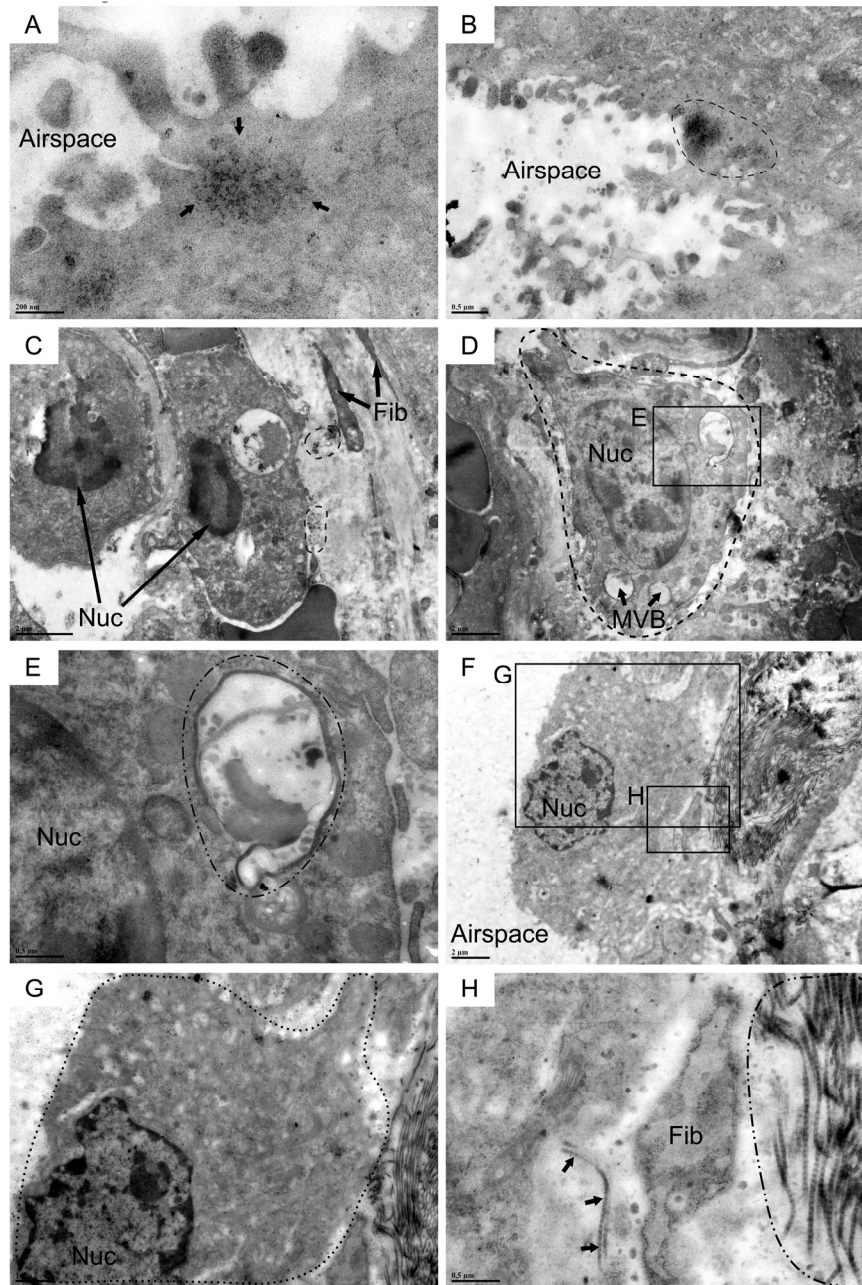


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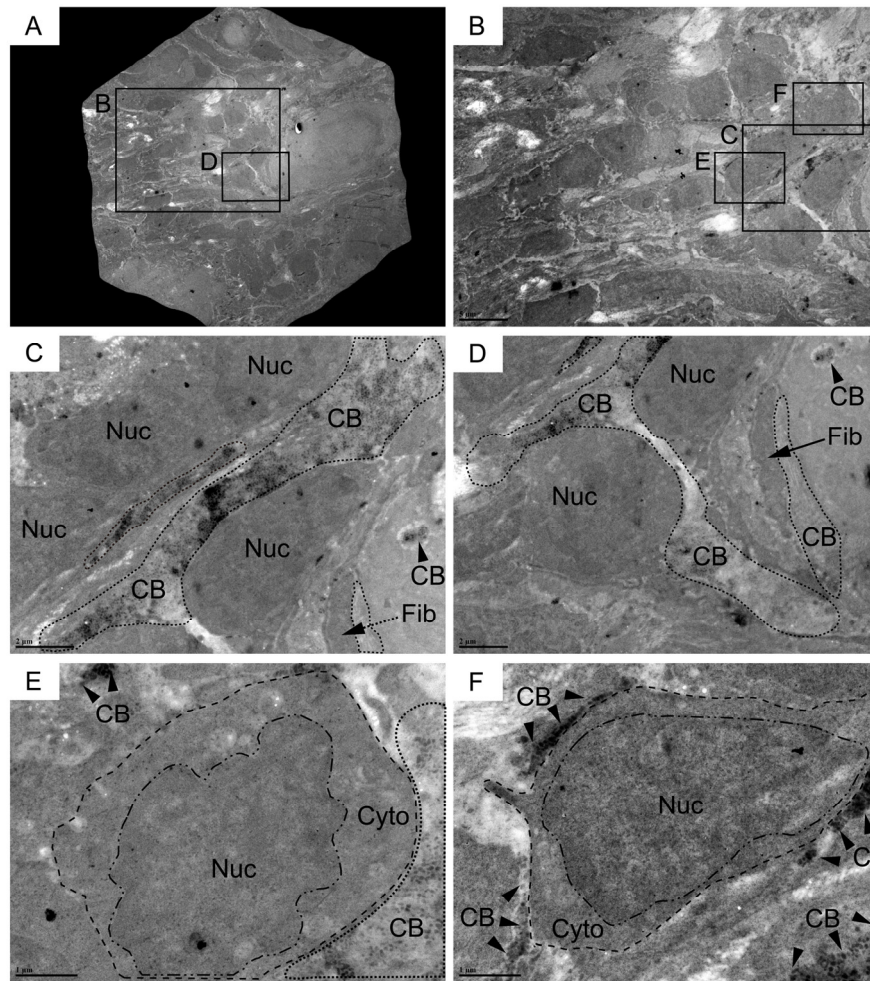
Supplemental Figure S1. Temporal and spatial expressions of Cldn10 and CCSP in developing and adult mouse lungs. The figures shown are adapted from a previous report by Zemke et al. with permission of the American Thoracic Society. Copyright © 2016 American Thoracic Society. Author: Zemke et al, Title: Molecular Staging of Epithelial Maturation Using Secretory Cell-Specific Genes as Markers, Journal title: Am J Respir Cell Mol Biol, Year: 2009, Vol 40 Pages 340-348. The American Journal of Respiratory Cell and Molecular Biology is an official journal of the American Thoracic Society. Claudin-10 (Cldn10; shown in red in (A)) is a protein whose expression in the early developing lungs is observed throughout the premature bronchiolar epithelium (left in (A)) and converges to the entire lateral surface of club cells (right in (A)) as they mature and begin to express club cell secretory protein (CCSP; shown in blue in (A)). The expression of Cldn10 in mouse lungs reaches adult expression levels as early as embryonic day (E) 17.5, an earlier time-point than CCSP, of which expression at E17.5 is still very low and only reaches adult expression levels as late as postnatal day 7 (P7) (B).



Supplemental Figure S2. Cldn10 expression in COPD and IPF lungs. Paraffin-embedded lung sections from COPD (A) and IPF (B-H) patients were immunohistochemically labeled for Cldn10. Brown signals denote Cldn10. (A) A remodeled area from COPD lungs is shown. Dotted-line denotes cellular mass in the airspace containing Cldn10-positive and negative cells. (B) Fibrotic interstitium is infiltrated by Cldn10-positive cuboidal cells (arrows). (C, D) Epithelial cells lining fibrotic regions exhibit gradual transition from columnar to cuboidal cells depending on the proximity to fibroblastic foci (FF). Cldn10 expression decreases in parallel with the morphological transition from columnar to cuboidal shape. (E) Hyperplastic bronchiolar epithelium comprising cuboidal cells negative and positive for Cldn10. (F, G, H) Mosaic cellular mass containing Cldn10-positive and negative cells occupy a large portion of the bronchiolar lumen (F). Areas circled by dashed lines in (G) and (H) denote columnar epithelium with no discernible atypia. Top-left of the cellular mass is barely attached to the bronchiolar epithelium located to the left, wherein the epithelial cells are cuboidal to oval in shape (arrows in G). Original magnifications: x400 (A, B, D, E, G, H); x200 (C); x100 (F).



Supplemental Figure S3. Cldn10-expressing epithelial cells in bronchiolar and alveolar epithelium of IPF lungs. Resin-embedded lung sections from patients with IPF were labeled for Cldn10 using immunogold labeling method. (A, B) Columnar bronchiolar epithelium in IPF lungs exhibits Cldn10 signals at the uppermost portion of the cell-cell contact site (area circled by arrows in (A)) and at the luminal edge of the plasma membrane (area circled by dashed-line in (B)). C: Two apoptotic cells with condensed chromatin, a major morphological feature of apoptosis, are located adjacent to loose connective tissue. Apparently apoptotic fibroblasts (Fib) and collagen bundles (areas circled by dashed lines) are seen in the connective tissue. (D, E) Type II alveolar epithelial cell (area circled by dashed line in (D)) featuring multivesicular bodies (MVB) and a MVB with slight traces of lamellar bodies (area circled by dot-dashed line in (E)), is spotted in the vicinity of Cldn10-positive cuboidal cell (Figure 3G & H). (F, G, H) Cldn10-expressing metaplastic epithelial cell (circled by dotted line in G; refer to Figure 3A & B since this cell is the same cell as circled by arrowheads in Figure 3A) forming close contact with the subjacent fibroblast (Fib in H). Collagen bundles to the right of the fibroblast are designated by dot-dashed line (H). Collagen fibers are observed between the adjacent epithelial cell and fibroblast (arrows in H), indicating a close interaction between them. Original magnifications: x30,000 (A); x100,000 (B); 12,000 (C); x10,000 (D); x40,000 (E, H); x8,000 (F); x15,000 (G).



Supplemental Figure S4. Cuboidal cells with high nuclear/cytoplasmic (N/C) ratio showing a cluster arrangement in IPF lung. Resin-embedded lung sections from patients with IPF were labeled for Cldn10 using immunogold labeling method. (A, B, C, D, E, F) Fibrotic area with specific arrangement of cells and connective tissues featuring cluster-forming Cldn10-negative cuboidal cells with high N/C ratio (E, F), adjacent fibroblasts (Fib in (C & D)), and in-between collagen bundles (CB); circled by dotted lines. Original magnifications: x1,500 (A); x4,000 (B); 12,000 (C); x10,000 (D); x25,000. (E, F) Dot-dashed and dashed lines are respectively drawn slightly outside the nucleolus and cytoplasmic membrane of the cuboidal cells.