Histology and development of the respiratory system

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Outline of the lecture

1. Structure of the trachea
2. Histology of different parts of the pulmonary tree
3. Alveoli and the air-blood barrier
4. Development of the lung
Cross section of trachea

- **S**: Smooth muscle
- **C**: Cartilage
- Glands

C-shaped hyaline cartilage with open ends pointing to the esophagus.

- The posterior side is flattened
- Adventitia (adipose tissue)
- Trachealis muscle
- Submucosal glands
- Vagus nerve
- Elastic lamina
- Lamina propria
- Basal lamina
- Epithelium
- Submucosa with seromucous glands
Hyaline cartilage of the trachea
The wall of the trachea

Columnar ciliated cell
The apical density represents the linear alignment of basal bodies that give rise to cilia extending into the lumen. Columnar ciliated cells are about 30% of the total cell population.

Goblet cell
The apical portion of the cell contains mucus secretion that is released by exocytosis into the lumen, forming part of a protective mucus gel layer. Goblet cells are about 30% of the total cell population.

Basal cell
This cell does not extend to the free surface and functions as a stem cell population for the epithelium. Basal cells are about 30% of the total cell population.

Bronchial cells of Kulchitsky
Neuroendocrine cells with small granules can be observed in the basal region of the epithelium. They are predominant at the bifurcation of the lobar bronchi.
Respiratory epithelium

- Goblet cell
- Cilia
- Basal bodies
- Lumen
- Columnar ciliated cell
- Pseudostratified columnar epithelium
- Goblet cell
- Basal cell
- Basal lamina with subjacent elastic lamina
- Lamina propria
Goblet cells and the secreted mucus

Goblet cells secrete mucins, large glycoproteins with gel-forming properties.
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Branches of the pulmonary tree

<table>
<thead>
<tr>
<th>Unit of lung</th>
<th>Bronchus tree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>Principal bronchus</td>
</tr>
<tr>
<td>Lobe of lung</td>
<td>Lobar (secondary) bronchus</td>
</tr>
<tr>
<td>Bronchopulmonary segment</td>
<td>Segmental (tertiary) bronchus</td>
</tr>
<tr>
<td>Pulmonary lobule</td>
<td>Terminal bronchus</td>
</tr>
<tr>
<td>Pulmonary acinus</td>
<td>Terminal bronchiolar</td>
</tr>
</tbody>
</table>
Cross section of a bronchus

1. Cartilage plates
2. Bundles of smooth muscle are located between the mucosa and the cartilage plates.
3. Submucosal gland

Pseudostratified columnar ciliated epithelium with goblet cells.
Pulmonary lobule in the cross section of the lung
Bronchiole

Respiratory passage smaller than 1 mm

Does not contain cartilage

Its epithelium is simple columnar

The epithelium is not folded when alive, the characteristic folding is a histological artefact

The lamina propria is thin, it does not contain glands

The surrounding circular and spiral smooth muscle bundles regulate ventilation

Pulmonary arterioles are often found next to bronchioles
Blood vessels and nerves in the pulmonary lobule
Course of smooth muscle bundles and elastic fibers along the respiratory passages
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The pulmonary acinus

200-300 alveoli / acinus
Section of acinus
Wall of the terminal bronchiole

- Elastic fibers
- Cuboidal epithelial cells
- Clara cells
- Smooth muscle
Secretory cell type of the terminal bronchiole: Club (Clara) cell
Alveoli and their blood supply
The wall of alveoli
Air-blood barrier

![Diagram of the air-blood barrier showing the lumen of capillary, lumen of alveolus, endothelial cell, basal lamina of capillary, basal lamina of alveolar cell, type I alveolar cell, surfactant, and red blood cell.]
Type II alveolar cell (type II pneumocyte)
Macrophages and fibroblasts in the alveoli

Alveolar macrophages (also called dust cells) can shuttle between the alveolar space and the alveolar interstitium.

Type II alveolar cells are polygonal-shaped, surfactant-producing epithelial cells.

Type I alveolar cells are simple squamous epithelial cells.
The roles of macrophages in the alveolar system

• Defense against pathogens (as member of the mononuclear phagocyte system)
• Removal of particles towards the pharynx: „dust cells”
• Digestion of red blood cells that pathologically appear in the alveoli
• Degradation of the surfactant layer (half life: 19 hours)
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Appearance of the respiratory diverticulum in 4 weeks old embryo

In response to signal from surrounding mesenchyma, transcription factor TBX4 is induced in some endodermal cells of the primitive ventral esophagus, which leads to their differentiation to respiratory diverticulum.
Early (embryonic) development of the lung

The respiratory diverticulum invaginates the surrounding mesenchyme. The mesenchyme continues to secrete inducing factors to guide the repetitive branching and growth of the developing airway, a process called branching (dichotomic) morphogenesis.
Developmental malformations: esophagus atresia and tracheo-esophageal fistula

A: Trachea and esophagus atresia
B: Tracheo-esophageal fistula
C: Distal part of esophagus
D: Bronchi
E: Tracheo-esophageal fistula
The epithelial components of the lung are derived from the endoderm, while the cartilaginous, muscular, and connective components come from the surrounding splanchnic (visceral) mesoderm. The lungs expand in the pleural cavities surrounded by the parietal and visceral pleura. The visceral pleura extends between the lobes of the lung.
## Stages of the development of the lung

<table>
<thead>
<tr>
<th>Name of the stage</th>
<th>Age</th>
<th>Major developmental events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudoglandular</td>
<td>5-16 weeks</td>
<td><em>Growth and branching</em> allows the setup of all pulmonary structures (including terminal bronchioli) with the exception of the elements needed for gas exchange.</td>
</tr>
<tr>
<td>Canalicular</td>
<td>17-26 weeks</td>
<td>The terminal bronchioles give rise to canaliculi that make up the <em>alveolar ducts</em>. Airspaces are multiplicated by partitioning (<em>septation</em>). <em>Differentiation</em> of the epithelium into secretory and flat cells. <em>Vascularization</em> also develops.</td>
</tr>
<tr>
<td>Saccular</td>
<td>27-40 weeks</td>
<td><em>Alveolar sacs</em> separated by primary septa are formed, which are <em>contacted by capillaries</em>.</td>
</tr>
<tr>
<td>Alveolar</td>
<td>41 weeks – 2 years</td>
<td>The alveolar sacs progressively divide into alveoli (<em>alveolarization</em>).</td>
</tr>
</tbody>
</table>
Stages of the maturation of the lung

Canalicular stage
- Respiratory bronchiolus
- Blood capillaries
- Cuboidal epithelium
- Terminal bronchiolus

Saccular stage
- Thin squamous epithelium
- Flat endothelium cell of blood capillary
- Cuboidal epithelium

Alveolar stage
- Thin squamous epithelium
- Blood capillary
- Mature alveolus
- Lymph capillary
- Terminal bronchiolus
Section of the fetal lung

bronchiolus  bronchus
Thank you for your attention!