



# Mouse Lung Tumor Workshop

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# Of Mice and Humans – The Lung

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## Gross Anatomy

- Mouse –
  - Right Lung – Four Lobes
  - Left – One Lobe
- Human
  - Right Lung – Three Lobes (upper, middle, lower)
  - Left Lung – Two Lobes (upper, lower)

Suarez, CJ, Dintzis, SM, Frevert, CW, Chapter 9 Respiratory **IN**: Comparative Anatomy and Histology, A Mouse and Human Atlas, Treuting, PM, Dintzis, SM, Eds Academic Press, Elsevier, New York, pp 129 – 134, 2012.

# Intrapulmonary Airways

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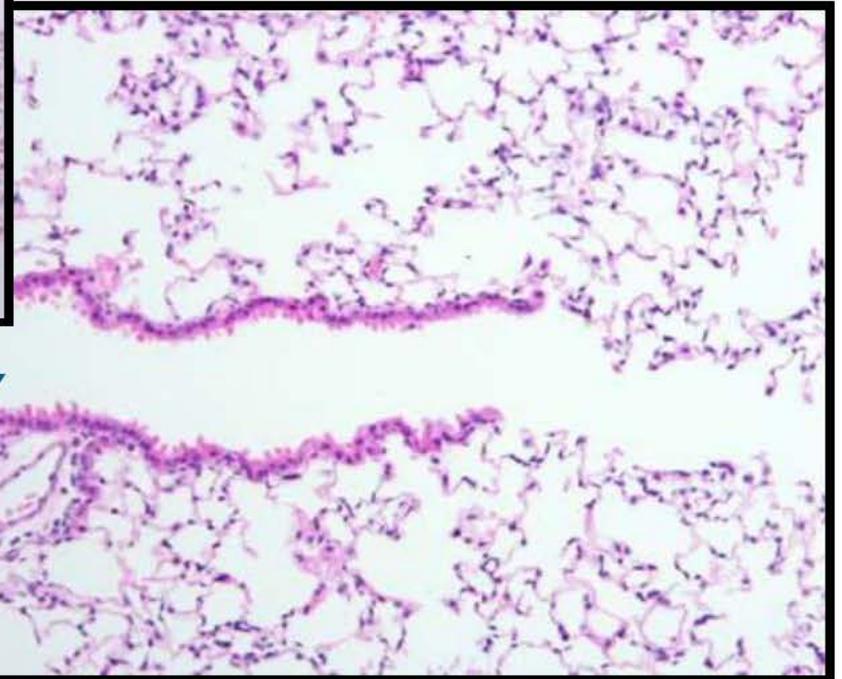
- Mouse –
  - Monopodial Branching 13 – 17 Generations
  - Intrapulmonary Bronchi Lack Cartilage
  - None or one Respiratory Bronchiole
- Human
  - Dichotomous Branching 17 – 21 Generations
  - Intrapulmonary Bronchi Have Cartilage
  - Several Orders of Respiratory Bronchioles

Suarez, CJ, et al Academic Press, New York, pp 129 – 134, 2012.

# Intrapulmonary Airways



**Asymmetrical branching  
In Mouse**



**Bronchus**

**Bronchus in Mouse Connects  
to Terminal bronchiole**

**COVANCE.**

# Proximal Intrapulmonary Epithelium (%)

Cell Type	Mouse	Humans
Ciliated	28-36	37
<b>Clara</b>	<b>59-61</b>	-
Mucus Globlet	<1	10
<b>Basal</b>	<1	<b>32</b>

Suarez, 2012; Fox, 2007; Plopper and Hyde, 2008

**COVANCE.**

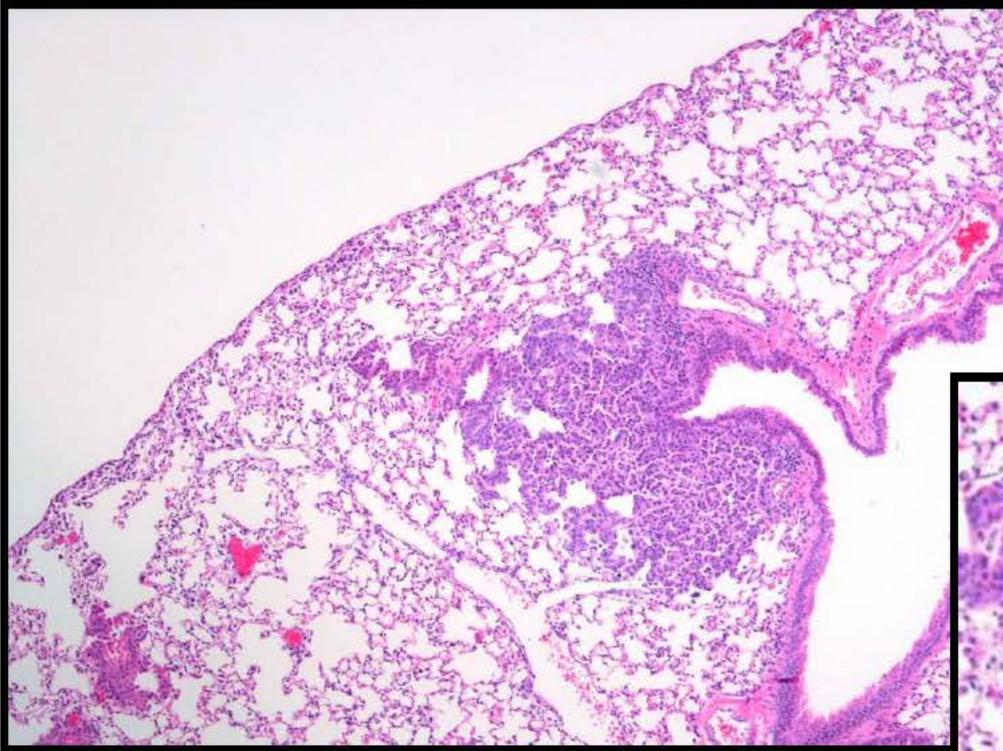
# Terminal Bronchiole Epithelium (%)

Cell Type	Mouse	Humans
Ciliated	20-40	52
<b>Clara</b>	<b>60-80</b>	-
Serous	0	35
Basal	<1	<1

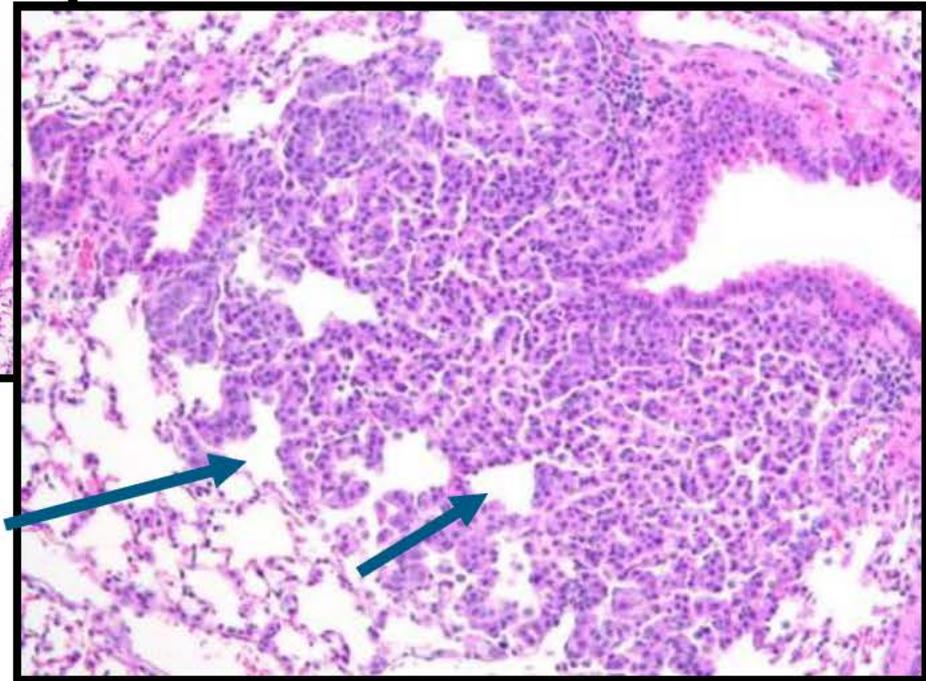
Suarez, 2012; Fox, 2007; Plopper and Hyde, 2008

**COVANCE.**

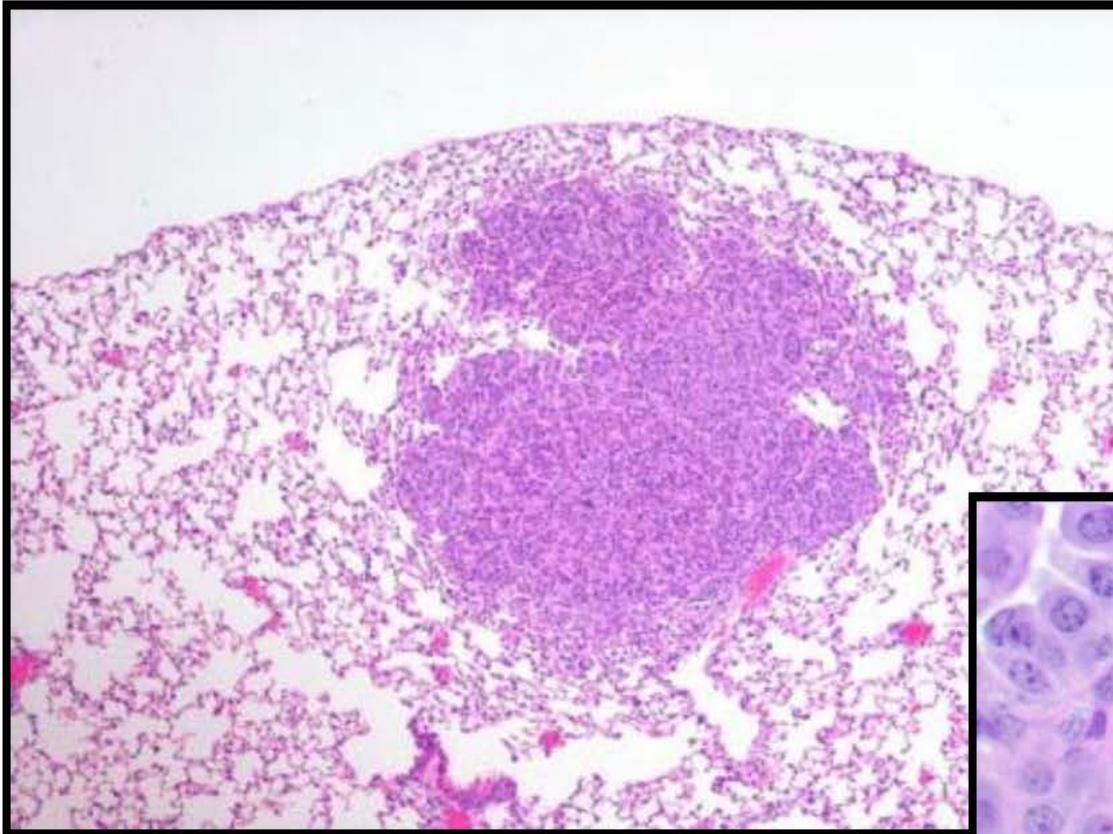
# Lung Hyperplasia in Mice



**Arises in periphery of lung;  
alveolar structures are visible**

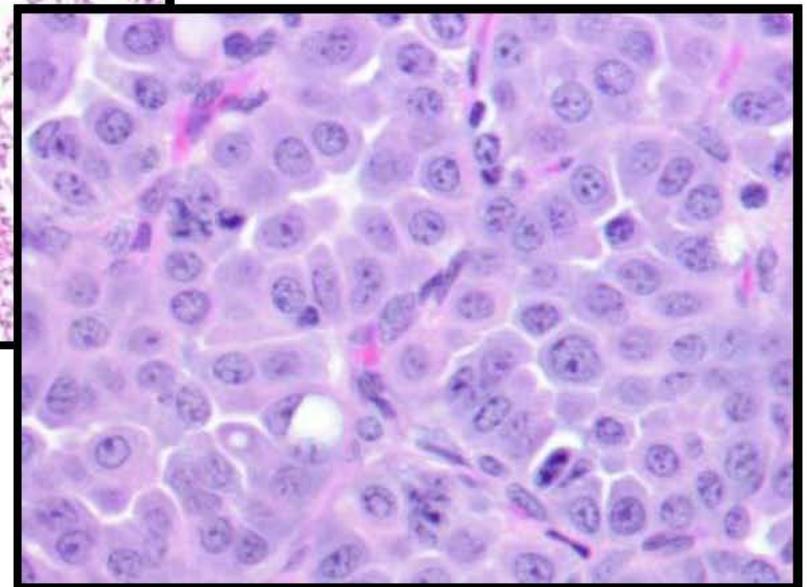


# Bronchioloalveolar Adenomas



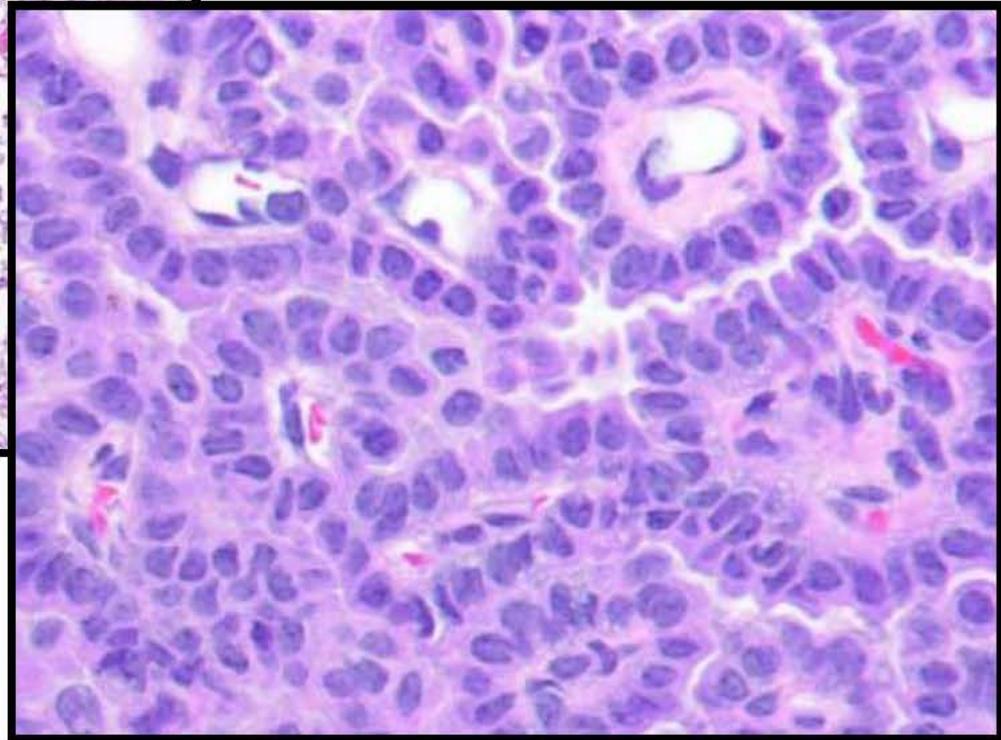
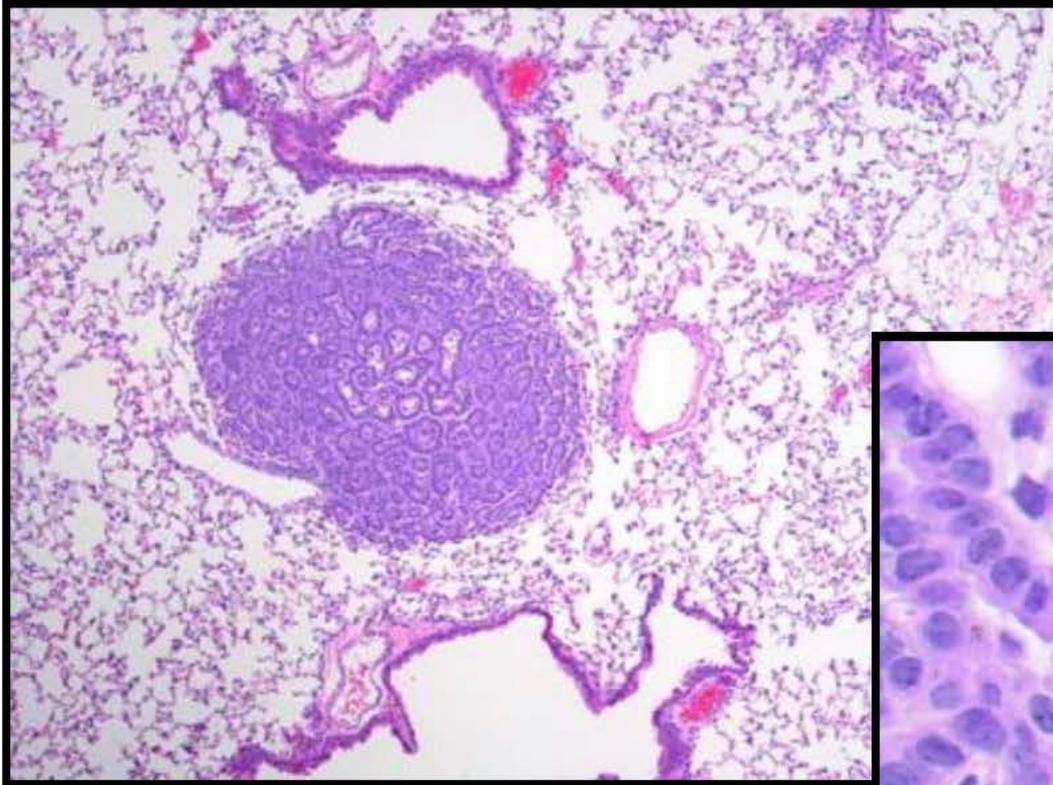
**Peripheral  
and Solid**

**Cells have Type II Appearance**



**COVANCE.**

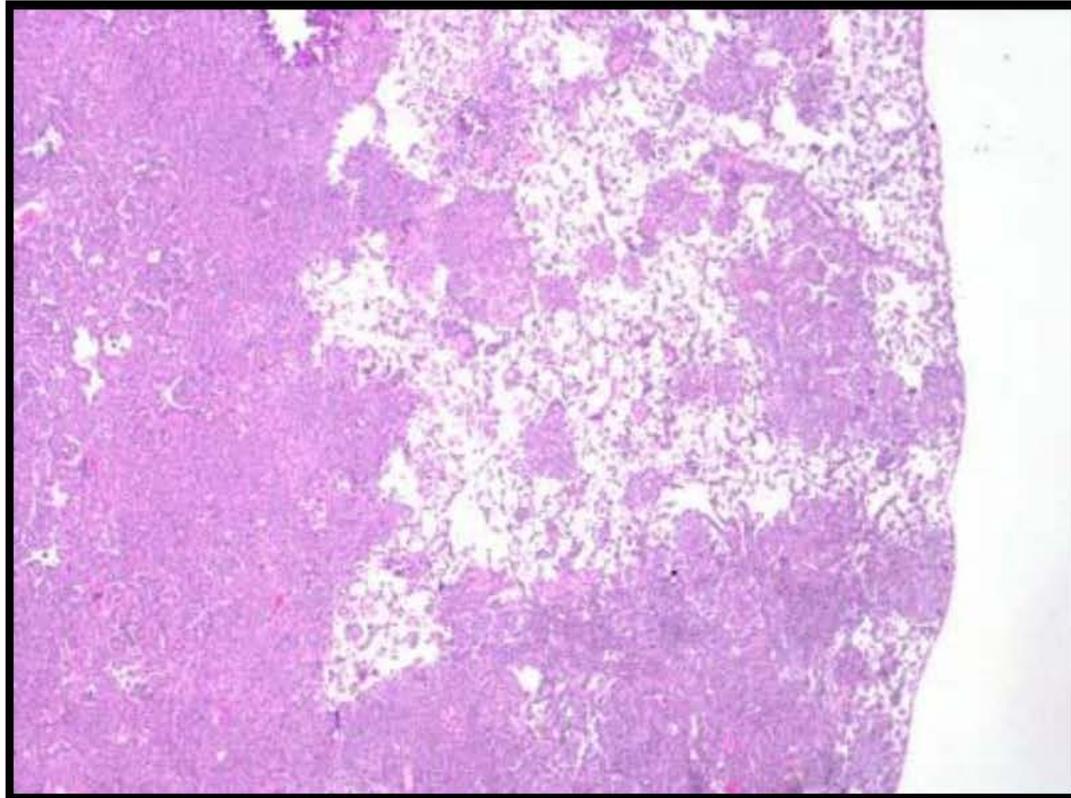
# Bronchioloalveolar Adenoma



**More Tubular Pattern  
May be Clara Cells**

# Bronchioloalveolar Carcinoma

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**Carcinomas Show Local Invasion, Extension Throughout the Lung and Distant Metastases**

# B/A Lung Tumor Incidences (%)

Mouse/Sex	Adenoma	Carcinoma
B6C3F1/Male	16.7 (8 – 36)	7.6 ( 0 – 16)
B6C3F1/Female	6.4 (0 – 14)	3.3 (0 – 12)
CD1/Male	13.7 (8 – 38)	5.8 (2 – 16)
CD1/Female	5.8 (2 – 16)	3.3 (1 – 20)
rasH2/Male	10.1 (0 – 24)	0.6 (0 – 8)
rasH2/Female	5.8 (0 – 24)	1.1 (0 – 4)

Maronpot et al., 1999; Charles River, 2014; Paranjpe et al., 2013



# Bronchioloalveolar Tumors Mice

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- Tumors arise in Periphery of Lung
- Originate from Type 2 and Clara Cells
- Rates are highly variable (Adenoma)
  - 8% to 36%: male B6C3F1 at 104 weeks (gps/25)
  - 8% to 38%: male CD-1 at 78-104 weeks (gps/50)
  - 0% to 24%: male rasH2 at 26 weeks (gps/25)
- Carcinoma is less common

# Lung Cancer in Humans

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- Bronchogenic Carcinoma: 90 – 95%
  - Squamous Cell Carcinoma (25 – 40%)
  - Adenocarcinoma (25 – 40%)
  - Small Cell Carcinoma (20 – 25%)
  - Large Cell Carcinoma (10 – 15%)
- Bronchial Carcinoid: 5%
- Mesenchymal and Other: 2 – 5%

Robbins, 6<sup>th</sup> Edition, 1999

# Lung Tumors in Mice and Humans

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- Mouse Tumors Originate Peripherally
  - Usually at terminal acinus
  - Type II Cell or Clara Cell Origin
  - May be Spontaneous or Chemically Induced
- Human Tumors Originate Centrally in Bronchi
  - 80 – 85% associated with smoking
  - Basal or Bronchial Cell Origin

# Conclusions

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- Mouse and Human Lung Tumors Differ
  - Location
  - Site of Origin
  - Predominate Cell Type
  
- Mouse has Mixed Record as a Predictive Model
  - A strain Mouse NTP study was not Predictive
  - NTP studies Variable Results

# Mouse Lung Tumor Models

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