@ATS RIS RESPIRATORY INNOVATION SUMMIT

What's Emerging in IPF/ILD: Challenges and Opportunities

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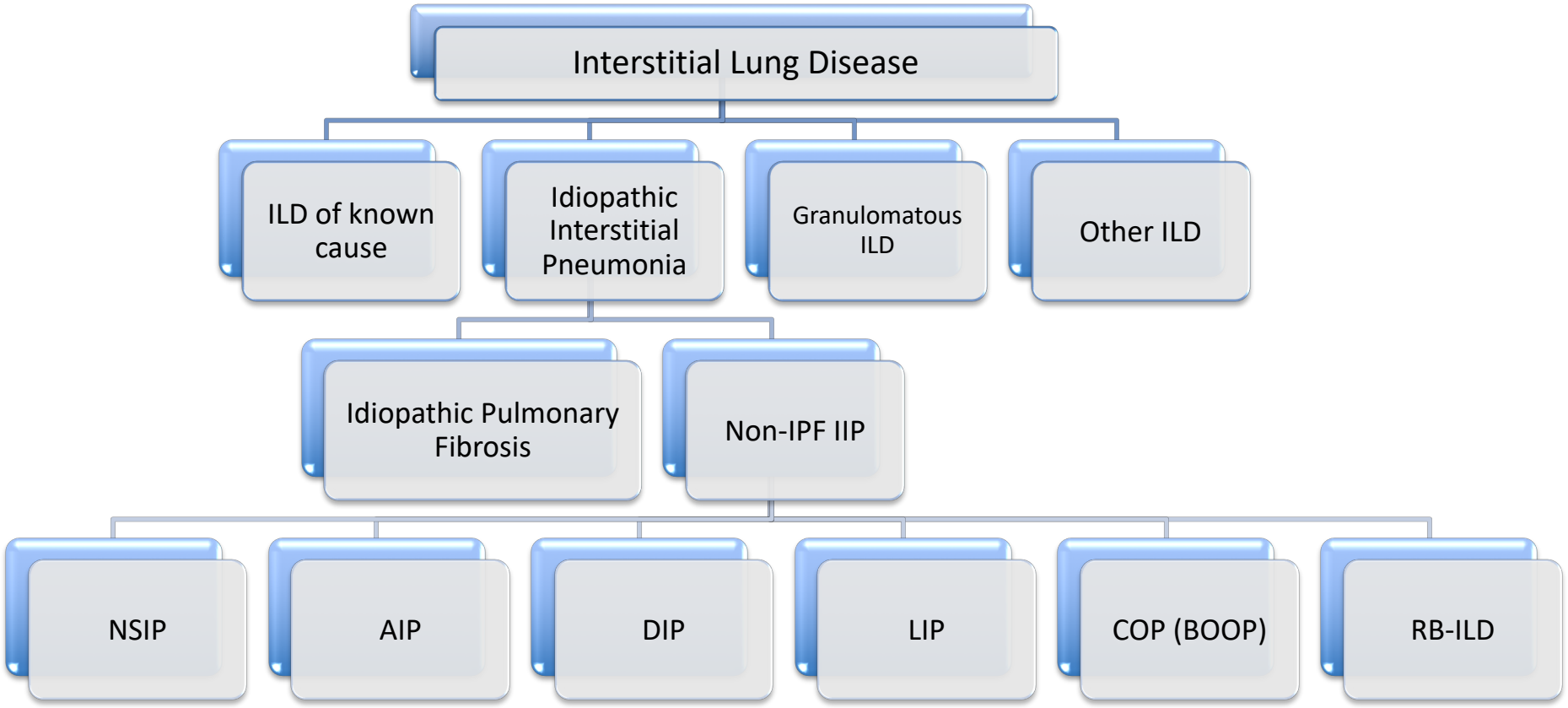
Disclosures

- Consultant – Boehringer-Ingelheim
- Steering Committee – Boehringer-Ingelheim
- Medical Advisory Board – Pulmonary Fibrosis Foundation
- Site PI or Co-I (past 3 years) – Afferent, Bellerophon, Boehringer-Ingelheim, Galapagos, Genentech, NIH, Pulmonary Fibrosis Foundation, Respivant,

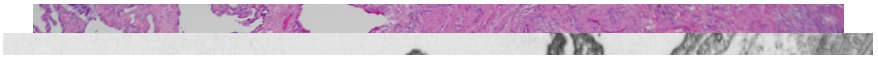
The Clinical Problem – Interstitial Lung Disease



Adapted from American Thoracic Society. *Am J Respir Crit Care Med.* 165:277-304, 2002

Interstitial Lung Disease

- Interstitium: microscopic space bounded by the basement membrane of alveolar epithelial cells and capillary endothelial cells
- Expanded by:
  - Inflammatory cells
  - Reparative cells (fibroblasts)
  - Extracellular matrix
- Often extends beyond the interstitium to involve alveoli, vasculature, and airways



cell type	average volume (μm^3)	BNID
sperm cell	30	109891, 109892
red blood cell	100	107600
lymphocyte	130	111439
neutrophil	300	108241
beta cell	1,000	109227
enterocyte	1,400	111216
fibroblast	2,000	108244
HeLa, cervix	3,000	103725, 105879
hair cell (ear)	4,000	108242
osteoblast	4,000	108088
alveolar macrophage	5,000	103566
cardiomyocyte	15,000	108243
megakaryocyte	30,000	110129
fat cell	600,000	107668
oocyte	4,000,000	101664

The Challenge(s) – for us

- What drives fibrosis?
  - Extracellular matrix (production, breakdown, signalling)
  - Cell death (epithelial cells) and proliferation (fibroblasts)
  - Inflammation
  - Auto-immunity (?)
  - Coagulation cascades
  - Microbiome (?)

- What defines “progression” of pulmonary fibrosis?

The **REAL** Challenge(s) – for the patients

- Dyspnea
- Cough
- Hypoxia
- Exercise intolerance
- Pulmonary hypertension
- Depression/anxiety

The Opportunity

- Must be able to quantify “progression”
- Must identify therapeutic target(s) that halt or reverse progression of disease (FVC)

BUT…

- Must address patients’ symptoms to make people feel better, live longer, and remain independent