

# Aging Lung

- ↓ Lung size
- ↓ Lung volume
- ↓ Muscle mass
- ↑ Pulmonary fibrosis
- Altered intracellular communications
  - Mitochondrial Dysfunction
  - Deregulated nutrient sensing
  - Loss of proteostasis (↑ misfolded, aggregated, & covalently modified proteins)
- Extracellular matrix dysregulation
  - Epigenetic alterations
  - Telomere attrition
- Stem cell exhaustion
  - Genomic instability
  - Cellular senescence

## Trachea, Bronchi, Bronchioles

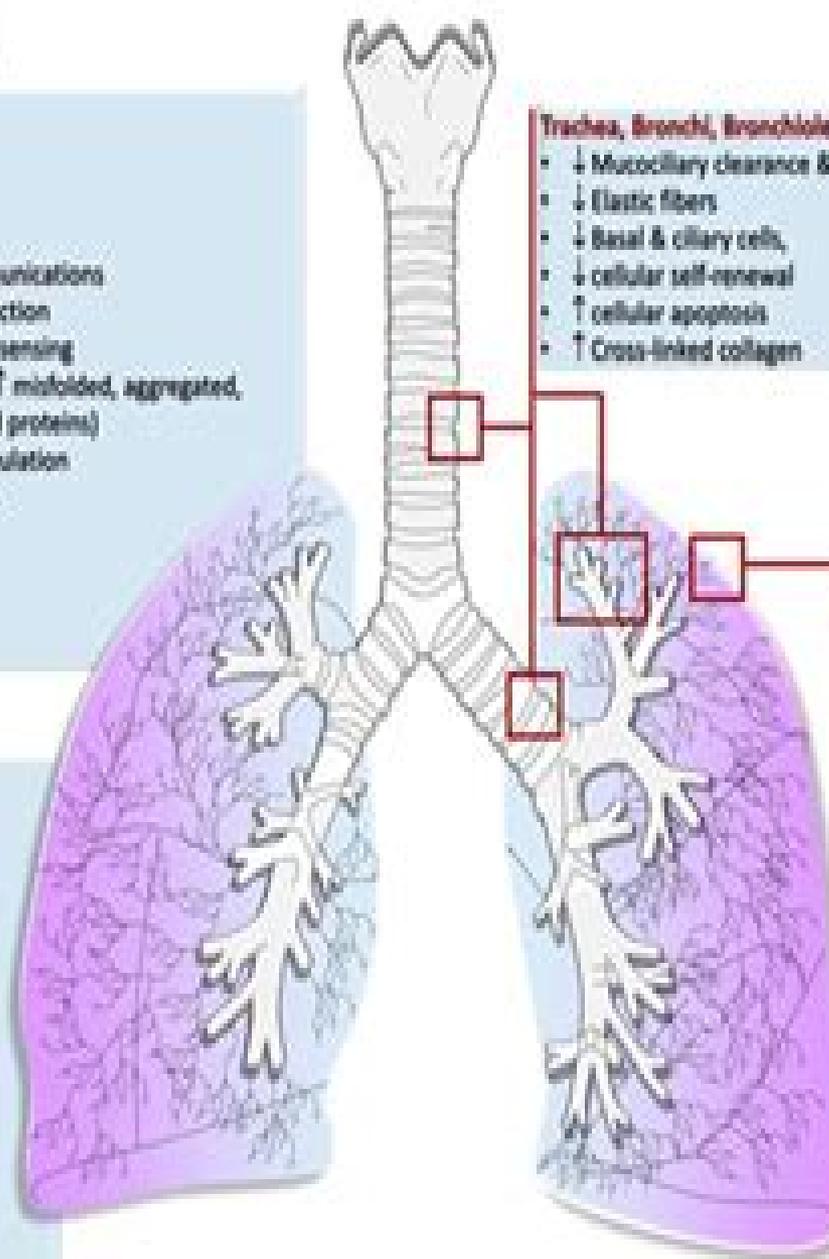
- ↓ Mucociliary clearance & ciliary beat
- ↓ Elastic fibers
- ↓ Basal & ciliary cells,
- ↓ cellular self-renewal
- ↑ cellular apoptosis
- ↑ Cross-linked collagen

## Alveolar Space

- Enlarged alveolar ducts and alveoli
- ↓ Alveolar septa
- ↓ Elasticity
- ↓ AT-I cell numbers (impaired differentiation of AT-I into AT-II)
- ↓ Cellular mitophagy
- Altered AM cell subpopulations, phagocytosis, PRR & other innate immune protein expression & function, cytokine secretion
- Changes in extracellular matrix
- ↑ AT-II cell senescence (e.g. ↑ endoplasmic reticulum stress, ↑ MHC-I, altered lipid metabolism with ↑ sterol synthesis, enlarged mitochondria with cristae loss & swelling)
- ↑ Apoptosis & makers of senescence
- ↑ Soluble & cellular inflammation
- ↑ Environmental & cellular oxidative stress. (e.g. ↑ NADPH oxidase, ↑ ROS)
- ↑ Fibroblast/Fibrosis

## Immunity

- ↓ Immune surveillance
- Dysfunctional NK cells with ↓ anti-microbial responses & cytotoxicity
- ↑ Dysfunctional AMs
- ↓ T & B cell development
- ↓ DC Ag-presentation & ↓ migration
- ↓ T cell priming, ↓ proliferation & function, ↓ cytotoxicity, ↓ CD28 expression, restricted Ag-receptor repertoire
- ↓ Neutrophils phagocytosis, ROS production, NET formation & apoptosis
- Dysregulated neutrophil infiltration related to ↑ tissue destruction
- ↓ B cell numbers, activation & Ab responses
- ↑ Basal inflammatory mediator levels
- ↑ Dysfunctional CD8+ T<sub>reg</sub> cells



# The Aging Lung Normal Function

**TD Snyder**



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