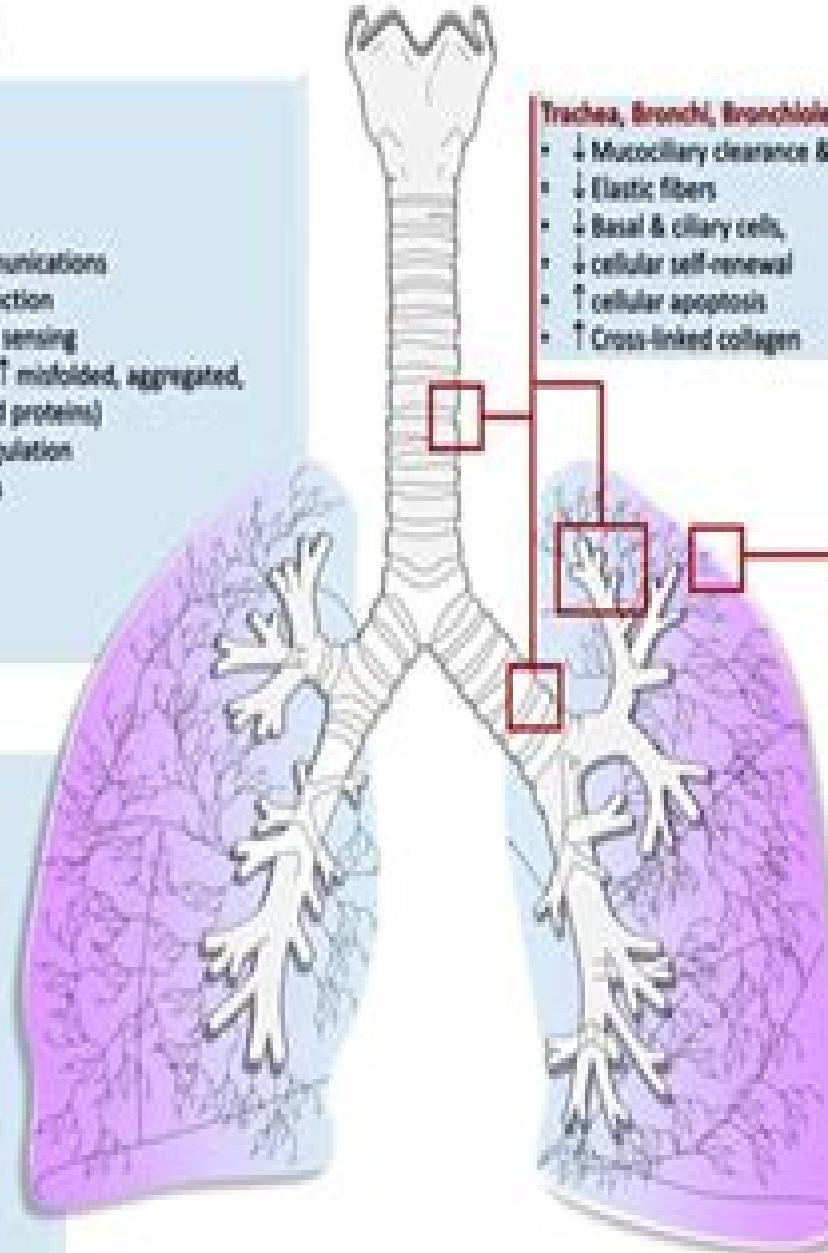


Aging Lung

- ↓ 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-II cell numbers (impaired differentiation of AT-II into AT-I)
- ↓ Cellular mitophagy
- Altered AT cell subpopulations, phagocytosis, PRX & other innate immune protein expression & function, cytokine secretion
- Changes in extracellular matrix
- ↑ AT-II cell senescence (e.g. ↑ endoplasmic reticulum stress, ↑ MHC-II, altered lipid metabolism with ↑ sterol synthesis, enlarged mitochondria with cristae loss & swelling)
- ↑ Apoptosis & markers 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 ATMs
- ↓ T & B cell development
- ↓ DC Ag-presentation & ↓ migration
- ↓ T cell priming, ↓ proliferation & function, ↓ cytotoxicity, ↓ CD38 expression, restricted Ag-receptor repertoire
- ↓ Neutrophils phagocytosis, ROS production, NET formation & apoptosis
- Dysregulated neutrophil infiltration related to ↑ tissue destruction
- ↓ B cell number, activation & Ab responses
- ↑ Basal inflammatory mediator levels
- ↑ Dysfunctional CD8+ T_{eff} cells

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1. Understanding the eBook The Aging Lung Normal Function
 - The Rise of Digital Reading The Aging Lung Normal Function
 - Advantages of eBooks Over Traditional Books
2. Identifying The Aging Lung Normal Function
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an The Aging Lung Normal Function
 - User-Friendly Interface
4. Exploring eBook Recommendations from The Aging Lung Normal Function
 - Personalized Recommendations

- The Aging Lung Normal Function User Reviews and Ratings
- The Aging Lung Normal Function and Bestseller Lists

5. Accessing The Aging Lung Normal Function Free and Paid eBooks

- The Aging Lung Normal Function Public Domain eBooks
- The Aging Lung Normal Function eBook Subscription Services
- The Aging Lung Normal Function Budget-Friendly Options

6. Navigating The Aging Lung Normal Function eBook Formats

- ePUB, PDF, MOBI, and More
- The Aging Lung Normal Function Compatibility with Devices
- The Aging Lung Normal Function Enhanced eBook Features

7. Enhancing Your Reading Experience

- Adjustable Fonts and Text Sizes of The Aging Lung Normal Function
- Highlighting and Note-Taking The Aging Lung Normal Function
- Interactive Elements The Aging Lung Normal Function

8. Staying Engaged with The Aging Lung Normal Function

- Joining Online Reading Communities
- Participating in Virtual Book Clubs
- Following Authors and Publishers The Aging Lung Normal Function

9. Balancing eBooks and Physical Books The Aging Lung Normal Function

- Benefits of a Digital Library
- Creating a Diverse Reading Collection The Aging Lung Normal Function

10. Overcoming Reading Challenges

- Dealing with Digital Eye Strain
- Minimizing Distractions
- Managing Screen Time

11. Cultivating a Reading Routine The Aging Lung Normal Function

- Setting Reading Goals The Aging Lung Normal Function
- Carving Out Dedicated Reading Time

12. Sourcing Reliable Information of The Aging Lung Normal Function

- Fact-Checking eBook Content of The Aging Lung Normal Function

- Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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