

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

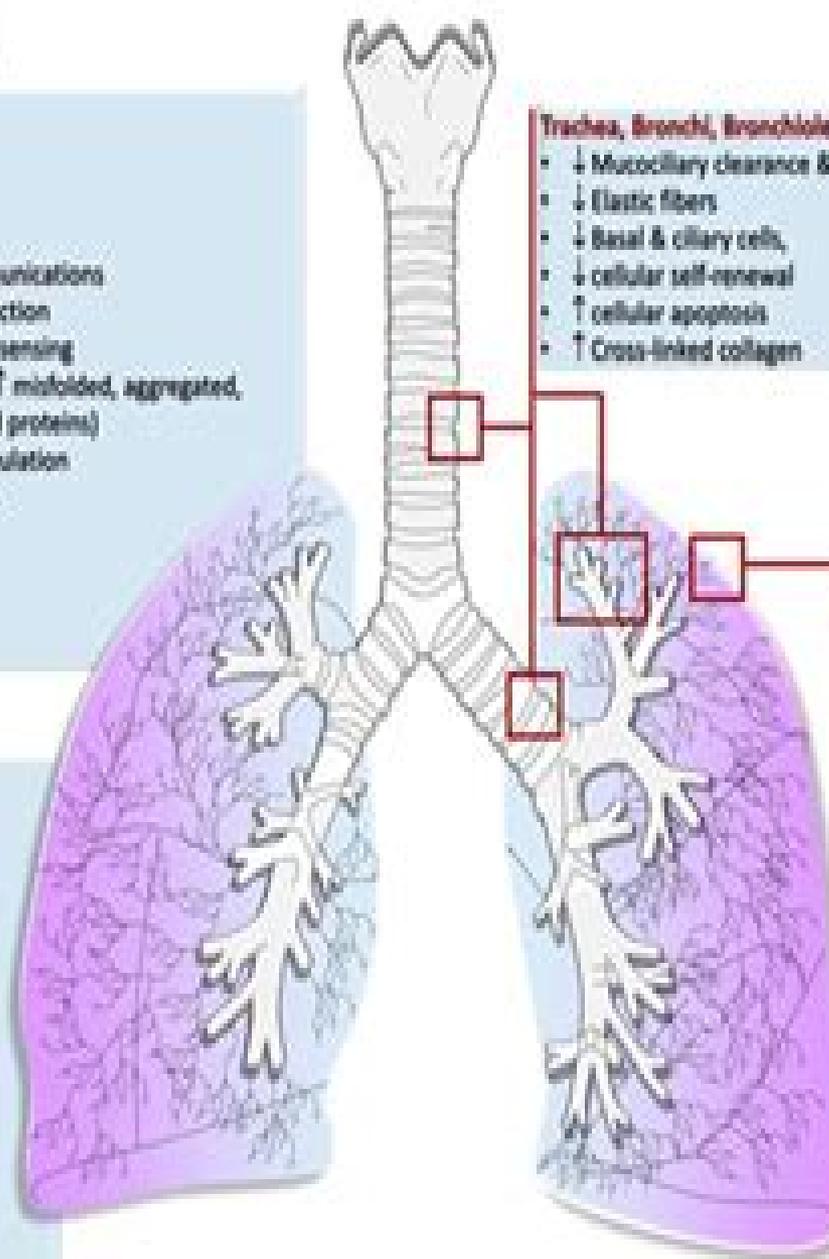
- ↓ Mucociliary clearance & ciliary beat
- ↓ Elastic fibers
- ↓ Basal & ciliary cells,
- ↓ cellular self-renewal
- ↑ cellular apoptosis
- ↑ Cross-linked collagen

Alveolar Space

- Enlarged alveolar ducts and alveoli
- ↓ Alveolar septa
- ↓ Elasticity
- ↓ AT-I cell numbers (impaired differentiation of AT-II into AT-I)
- ↓ 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_{reg} cells



The Aging Lung Normal Function

Ian Pickup



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Table of Contents The Aging Lung Normal Function

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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