Research in Lung Aging and Critical Care at NHLBI

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National Heart, Lung, and Blood Institute

Lung Aging at NHLBI

Interest of NHLBI in Lung Aging Research

- What is “normal lung aging”?
- How do mechanisms of lung aging relate to (non-cancer) disease pathobiology?
- How can we treat and care for patients with aging-related lung diseases?

Ongoing program funded by NHLBI and NIA to understand the molecular landscape of lung aging: https://www.youtube.com/watch?v=3GVn4SBzTqQ

How do “hallmarks of aging” in the lung lead to disease?

Aging

Cell types
Exposures
Behaviors
Infection
Genetics
Lung structure

?

Disease

COPD

IPF

Pulmonary Hypertension

ARDS/ALI

Pneumonia

HIV

COVID-19

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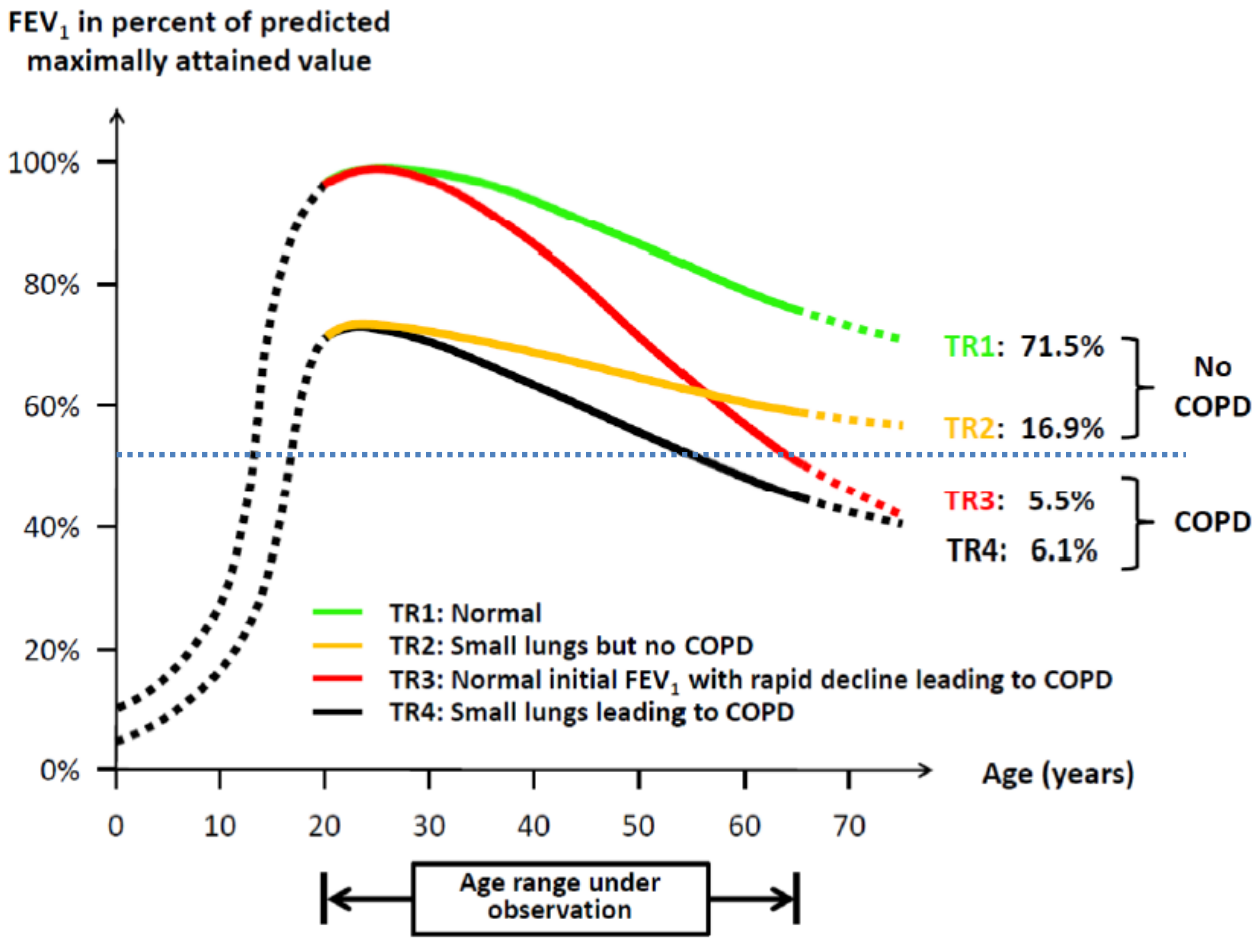
López-Otín et al, Cell Volume 153, Issue 6, 6 June 2013, Pages 1194-1217

Lung function decline through the life course



Lange et al N Engl J Med 2015; 373:111-122

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NHLBI/NIA Workshop: Intersection of Aging Biology and Pathobiology of Lung Disease

Recommendations:

- Use aged animals for the study of aging-related lung diseases
- Understand mechanisms of normal aging in the lung
- Develop integrative systems-based platforms that can incorporate multi-omics data sets of the aging lung
- Understand why hallmarks of aging can lead to different phenotypes and diseases (why are both COPD and IPF diseases of aging despite distinct mechanisms)

J Gerontol A Biol Sci Med Sci, Volume 72, Issue 11, November 2017, Pages 1492–1500

NHLBI Workshop: DNA Damage, Senescence, and Lung Disease

Recommendations:

- Identify biomarkers for senescent cells of different cell types and biomarkers of senescence that results from different types of inducers
- Identify the role of different senescent cell type in senescence-associated diseases of the lung such as IPF and COPD
- Develop cell type-specific senolytics and senomorphics as well as other methods for clearing senescent cells, including immunotherapies
- Use NIH-funded aging cohorts to better understand the role of aging in lung diseases

NHLBI Workshop: Adult Pulmonary and Critical Care Research Priorities

Recommendations:

- Understand the clinical, physiological, and biological underpinnings of adult pulmonary critical care heterogeneity and disease
- Optimize preclinical models by incorporating comorbidities, cointerventions, and organ failure and support
- Use adaptive and platform clinical study designs
- Incorporate measurement of long-term patient-important outcomes and potential surrogate outcomes

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Semler et al, American Journal of Respiratory and Critical Care Medicine 2020 Mar 9;202(4):511-523

NHLBI/NIGMS ARDS, Pneumonia, and Sepsis Phenotyping Consortium

- Notices of Intent to Publish FOAs for Clinical Centers and Coordinating Center: March 17, 2021
- Estimated FOA publication date: January 14, 2022
- Cooperative multi-site Acute Respiratory Distress Syndrome (ARDS), Pneumonia, and Sepsis Phenotyping Consortium (**APS Consortium**)
- Prospective, longitudinal observational study with common data and biospecimen collection of 5,000 hospitalized adults with ARDS, pneumonia, or sepsis from hospitalization to 1 year
- Approximately half of the surviving participants will have follow-up at 3, 6, and 12 months
- Inquiries to: Lora Reineck (Lora.Reineck@nih.gov)

NOSIs : ARDS/ALI and Patient Care

- Notice of Special Interest (NOSI): The Influence of Host Resilience on Heterogeneity of Acute Respiratory Distress Syndrome/Acute Lung Injury (ARDS/ALI)
- Notice of Special Interest (NOSI): Palliative Care in Heart, Lung, Blood, and Sleep Diseases
- Notice of Special Interest: Advancing the Science of Geriatric Palliative Care

Other relevant NOSIs and FOAs

- Notice of Special Interest (NOSI): Integrative Omics Analysis of NHLBI TOPMed Data (Parent R01 Clinical Trial Not Allowed)
- Notice of Special Interest (NOSI): Heart, lung, blood and sleep focused ancillary studies to large ongoing clinical studies
- Secondary Analysis of Existing Datasets in Heart, Lung, and Blood Diseases and Sleep Disorders (R21 Clinical Trial Not Allowed)
- Disease Modifying Therapies for Chronic Lung Disease (R61/R33 Clinical Trial Required)

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