Patient Education

October 30th, 2019

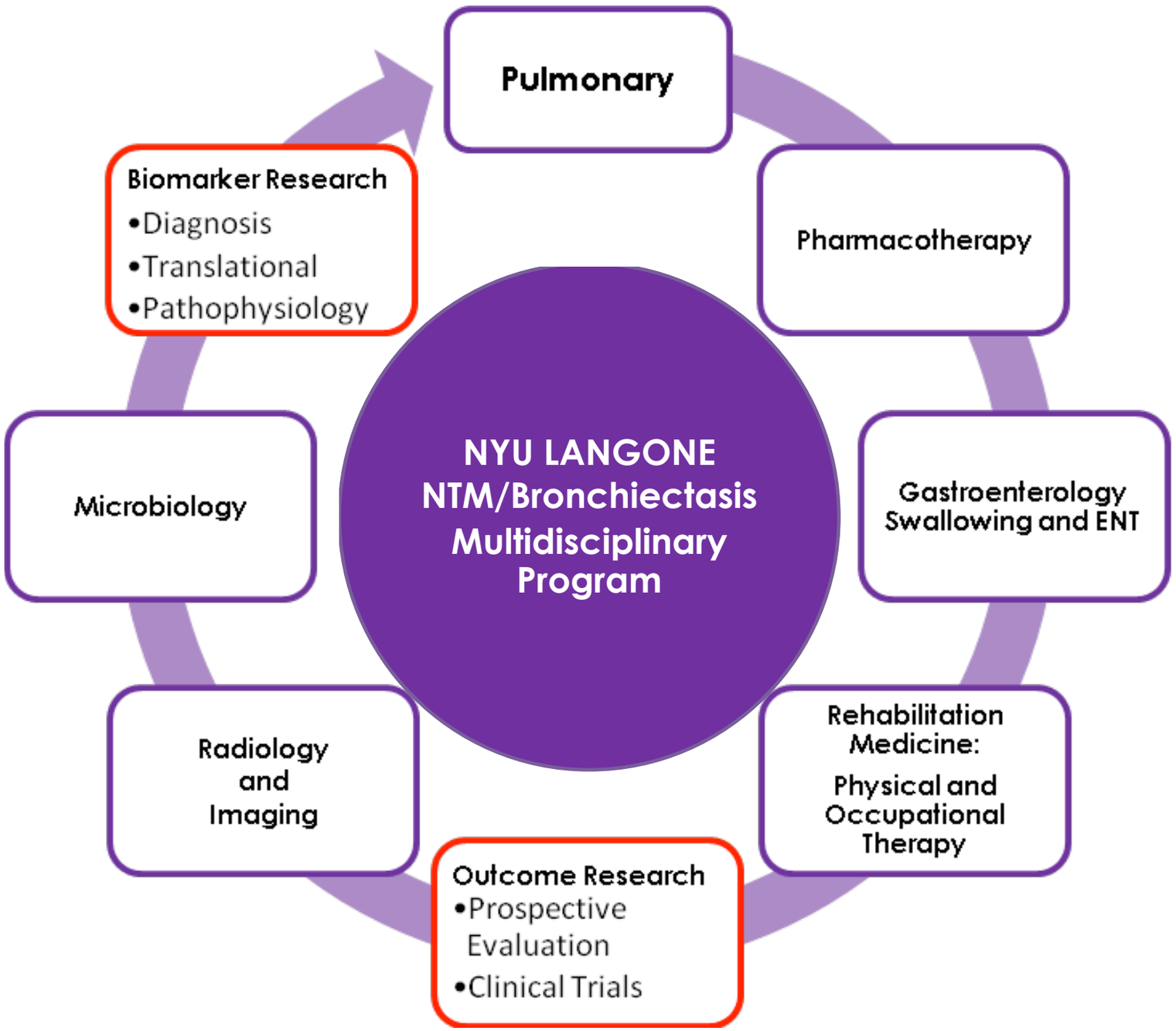
NYU Non-Tuberculous Mycobacteria Program
Research

Leopoldo N. Segal, MD, MS

Division of Pulmonary and Critical Care Medicine

Program Co-Directors

Research Director



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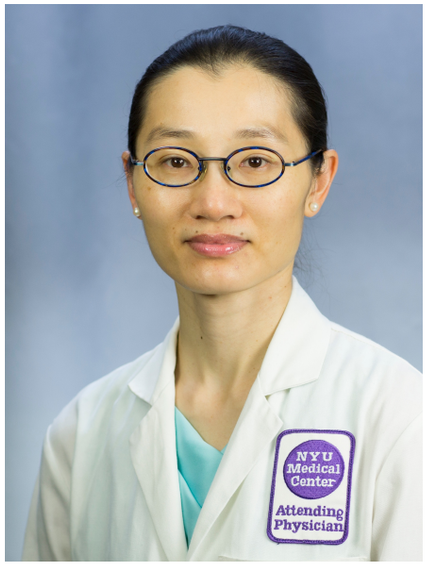
NYU NTM/Bronchiectasis Program



Stephanie Lau, MD

Amy Levinger, NP

Adrienne Scott, MS

Rosemary Schluger, RN

Ashley Drengler, BSc

Emily Clementi, BSc

Marla Sagatelian, BSc

Danielle Harris

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NYU NTM/Bronchiectasis Program (Segal Lab)

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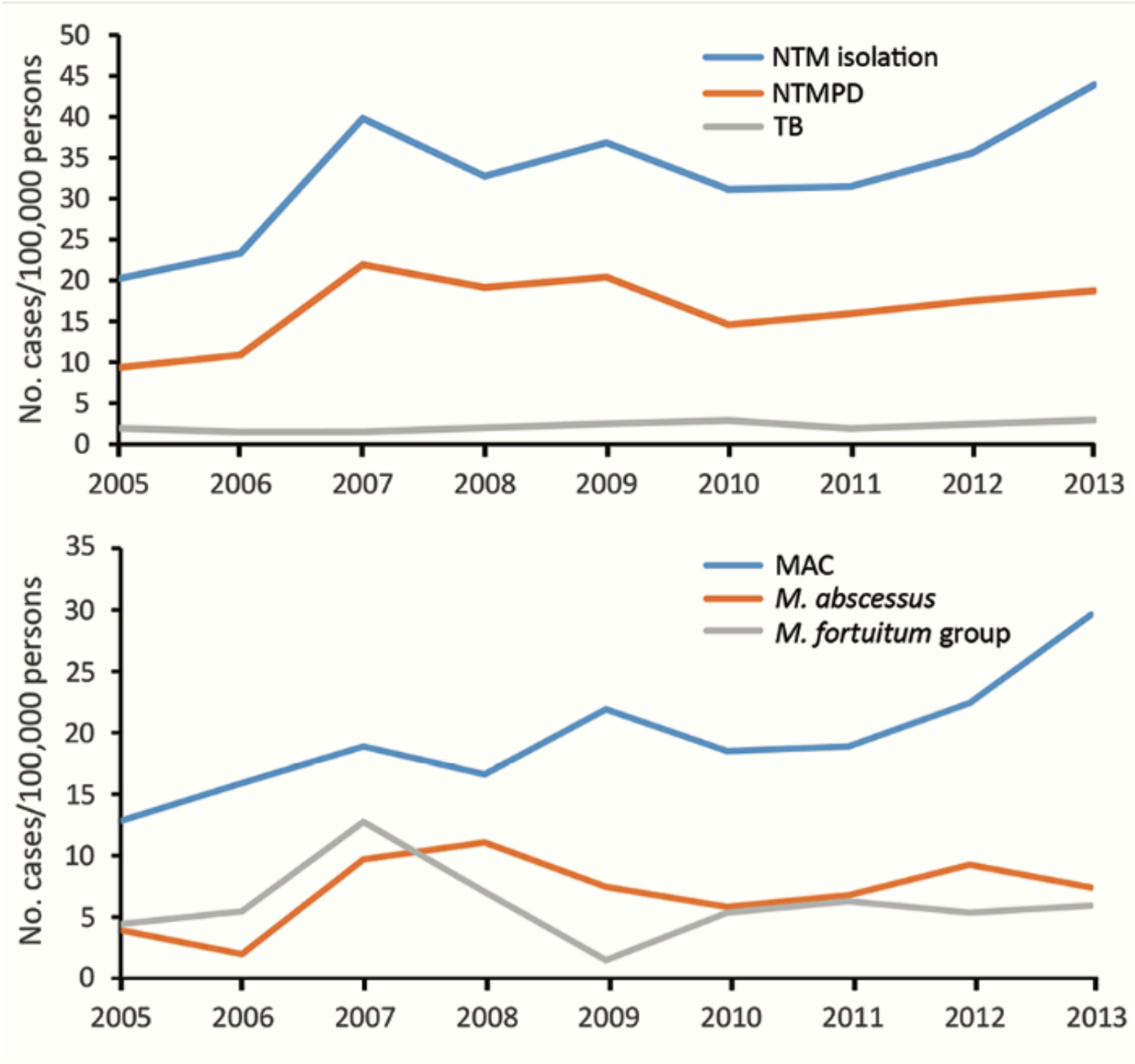
NTM bronchiectasis: Increasing problem in US

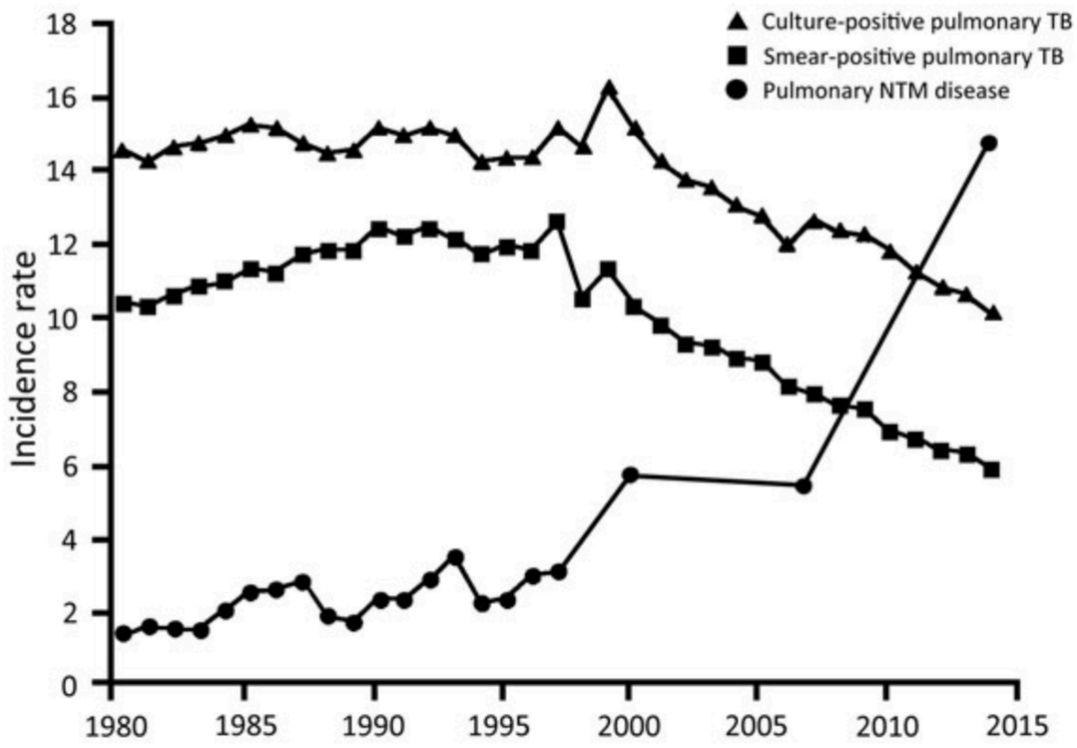


Adjemian et al. Emerg Infect Dis. 2017

NTM bronchiectasis: Increasing problem Worldwide

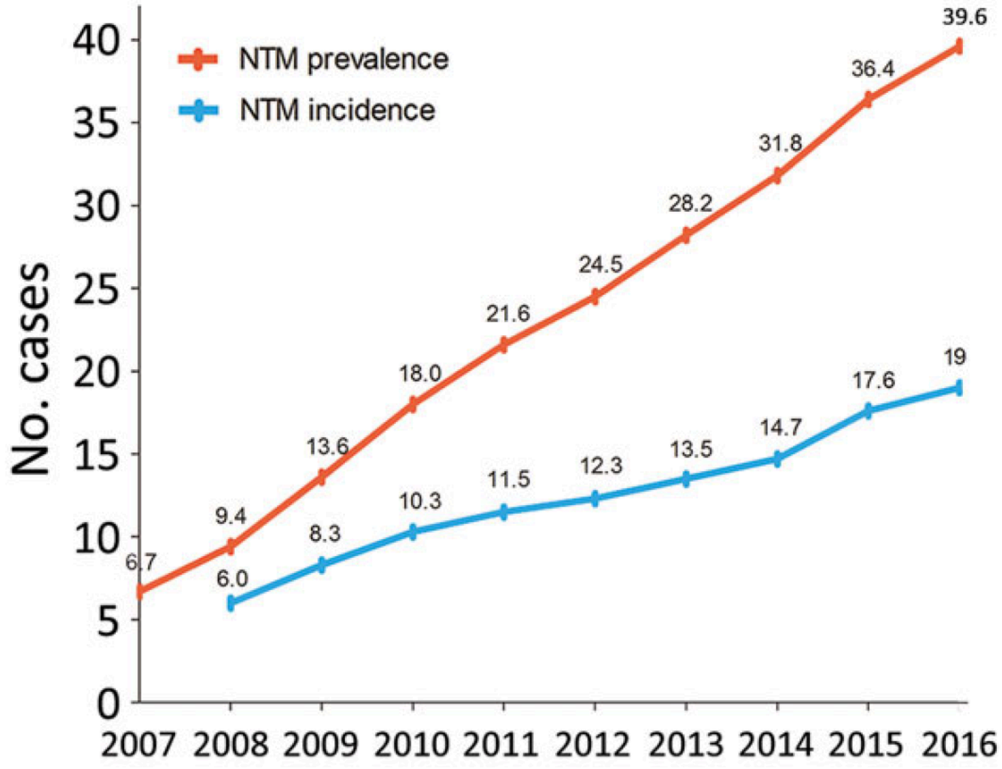
Japan

Figure

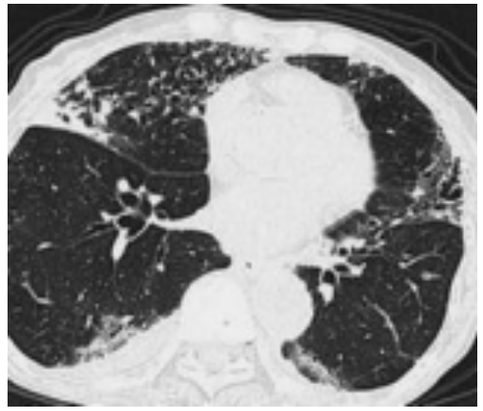


South Korea

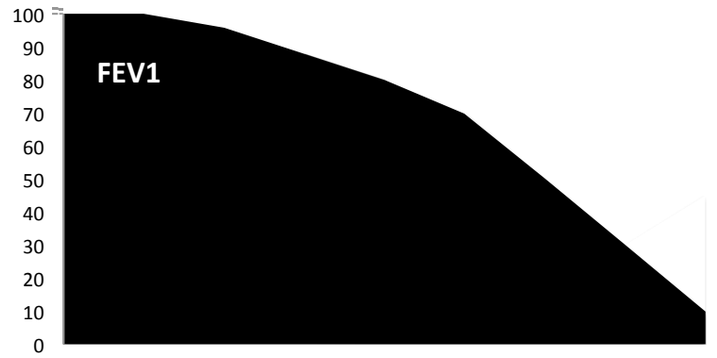
Figure 1



Cough and Sputum Production



Structural Damage of the Lung



Decline in Lung Function

Diagnosis

F/U and Prognosis

Treatment

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NYU Langone Lung & Airways Disease Registry

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Bronchiectasis and NTM Initiative

Bronchiectasis is a chronic lung disease that affects hundreds of thousands of people in the U.S. It is characterized by the widening of the small airways, which allows for the collection of mucus in the airways, and in turn causes recurring lung infections. Nontuberculous Mycobacterial (NTM) lung disease is common in individuals with Bronchiectasis. NTM are naturally occurring bacteria, some of which cause lung infections.

In an effort to meet the needs of the Bronchiectasis and NTM communities, the COPD Foundation has created the **BRONCHIECTASIS AND NTM INITIATIVE**, which comprises of BronchandNTM360social, educational information and materials, and research programs such as the Bronchiectasis and NTM Research Registry.

Click the orange links below to visit the pages specific to each program.

BRONCHANDNTM360SOCIAL is a global, online community for individuals affected by Bronchiectasis and NTM. It serves as an online home where community members can interact, ask questions, read and comment on blog posts, and more.

THE BRONCHIECTASIS AND NTM RESEARCH REGISTRY is a clinical registry of over 2,000 patients. The goal of the Registry is to support collaborative research and clinical trials

Visit **WWW.BRONCHIECTASISANDNTMINITIATIVE.ORG** to learn more about these excellent resources!

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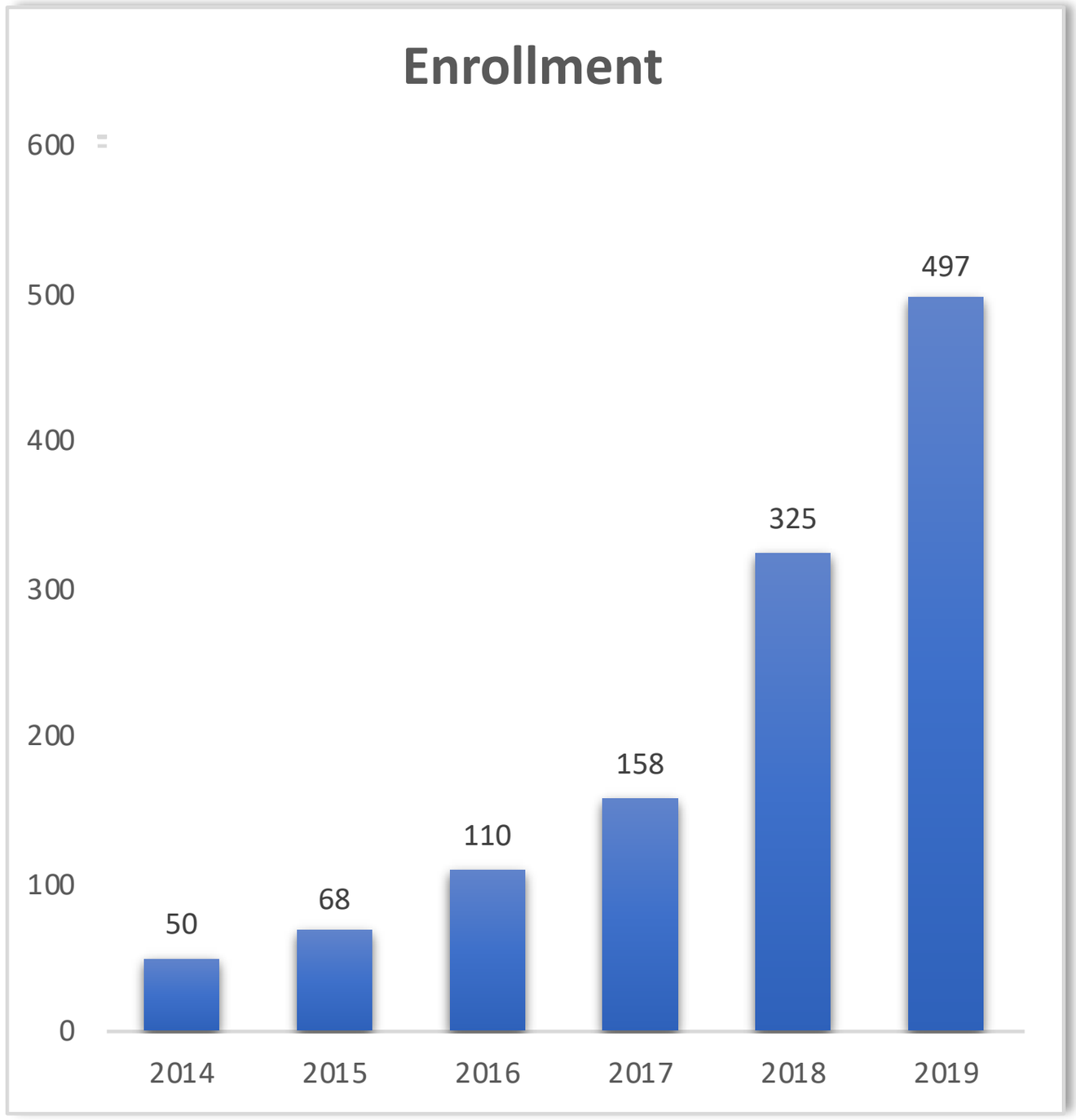
Exponential growth of enrollment



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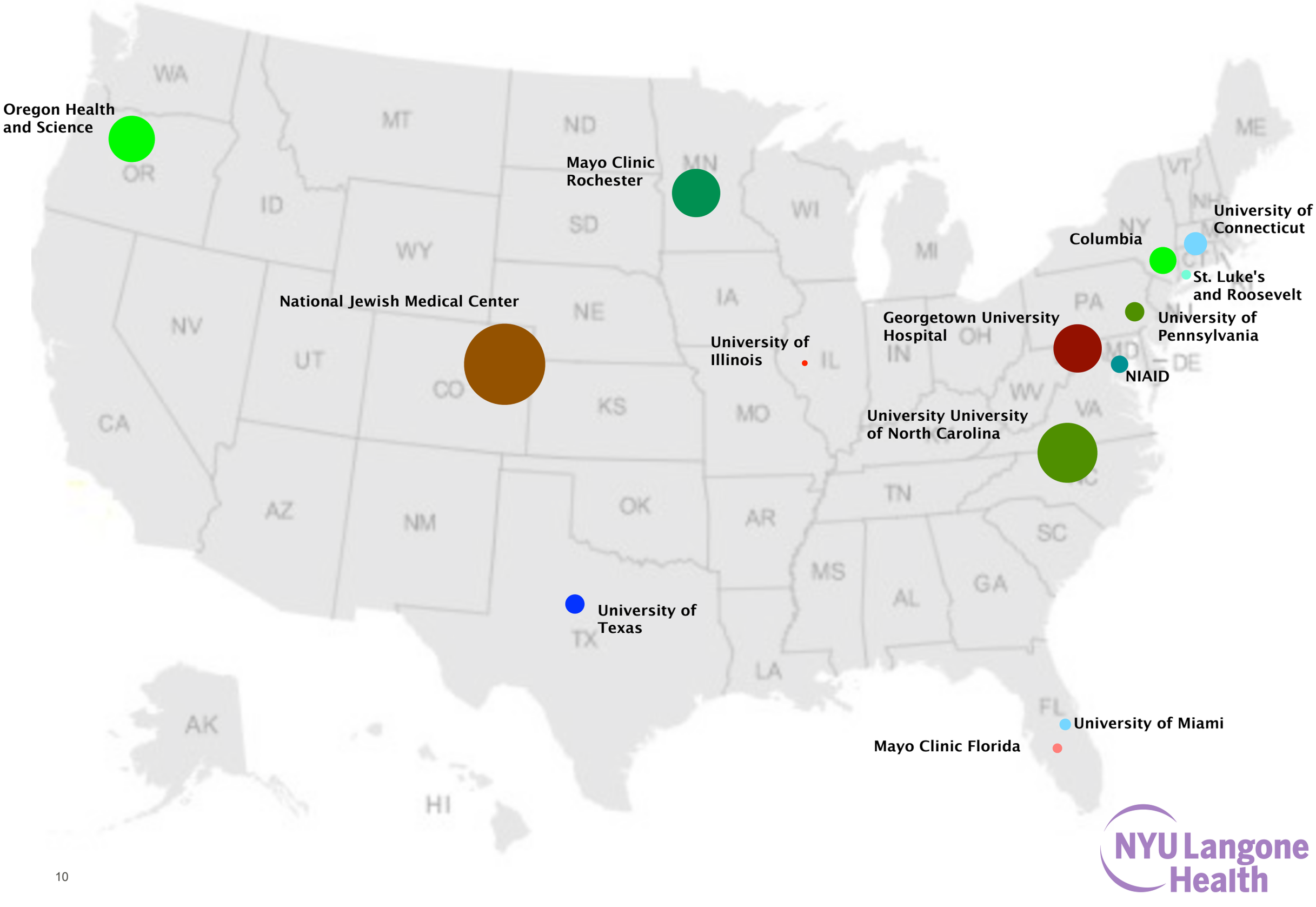
NYU Langone Lung & Airways Disease Registry



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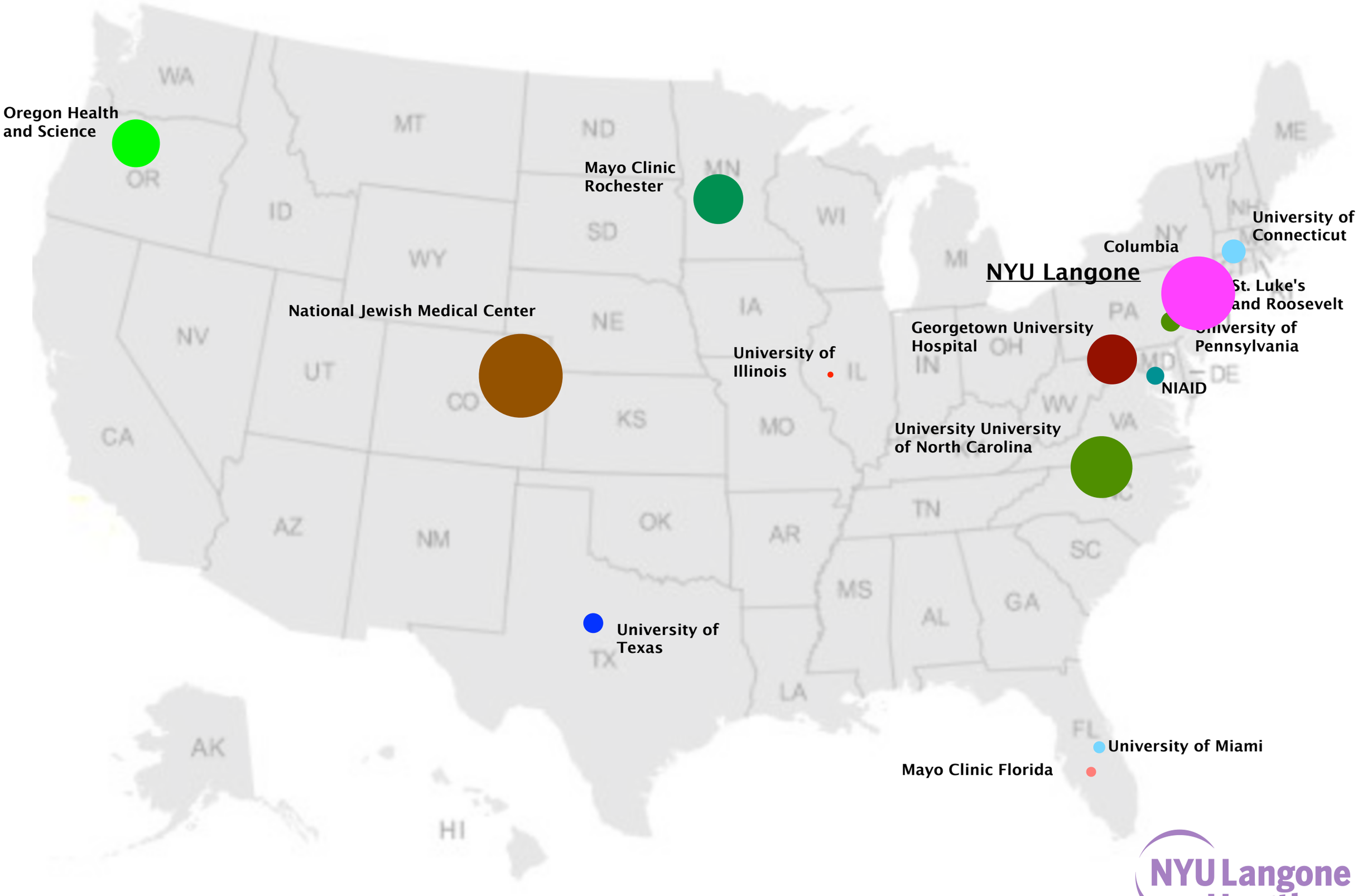
NYU Langone Lung & Airways Disease Registry



Accomplishments: Registry

Chronic Obstructive Pulmonary Diseases:
Journal of the COPD Foundation

Original Research

The Clinical Features of Bronchiectasis Associated with Alpha-1 Antitrypsin Deficiency, Common Variable Immunodeficiency and Primary Ciliary Dyskinesia–Results from the U.S. Bronchiectasis Research Registry

Edward Eden, MBBS[1] Radmila Choate, MPH[2] Alan Barker, MD[3] Doreen Addrizzo-Harris, MD[4]
Timothy R. Aksamit, MD[5] Charles L. Daley, MD[6] M. Leigh Anne Daniels, MD, MPH[7] Angela DiMango, MD[8]
Kevin Fennelly, MD[9] David E. Griffith, MD[10] Margaret M. Johnson, MD[11] Michael R. Knowles, MD[7]
Mark L. Metersky, MD[12] Peadar G. Noone, MD[7] Anne E. O'Donnell, MD[13] Kenneth N. Olivier, MD, MPH[9]
Matthias A. Salathe, MD[14] Andreas Schmid, MD[15] Byron Thomashow, MD[8] Gregory Tino, MD[16]
Gerard M. Turino, MD[1] Kevin L. Winthrop, MD, MPH[3,17]

Chronic Obstr Pulm Dis. 2019 Apr 9;6(2):145-153

Accomplishments: Clinical Trials

A phase 3 randomized, double-blind, placebo-controlled study of liposomal amikacin for inhalation (Arikase®) in patients with resistant NTM lung disease

IINS-212: A Randomized, Open-Label, Multi-center Study of Liposomal Amikacin for Inhalation (LAI) in Adult patients with NTM Lung Infections caused by MAC that are Refractory to Treatment

INS-312: An Open-Label Safety Extension Study to a Multi-center Study of Liposomal Amikacin for Inhalation (LAI) in Adult Patients with NTM Lung Infections caused by MAC that are Refractory to Treatment

Now Closed

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Accomplishments: Clinical Trials

ORIGINAL ARTICLE

Amikacin Liposome Inhalation Suspension for Treatment-Refractory Lung Disease Caused by *Mycobacterium avium* Complex (CONVERT)

A Prospective, Open-Label, Randomized Study

David E. Griffith[1], Gina Eagle[2], Rachel Thomson[3], Timothy R. Aksamit[4], Naoki Hasegawa[5], Kozo Morimoto[6], Doreen J. Addrizzo-Harris[7], Anne E. O'Donnell[8], Theodore K. Marras[9], Patrick A. Flume[10], Michael R. Loebinger[11], Lucy Morgan[12], Luigi R. Codecasa[13], Adam T. Hill[14], Stephen J. Ruoss[15], Jae-Joon Yim[16], Felix C. Ringshausen[17], Stephen K. Field[18], Julie V. Philley[1], Richard J. Wallace, Jr.[1], Jakko van Ingen[19], Chris Coulter[20], James Nezamis[2], and Kevin L. Winthrop[21]; for the CONVERT Study Group*

[1]The University of Texas Health Science Center at Tyler, Tyler, Texas; [2]Insmed Incorporated, Bridgewater, New Jersey; [3]University of Queensland, Gallipoli Medical Research Institute, Brisbane, Queensland, Australia; [4]Pulmonary Disease and Critical Care Medicine, Mayo Clinic, Rochester, Minnesota; [5]Keio University Hospital, Tokyo, Japan; [6]Fukujuji Hospital, Japan Anti-Tuberculosis Association, Tokyo, Japan; [7]Division of Pulmonary, Critical Care and Sleep Medicine, New York University School of Medicine, New York, New York; [8]Division of Pulmonary, Critical Care and Sleep Medicine, Georgetown University Hospital, Washington, District of Columbia; [9]Department of Medicine, University of Toronto, and Toronto Western Hospital, University Health Network, Toronto, Ontario, Canada; [10]Medical University of South Carolina, Charleston, South Carolina; [11]Host Defense Unit, Royal Brompton Hospital, and Imperial College, London, United Kingdom; [12]Concord Clinical School, University of Sydney, Sydney, New South Wales, Australia; [13]TB Reference Centre, Villa Marelli Institute/Niguarda Hospital, Milan, Italy; [14]Department of Respiratory Medicine, Royal Infirmary of Edinburgh and Queen's Medical Research Institute, University of Edinburgh, Edinburgh, United Kingdom; [15]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, California; [16]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, South Korea; [17]Department of Respiratory Medicine, Hannover Medical School, and German Center for Lung Research, Hannover, Germany; [18]Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada; [19]Department of Medical Microbiology, Radboud University Medical Center, Nijmegen, the Netherlands; [20]Queensland Mycobacterium Reference Laboratory, Pathology Queensland, Brisbane, Australia; and [21]OHSU-PSU School of Public Health, Portland, Oregon

ORCID ID: 0000-0003-0686-171X (R.T.).

Am J Respir Crit Care Med Vol 198, Iss 12, pp 1559–1569, Dec 15, 2018

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Clinical Trials

Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multi-Center Study to Assess the Efficacy, Safety and Tolerability, and Pharmacokinetics of INS1007 Administered Once Daily for 24 Weeks in Subjects with Non-C Fibrosis Bronchiectasis)	
Double-blind, placebo-controlled, multi-centre, A PILOT STUDY TO EVALUATE THE USE OF THE VEST® SYSTEM FOR TREATMENT OF NON-CYSTIC FIBROSIS BRONCHIECTASIS PATIENTS IN THE HOME SETTING	***Open***
Multi-center randomized pragmatic clinical trial comparing 2- versus 3-antibiotic therapy for pulmonary Mycobacterium avium complex disease	

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NTM disease is associated with micro aspiration

Respiratory Medicine (2006) 100, 1663–1665

respiratoryMEDICINE

CASE REPORT

Non-tuberculous mycobacteria masquerading as aspiration pneumonia in patients with gastrointestinal problems

Alistair Colin Church[a,*], Simon Watkin[b]

[a]Papworth Hospital, Papworth Everard, Cambridge CB3 8RE, UK
[b]Respiratory Department, Norfolk and Norwich University Hospital, Colney lane, Norwich NR4 7UY, UK

Received 28 November 2005; accepted 31 December 2005

Original Research

MYCOBACTERIAL DISEASE

Prevalence of Gastroesophageal Reflux Disease in Patients With Nontuberculous Mycobacterial Lung Disease*

Won-Jung Koh, MD; Jun Haeng Lee, MD; Yong Soo Kwon, MD; Kyung Soo Lee, MD; Gee Young Suh, MD; Man Pyo Chung, MD; Hojoong Kim, MD, FCCP; and O. Jung Kwon, MD

CHEST

Original Research

RESPIRATORY INFECTIONS

Gastroesophageal Reflux Disease, Acid Suppression, and *Mycobacterium avium* Complex Pulmonary Disease*

Rachel M. Thomson, MBBS; John G. Armstrong, MBBS, PhD; and David F. Looke, MBBS

Microaspiration

Pharyngeal Aspiration in Normal Adults and Patients with Depressed Consciousness

ELIOT J. HUXLEY, M D.*
JOSE VIROSLAV, M.D.
WILLIAM R. GRAY, M.D.
ALAN K. PIERCE, M.D
Dallas, Texas

From the Pauline and Adolph Weinberger Laboratory for Cardiopulmonary Research, Department of Internal Medicine, and the Department of Nuclear Medicine, University of Texas Health Science Center at Dallas, and the Department of Internal Medicine, St. Paul Hospital, Dallas, Texas.
This study was supported by grants from the St Paul Hospital Foundation, Inc , and U S. Public Health Service Grant 1-MOI-RR00633. Requests for reprints should be addressed to Dr Alan K Pierce, 5323 Harry Hines Boulevard H8 122, Dallas, Texas 75235. Manuscript accepted August 9, 1977.

Present address: Mt. Sinai Professional Building, 1218 West Kilbourn Avenue, Suite 207, Milwaukee, Wisconsin 53233

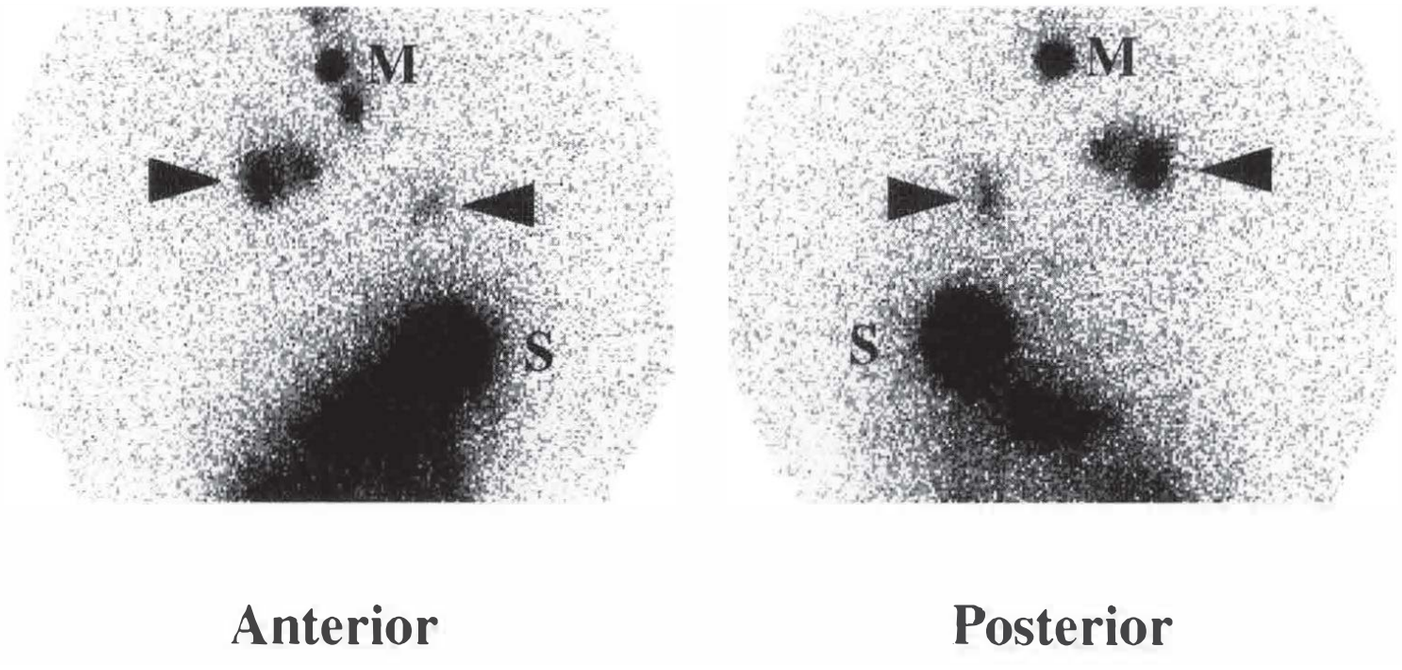
* Fellow of the American Lung Association

Quantitative Aspiration During Sleep n Normal Subjects*

evin Gleeson, MD; ouglas . Eggli, MD; and Steven L. Maxwell, DO, CCP

Gleeson et al. Chest 1997

Radioactive ^{99m}Tc tracer



Anterior **Posterior**

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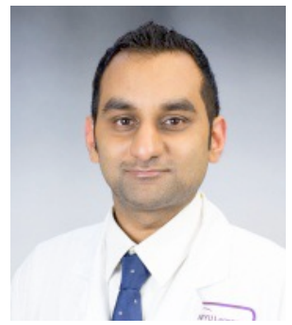
Swallow and NTM
"Role of aerodigestive dysmotility on airway dysbiosis in NTM disease"



Ashwin Basavaraj, MD

David Kamelhar, MD

- Subjects with Bronchiectasis undergoing swallow or upper GI evaluation
- Swallow studies standardized to determine role of micro aspiration and GI motility
- Paired evaluation of airway microbiota

Matina Balou, PhD

Abraham Khan, MD

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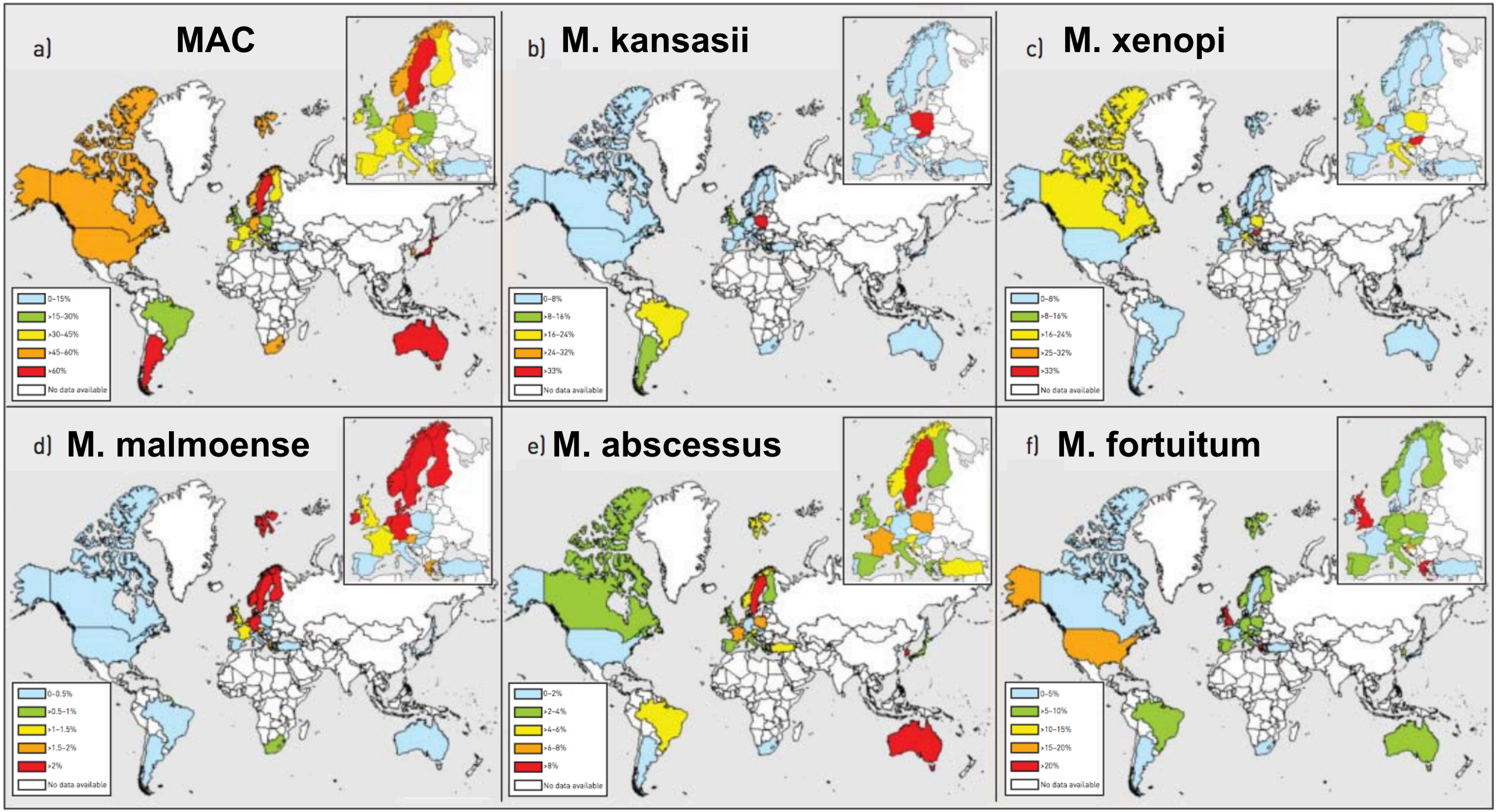
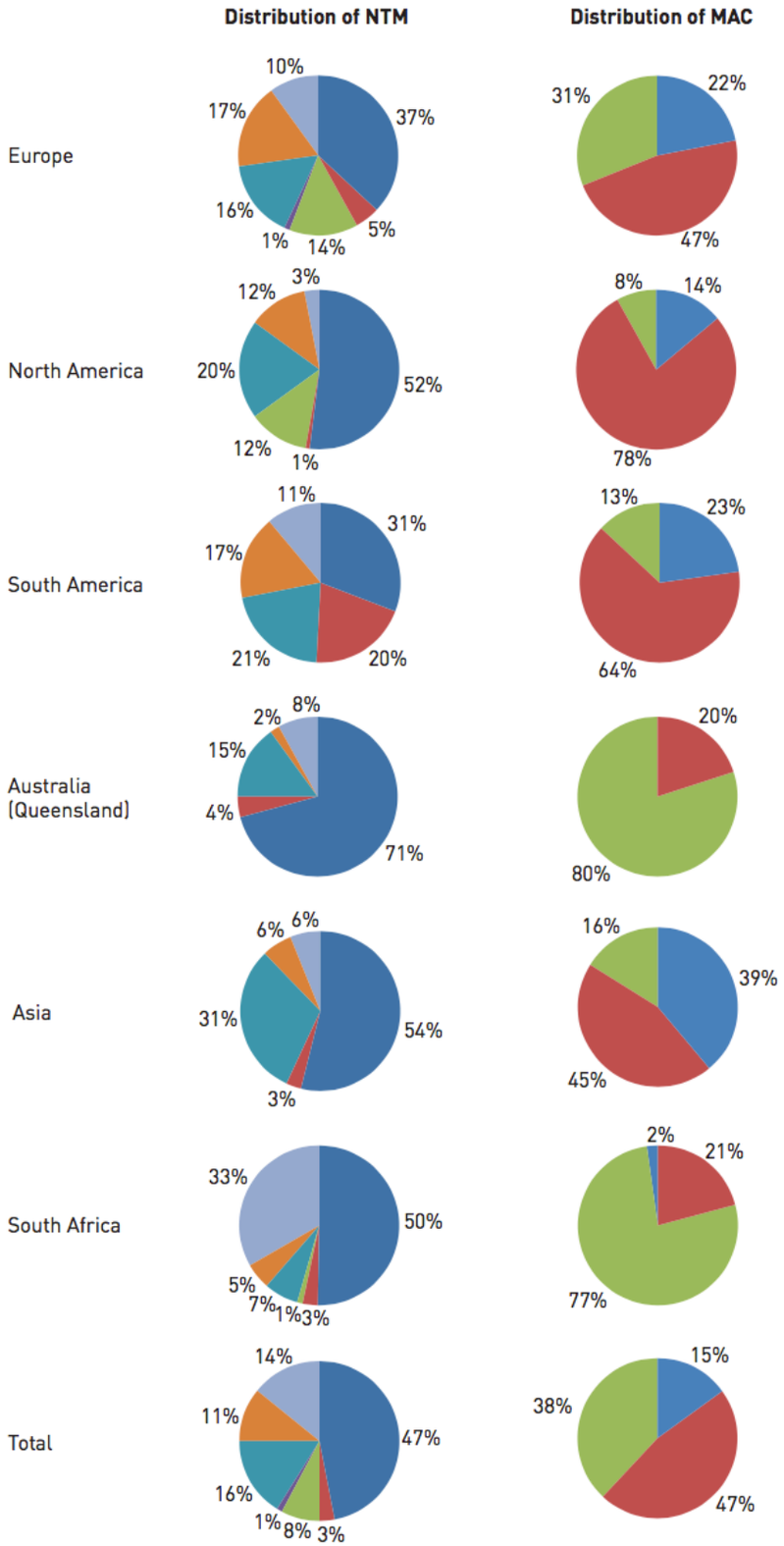
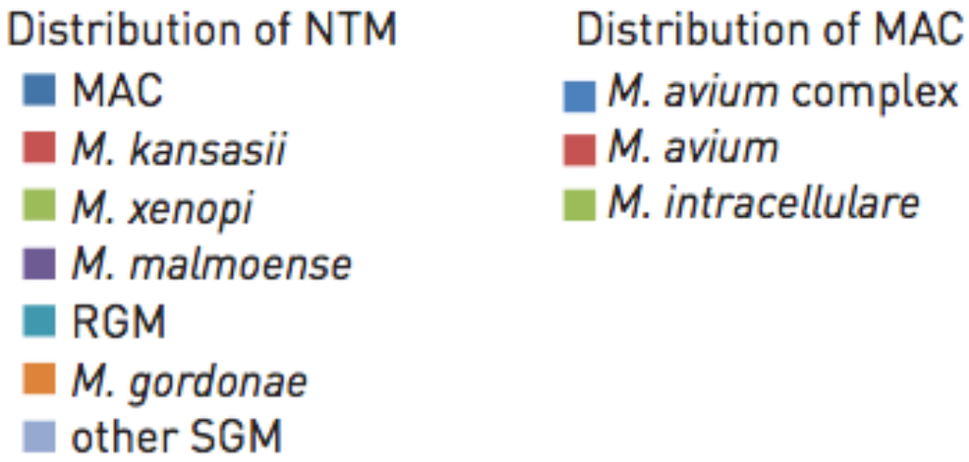
NTM bronchiectasis: Increasing problem Worldwide

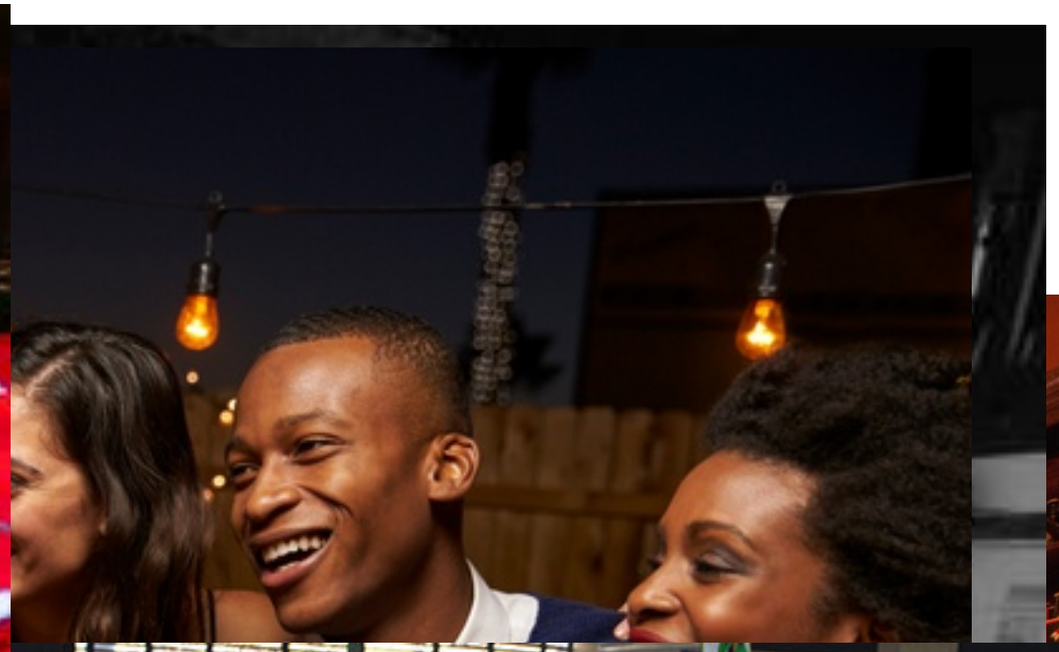


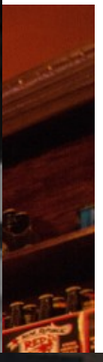
NTM bronchiectasis: Increasing problem Worldwide



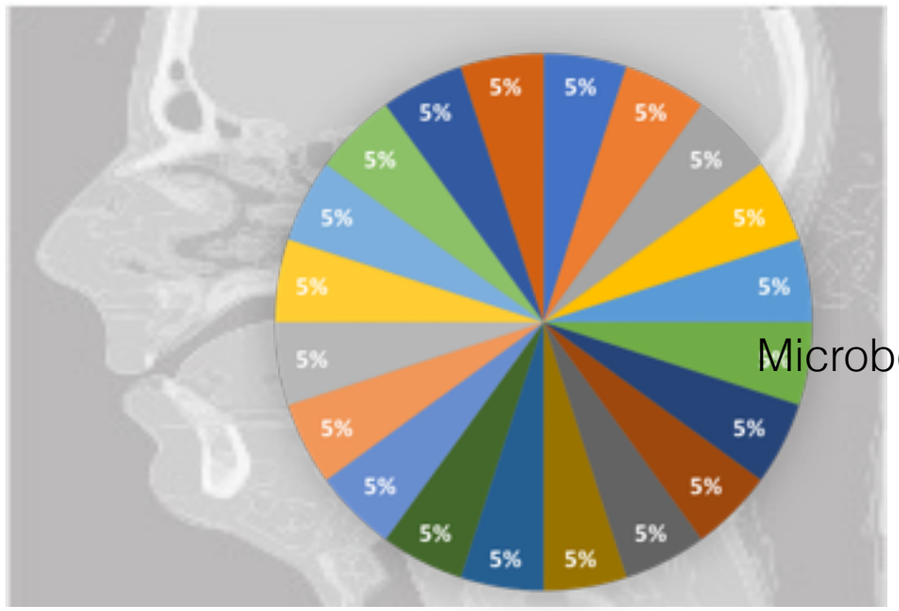


The lower airways are like bars

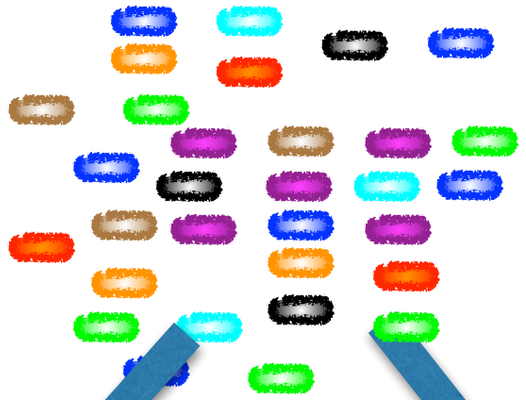




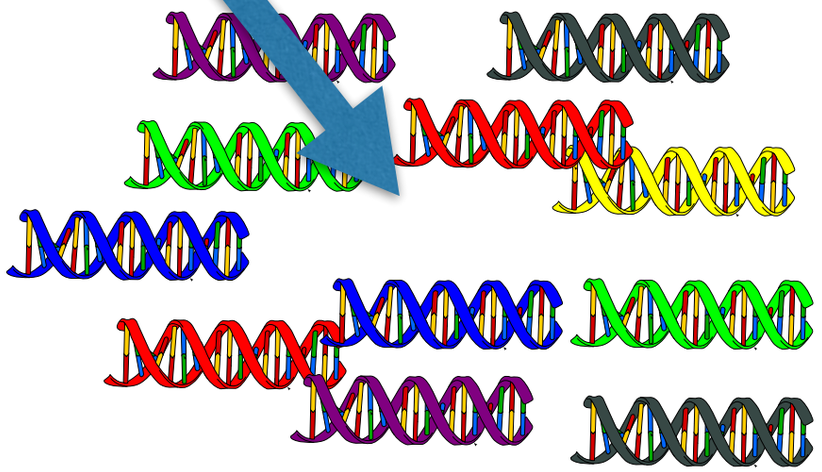
Microbiome: comprehensive characterization of the microbial communities

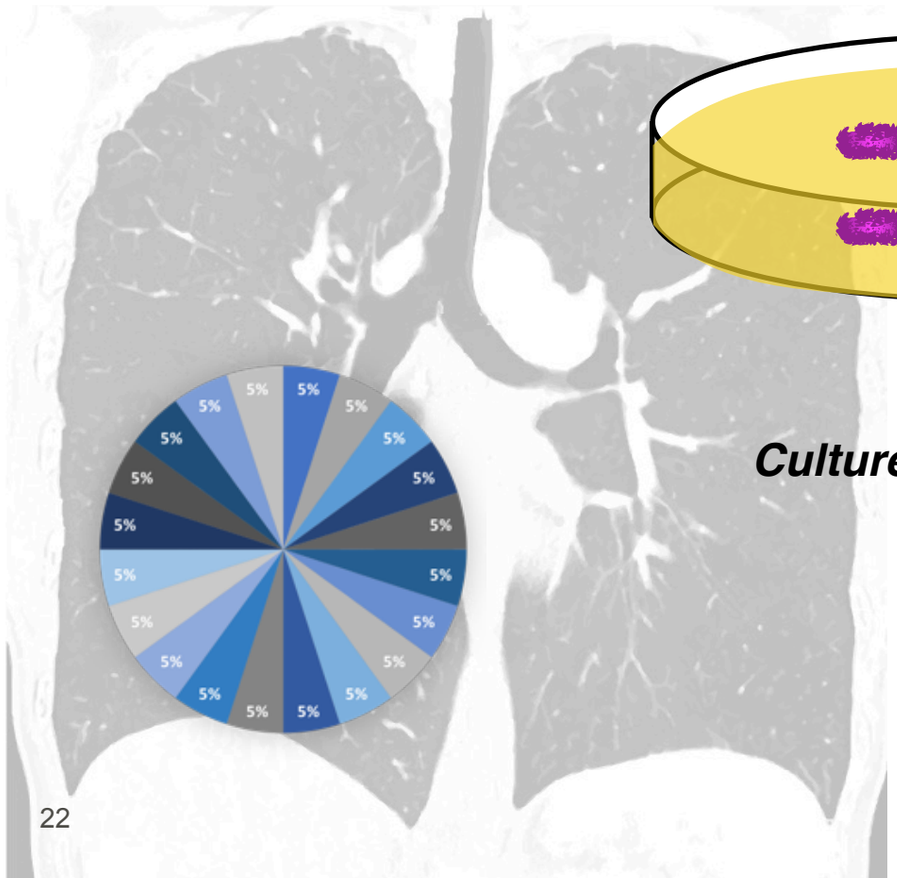


Microbe Isolation



Microbial Product Identification





Culture Dependent

Culture Independent

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Cough and Sputum Production

Diagnosis

1) NTM identification?

2) Non-NTM pathogens?

3) Patient susceptibility?

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Accomplishments: Translational Research

> 300 subjects with non invasive airway sampling

> 100 subjects with invasive airway sampling

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Accomplishments: Translational Research

ORIGINAL ARTICLE
LUNG INFECTION

Evaluation of the airway microbiome in nontuberculous mycobacteria disease

Imran Sulaiman[1], Benjamin G. Wu[1], Yonghua Li[1], Adrienne S. Scott[1], Patrick Malecha[1], Benjamin Scaglione[1], Jing Wang[1], Ashwin Basavaraj[1], Samuel Chung[1], Katrina Bantis[1], Joseph Carpenito[1], Jose C. Clemente[3,4], Nan Shen[3], Jamie Bessich[1], Samaan Rafeq[1], Gaetene Michaud[1], Jessica Donington[1], Charissa Naidoo[5], Grant Theron[5], Gail Schattner[1], Suzette Garofano[1], Rany Condos[1], David Kamelhar[1], Doreen Addrizzo-Harris[1] and Leopoldo N. Segal[1,2]

Eur Respir J. 2018 Oct 25;52(4)

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Pathogen Control

Pathogen Susceptibility

Increasing Anaerobes/SCFA

IFN-ɣ production

IL-17A production

IFN-ɣ inhibition

IL-17A inhibition

CD4

CD4

CD8

CD4

CD4

CD4
FoxP3

CD8
FoxP1

CD4

HO

NTM Antigen

Segal et al. Cell Host & Microbe 2017

DC 11/26/2019

The lower airways are like bars

Hypothesis

- *Bronchiectasis is a heterogenous disease*

- *We hypothesize that in NTM related bronchiectasis lower airway dysbiosis affects host immune phenotype and susceptibility to pathogens*

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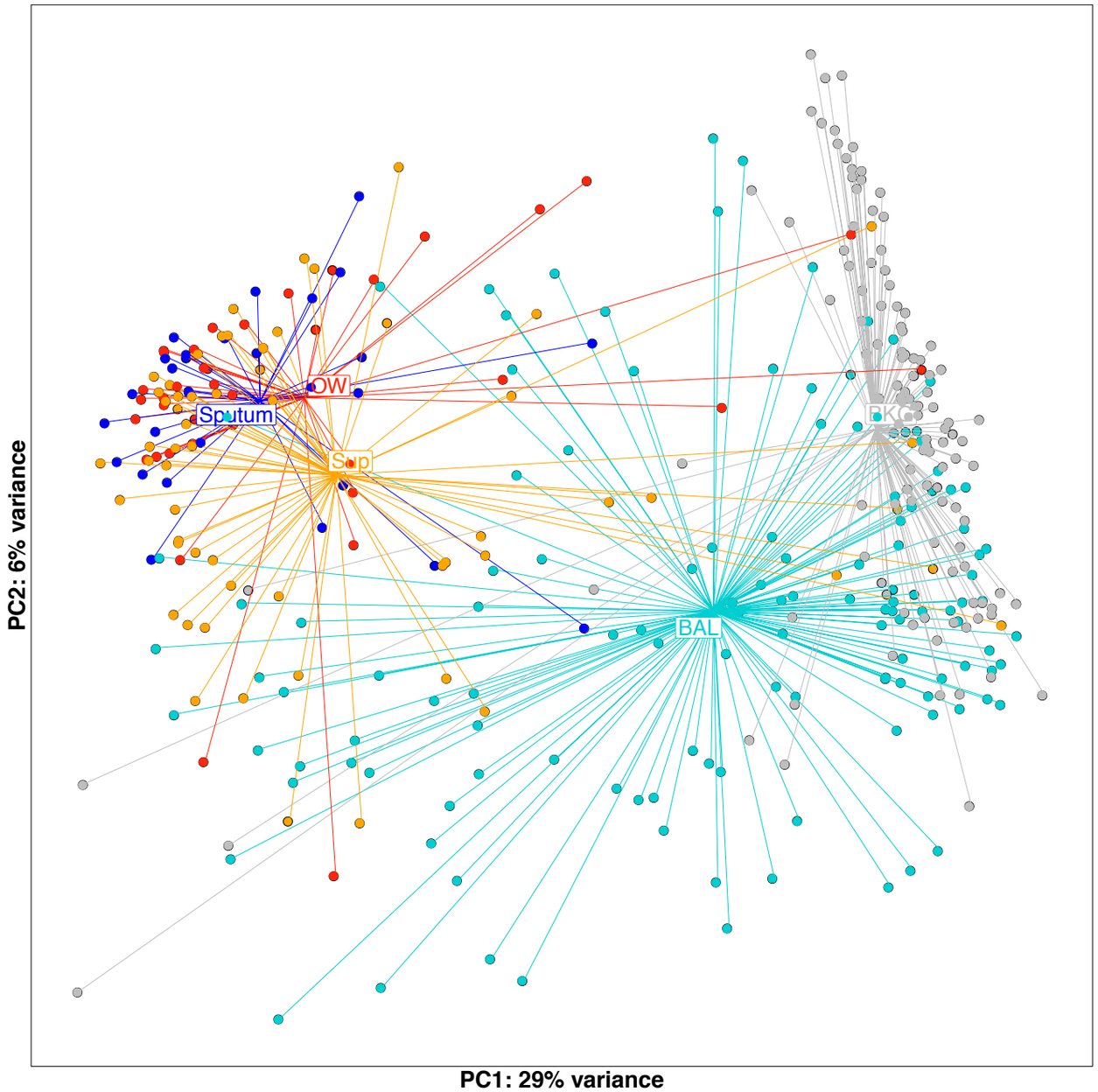
Growing cohort of patients with bronchiectasis with lower airway samples

Bronchiectasis Cohort	
n	89
Age	67[57-73]
Gender	70(78%)
Spirometry	
FVC (% Predicted)	94[85-104]
FEV1 (% Predicted)	88[77-100]
FEV1/FVC	76[70-81]
Culture	
Non-Tuberculous Mycobacterium	22 (24%)
NTM + second pathogen	14(15%)
Haemophilus	6(6%)
Pseudomonas	5(5%)
Candida	4(4%)
Aspergillus	3(3%)
Streptococcus	3(3%)
Negative	28(31%)
Other	4(4%)



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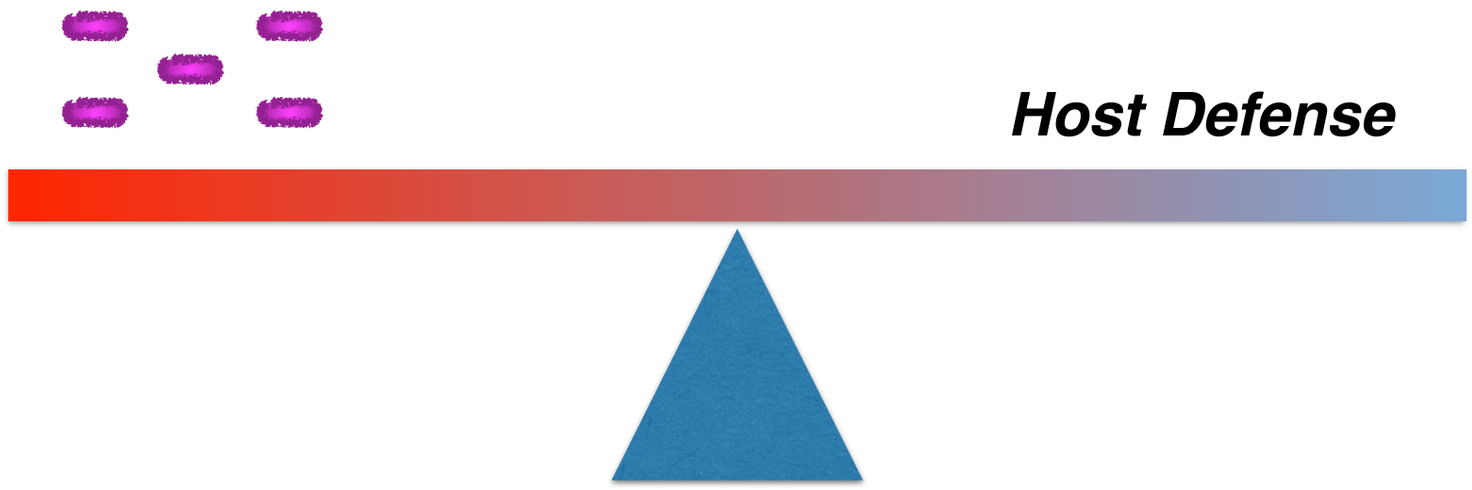
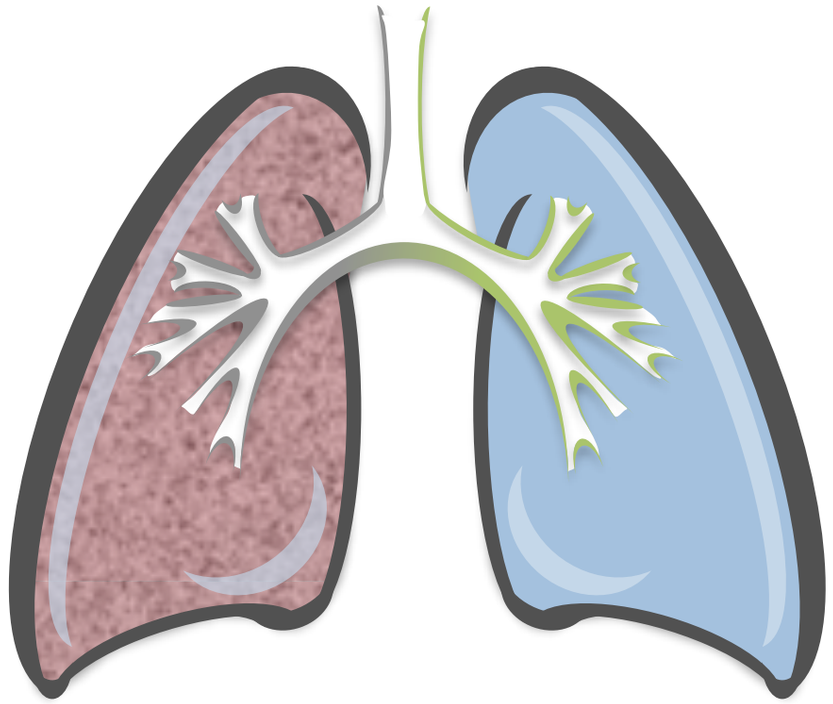
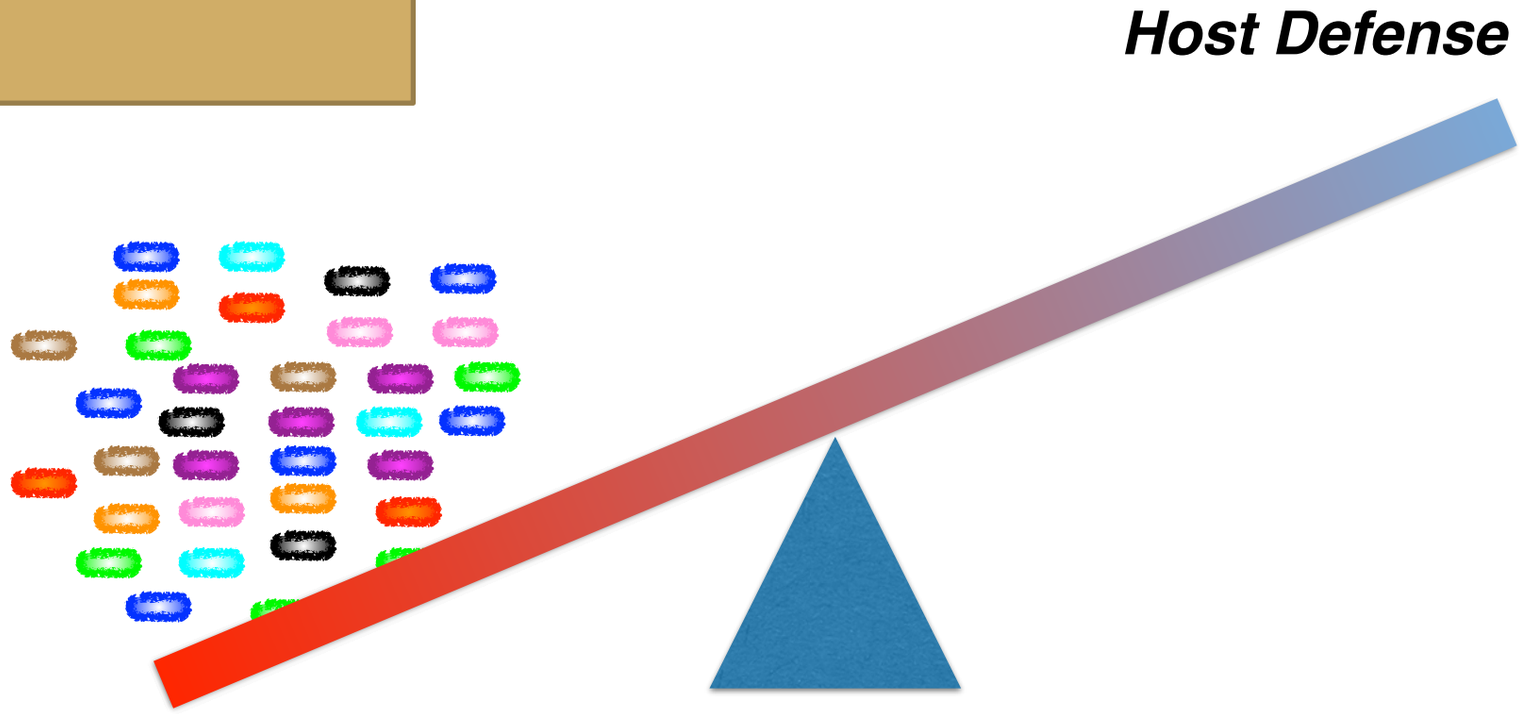
Evaluation of the Airway Microbiome In NTM



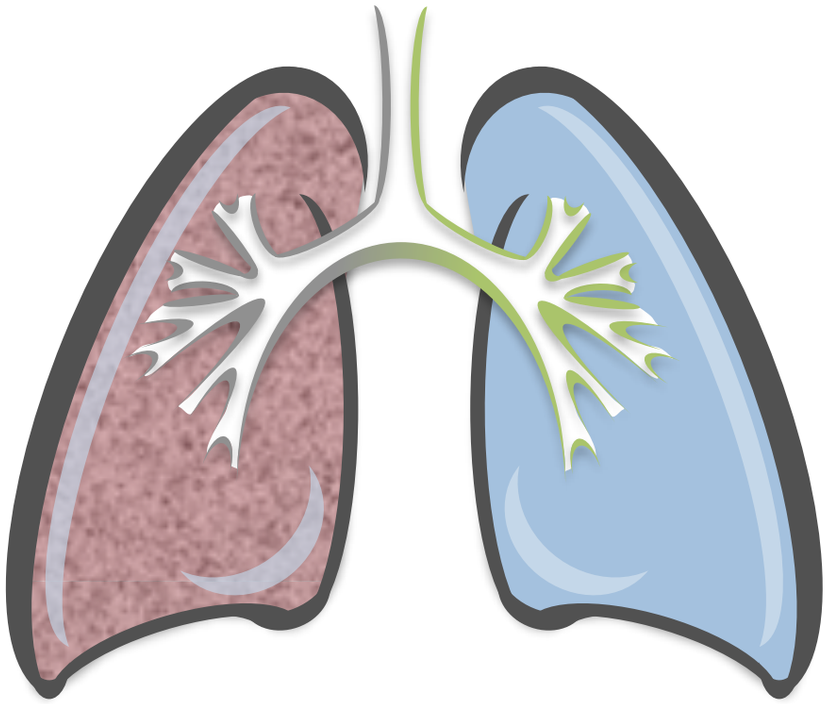


Disease **Health**

Microbial environment:
e.g. Biofilm

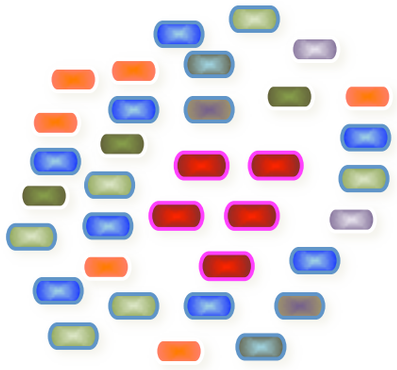


Microbial Dynamics:
- **GERD**
- **Impaired clearance**

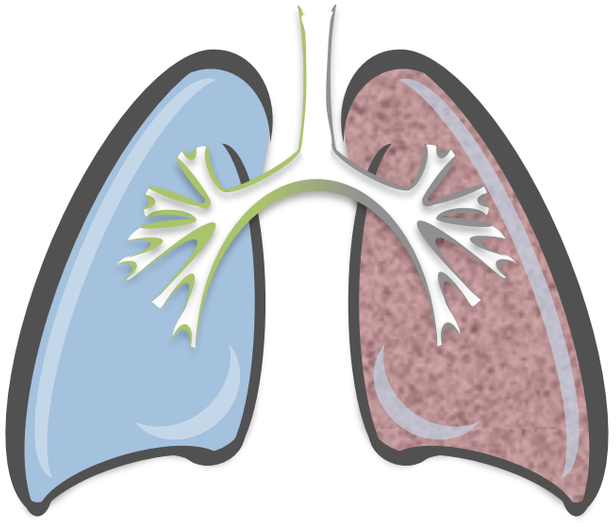


Disease **Health**

A new challenge for Koch Postulate



+ ***Host Factors*** =



Health Disease

Oral Microbiome ⟷ **Lung Microbiome**

Biomarker

Therapeutic

Antibiotics

Pro-Biotics

Pre-Biotics

Phage

Be involved!! Ask us about research opportunities

NYU Langone NTM/Bronchiectasis Program

Funding Support:
NIH/NIAID
Chest Foundation

We would like to acknowledge the generous support of donors to the NYU Langone NTM/bronchiectasis program:

NTM Info & Research
Helaine Lerner
The Chelnik family in honor of Harriette and Martin Chelnik
Beatrice Ifshin
Barbara Goldstein Amster
Wandler Family
Karen Elliott House
Leeam Lowin
Sandra Pearl
Lonuzzi Family
Alan Manheimer
Arthur Press
Anonymous

For more information about the program or opportunities for involvement, please contact Yodalis Moran (yodalis.Moran@nyulangone.org) or call 212-404-3538.

e-mail: leopoldo.segal@nyumc.org