

**The Lung Microbiome
in Asthma and COPD**

**Richard J. Martin, M.D.
Chairman, Department of Medicine
National Jewish Health**

**Edelstein Chair in Pulmonary Medicine
Professor of Medicine
National Jewish Health
University of Colorado Denver**

**What do we know about the lung
microbiome?**

- Very little
- Could be exceedingly important
- Vast majority of bacteria are non-cultured
- PCR to identify species is limited to detect anticipated bacteria
- 16S ribosomal RNA chips better (validation needed)
 - ~8,500 taxa

Les Dethlefsen, et al. Nature 2007;449:881-8. Turnbaugh, et al. Nature 2007; 449: 804-10. Turnbaugh, et al. Nature 2009;457:480-4.

**What do we know about the lung
microbiome?**

- Structural complexity of microbial communities, rather than simply the presence of individual species, can be important in determining states of health vs. disease.
- Difference in the structure or composition of a microbial community affects function exerted by the community.

Les Dethlefsen, et al. Nature 2007;449:881-8. Turnbaugh, et al. Nature 2007; 449: 804-10. Turnbaugh, et al. Nature 2009;457:480-4.

Our microbiome

- Our immunologic fate is intertwined with the microorganisms we evolved with
- Outnumbered 100 trillion bacterial cells in our bodies to 10 trillion of our own cells
- Commensal organisms promote absorption of nutrients, aid in vitamin metabolism, and protect mucosal surface from pathogenic organisms
 - **Modulate immune function and maintenance of mucosal homeostasis**

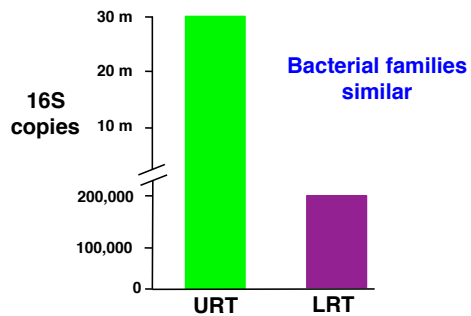
Endt, et al. PLoS Pathog 2010;6. Oyama N, et al. JACI 2001;107:153-9.

Germ free mice

- **Allergen challenge** produces more AHR, TH2 cytokine expression, and airway inflammation than mice under pathogen free conditions
 - Alterations in dendritic cells (antigen presenting cells) and macrophages occur
- **Dendritic cells extend outside epithelium into lumen to sample bacteria without disruption of the integrity of epithelial barrier**

Herbst, et al. AJRCCM 2011;184.
Rescigno M, et al. Nat Immunol 2001;2:361-7.

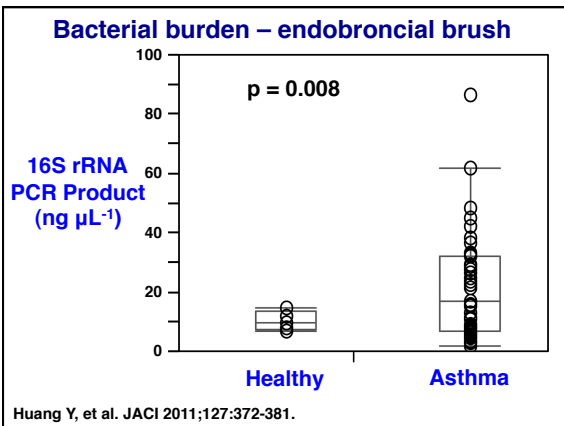
Upper respiratory tract (URT) vs. lower (LRT) in normal healthy individuals

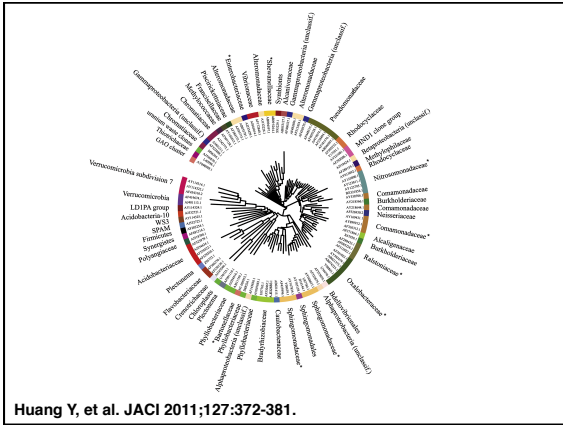


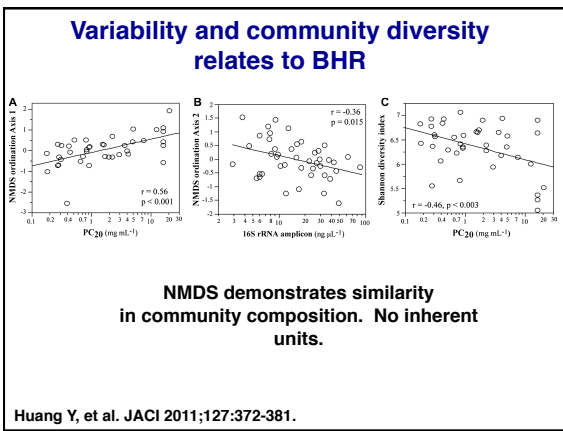
Charlson, et al. AJRCCM 2011;184:957-63.

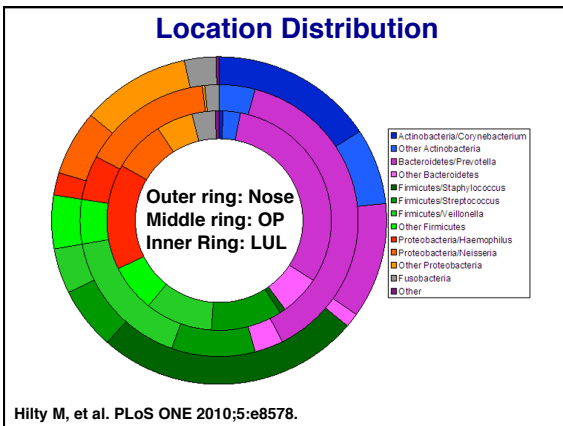
Asthma

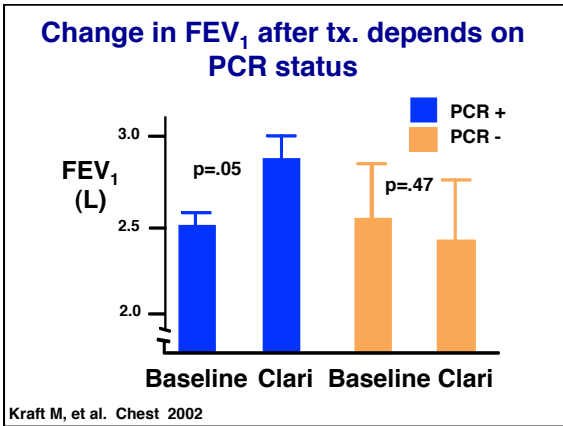
Is Asthma an infectious Disease?

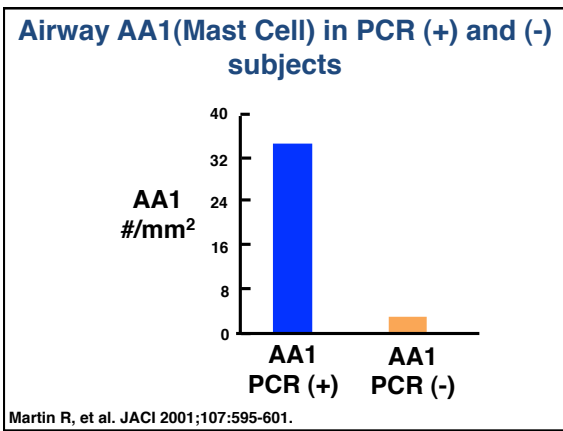




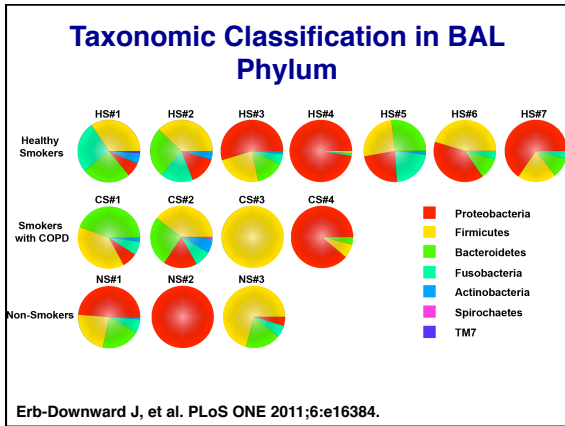


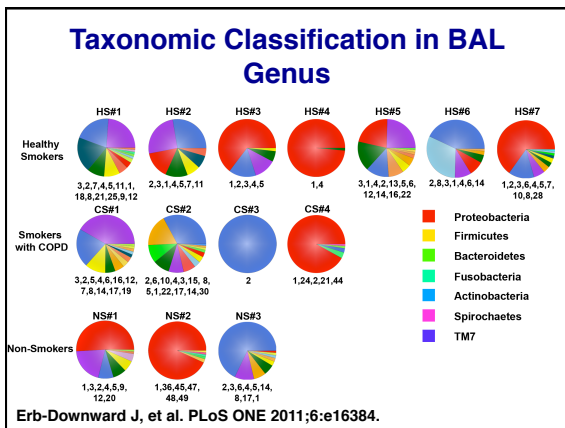






COPD

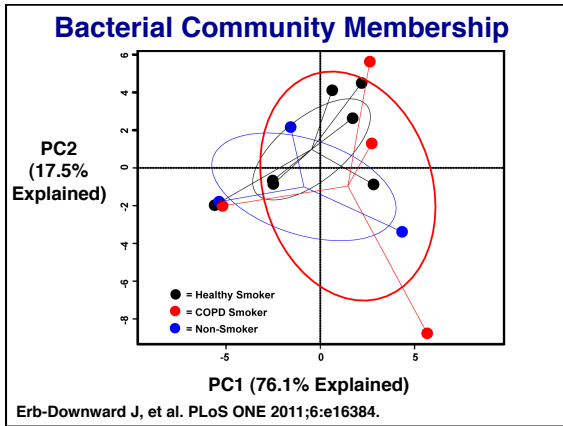


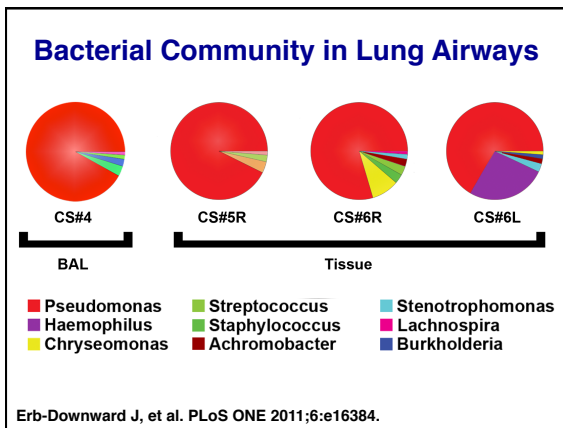


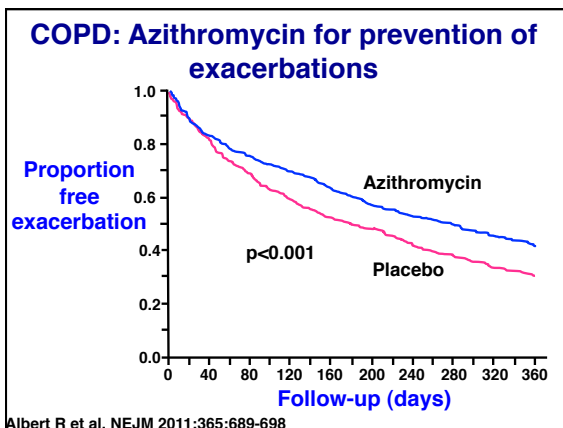
BAL Abundance Table. Top 10 of 51

Rank	Name	Total # Sequences	# Subjects Occurred/Total
1	Pseudomonas	78319	12/14
2	Streptococcus	23253	12/14
3	Prevotella	19916	10/14
4	Fusobacterium	8784	11/14
5	Veillonella	5937	9/14
6	Porphyromonas	4366	8/14
7	Leptotrichia	3801	5/14
8	Haemophilus	2765	8/14
9	Oribacterium	1577	6/14
10	Actinobacillus	1539	4/14

Erb-Downward J, et al. PLoS ONE 2011;6:e16384.







Conclusion

- A totally new area of important research to determine the lung microbiome and how alterations affect, propagate, and/or induce asthma and COPD
- New therapies to return microbiome to normal so as to improve and/or eliminate disease
