Looking Ahead: The Impact of Occupational Exposure and Health on the Human Microbiome

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UNMC COLLEGE OF PUBLIC HEALTH

Outline:

- **Introduction**
- Human microbiome vs. the exposome
- Current technology: exposure assessment to biologicals
- The future: advancements in monitoring and technology
  - microbiome and exposome
- Conclusions: cautionary tale

Introduction

- Graduate School – Industrial Hygiene
  - NIOSH ERC
- Faculty – Assistant Professor (2007 – 2011)
  - K01 Award – NIOSH Biotechnology
    - Thank you, mentors – S. Reynolds and J. Levin
- Faculty – Associate Professor (2011 – 2022)
- Faculty – Professor (2023 – Current)

Mentor – Steve Reynolds, PhD, CIH

Acknowledgments: CDC/NIOSH!!!

- CDC/NIOSH ERC T42OH008491 – Heartland Center (Many PIs – Sprince, O'Shaughnessy)
- NIOSH/CDC: - 1K01OH009674, Measures of Dust, Endotoxin, and Exhaled Nitric Oxide among Dairy Farm Workers (Nonnenmann, PI)
- NIH/NIEHS - P30 ES005605 Environmental Health Sciences Research Center, Determining concentrations of aerosolized influenza A (H1N1) utilizing RNAlater® as a sampling matrix. (Nonnenmann, PI)
- CDC/NIOSH - U54OOH007541 Southwest Center for Agricultural Health, Injury Prevention and Education (Center PI – Levin) Educational Approach to Increase Respirator Use among Broiler Chicken Workers. (Nonnenmann, PI)
- CDC/NIOSH - 2U54OH007548 - Great Plains Center for Agricultural Health and Safety (Center PI – Anthony) Air Quality Improvements in Livestock Production Buildings (Project PI - Nonnenmann)
- CDC/NCEZID – University of Chicago, COVID Supplement (CK000557/CK18-001). Evaluation of the effectiveness of face shield personal protective equipment when challenged with virus aerosol. (PI: Nonnenmann)
- CDC/NCEZID - 1 NU50 CK000623 Strengthening Healthcare Infection Prevention and Control and Improving Patient Safety in the United States (Herwaldt, PI) Role: Project PI – Nonnenmann
- CDC/NIOSH – 2 U54OH007548 - Great Plains Center for Agricultural Health and Safety (Anthony, Center PI) - Design and Evaluation of a Control Technology for Dust and Bioaerosol in Swine Buildings: Project PI – Nonnenmann
- *CDC/NIOSH - 1U54OH010162 – Central States Center for Agricultural Safety and Health (Rautiainen, Center PI) - Distribution of worker educational materials and personal protective equipment in response to Highly Pathogenic Avian Influenza (HPAI) in dairy and poultry production – Project PI - Nonnenmann*

Research Focus

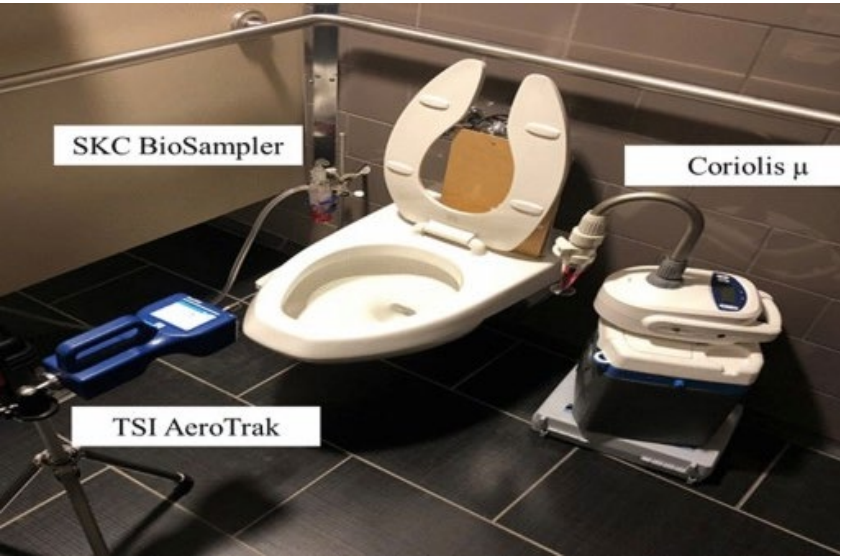
- Characterizing bioaerosols
  - Occupational and environmental
    - 16s Pyrosequencing - 2010
    - Application of DNA sequencing technology to inhalable samples - 2016
    - Field characterization – agricultural workers/health care 1997 - current
- Developing and evaluating bioaerosol exposure control technology – PPE, Administrative and Engineering Controls

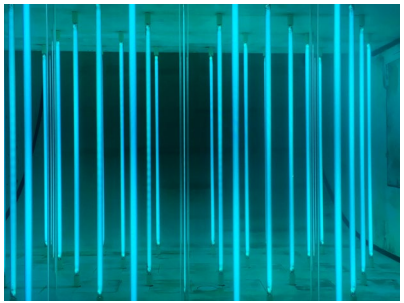
Airborne Influenza A Is Detected in the Personal Breathing Zone of Swine Veterinarians

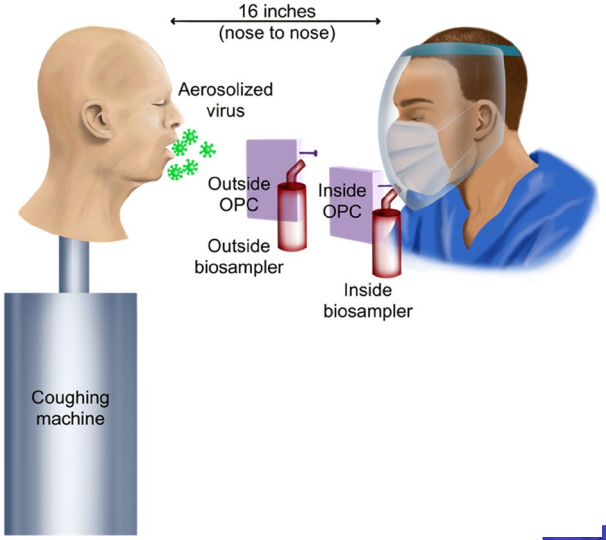
Kate M. O'Brien, Matthew W. Nonnenmann*

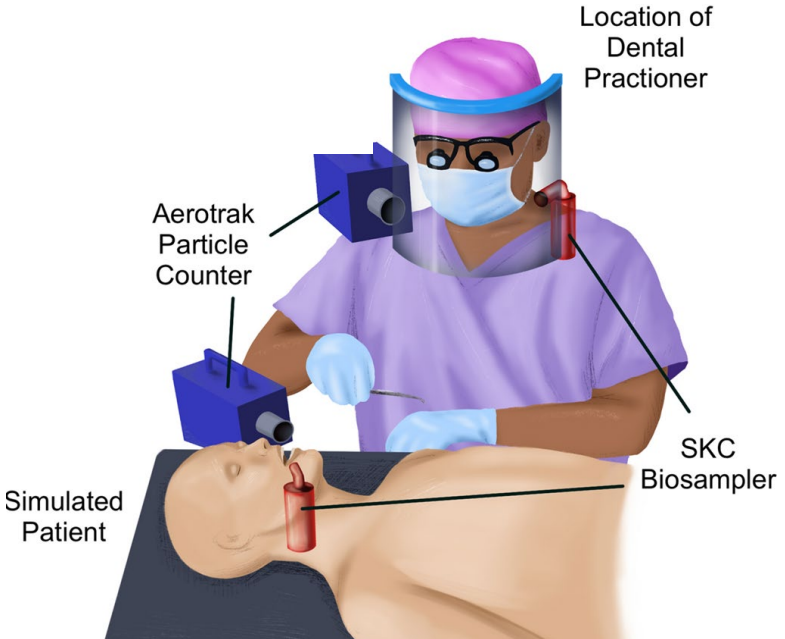
Department of Occupational and Environmental Health, College of Public Health, University of Iowa, Iowa City, Iowa, United States of America

Research Focus









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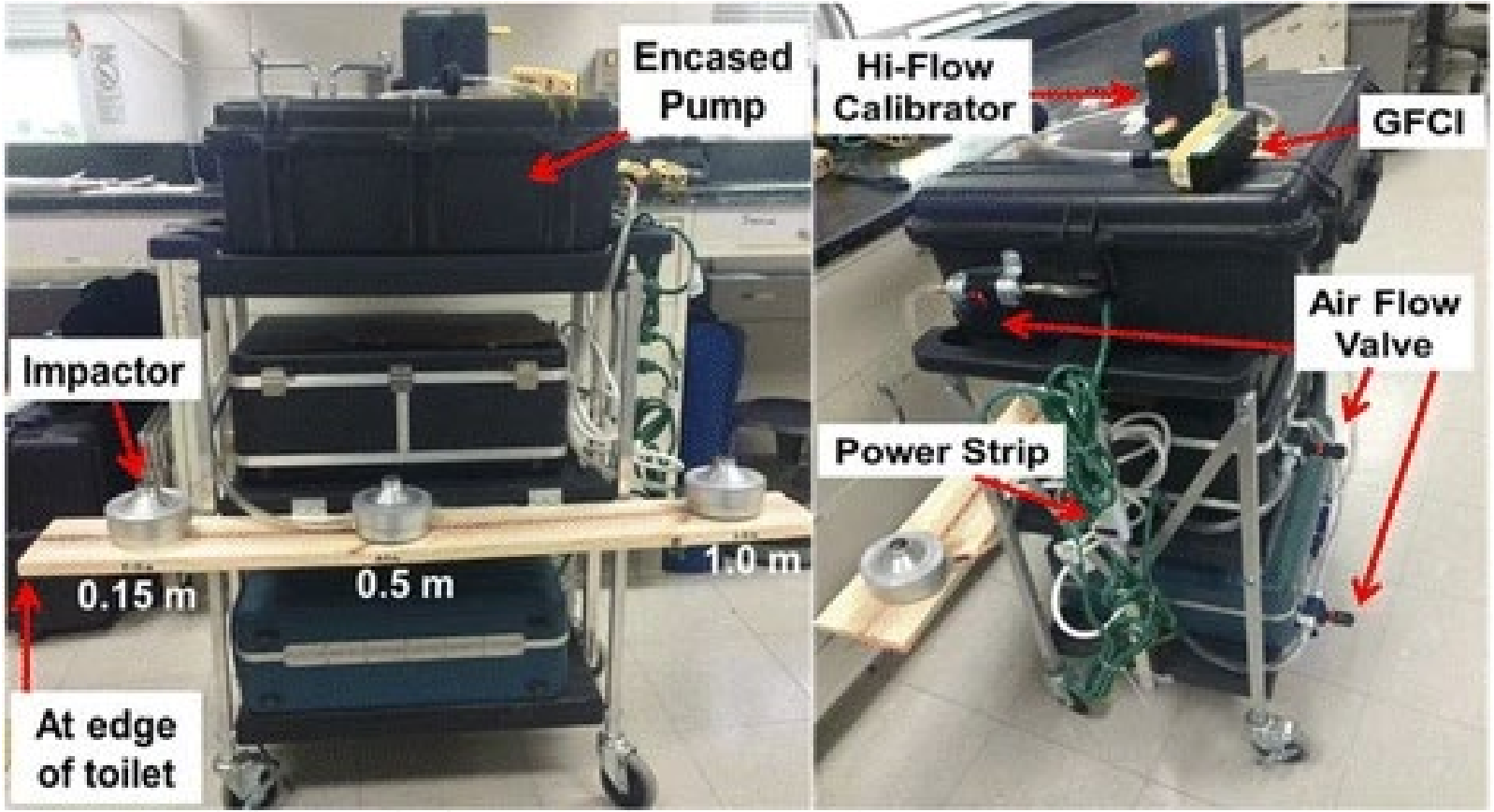

Research Focus – Dairy Industry

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Human Microbiome vs. Exposome

As Dr. Boles mentioned…

- The human microbiota is the collection of all the microbes living in association with the human body
  - Includes archaea, bacteria, viruses, and some unicellular eukaryotes

    - NIEHS, 2025

Source: Nathalie Ruaux

Human Microbiome vs. Exposome

- The exposome “includes chemical, physical, and biological stressors as well as lifestyle and social environments.”
  - NIEHS, 2025

- NIEHS Laboratory (@ Duke) has been created for environmental sampling for exposome research
  - Not aware of work including biological exposures

Source: Nathalie Ruaux

Natural Questions(?)

- What happens to the microbiome of people are exposed to occupational hazards?
- What is a “normal” microbiome in the lung, gut, oral cavity?
- Microbiome characterization includes concepts from biomonitoring
  - Biomarkers of exposure (e.g., manure)
    - e.g., presence of organisms from exposure to occupational environment (e.g., *E. coli*)
  - Biomarkers of effect
    - Exposure to a hazard (e.g., irritant gases) results in changes in the distribution of organisms the lung microbiome
    - Presence of antibodies (e.g., H5N1)
  - Biomarkers of susceptibility
    - ***Abnormal*** distribution of lung microbiome (e.g., presence of lung inflammation/disease)

Source: Wiki

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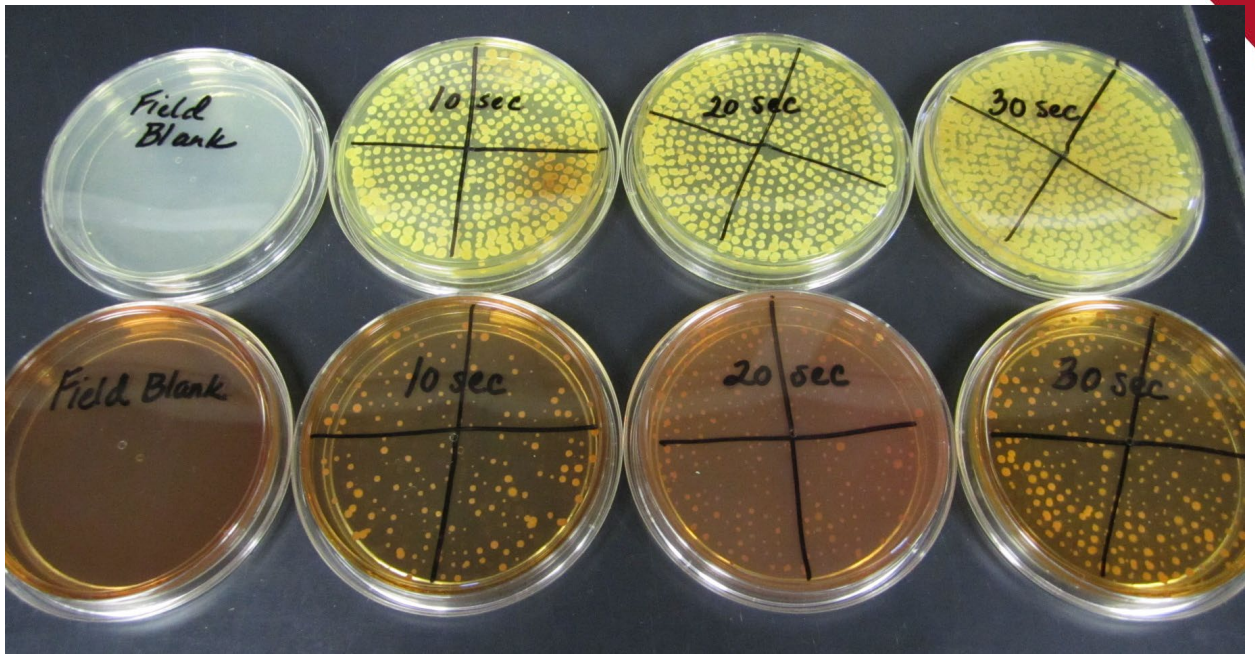
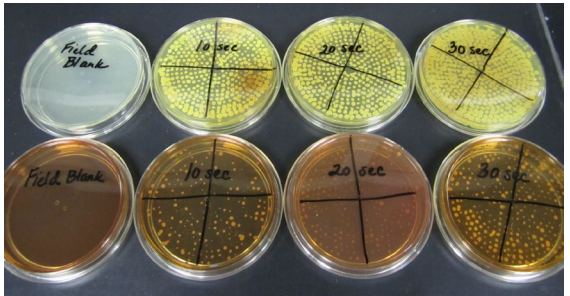


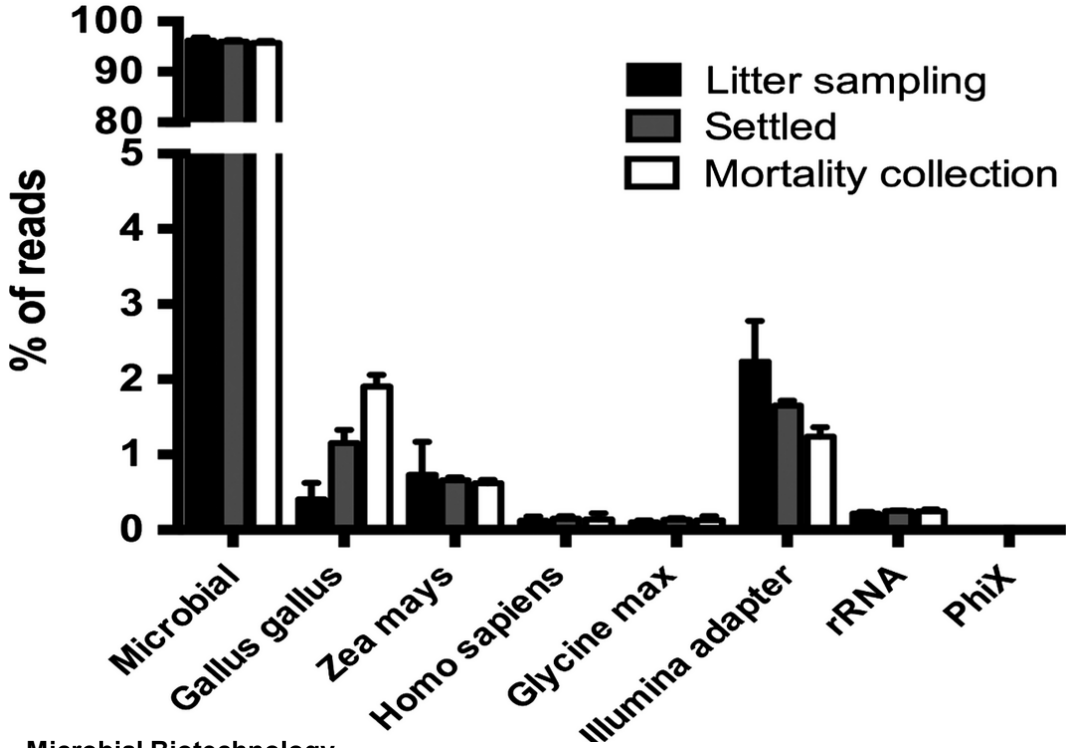
Concentrations range from 10^6 – 10^9 cfm/m^3

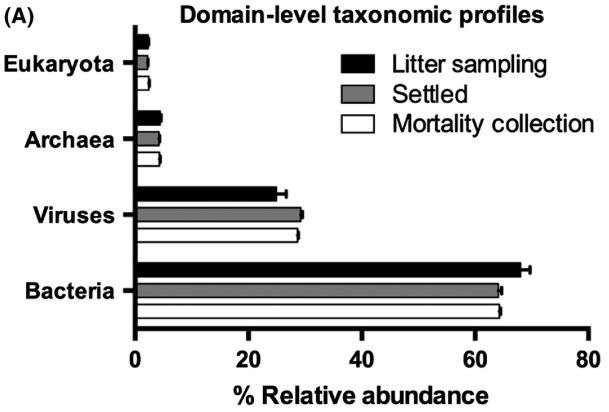
Current Technology: Biases?

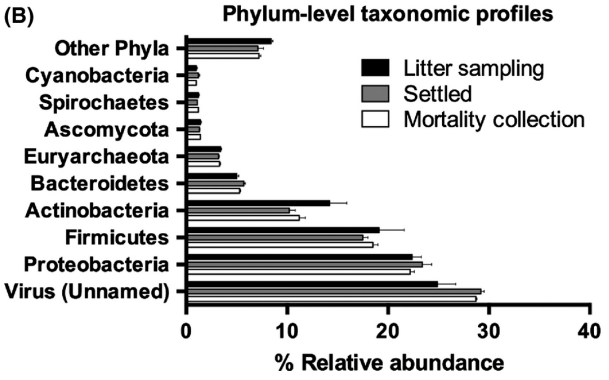
- What organisms are intact after sampling (-)
- What grows on the media (*i.e.*, food to eat) (-)
- What grows under the culture conditions (*i.e.*, temp, oxygen) (-)
- Sampling frame (10 seconds) (-)
- Breathing Zone (-)
- Personal inhalation exposure (-)
- Only bacteria/archaea (-)
- What grows the fastest (*i.e.*, 12 hours) (+)



New Methods: Metagenomics



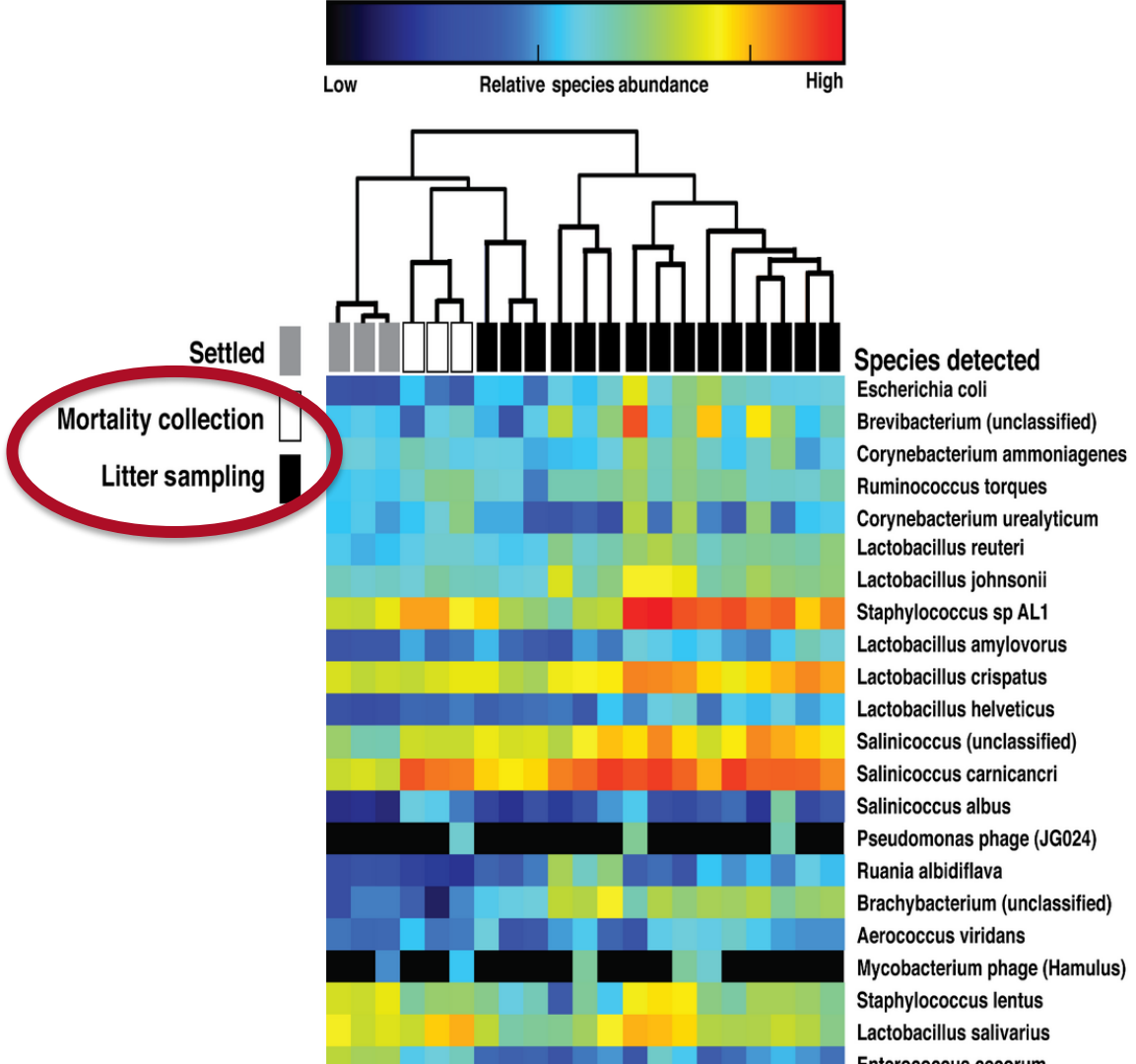




Microbial Biotechnology
28 JUL 2016 DOI: 10.1111/1751-7915.12380
http://onlinelibrary.wiley.com/doi/10.1111/1751-7915.12380/full#mbt212380-fig-0001

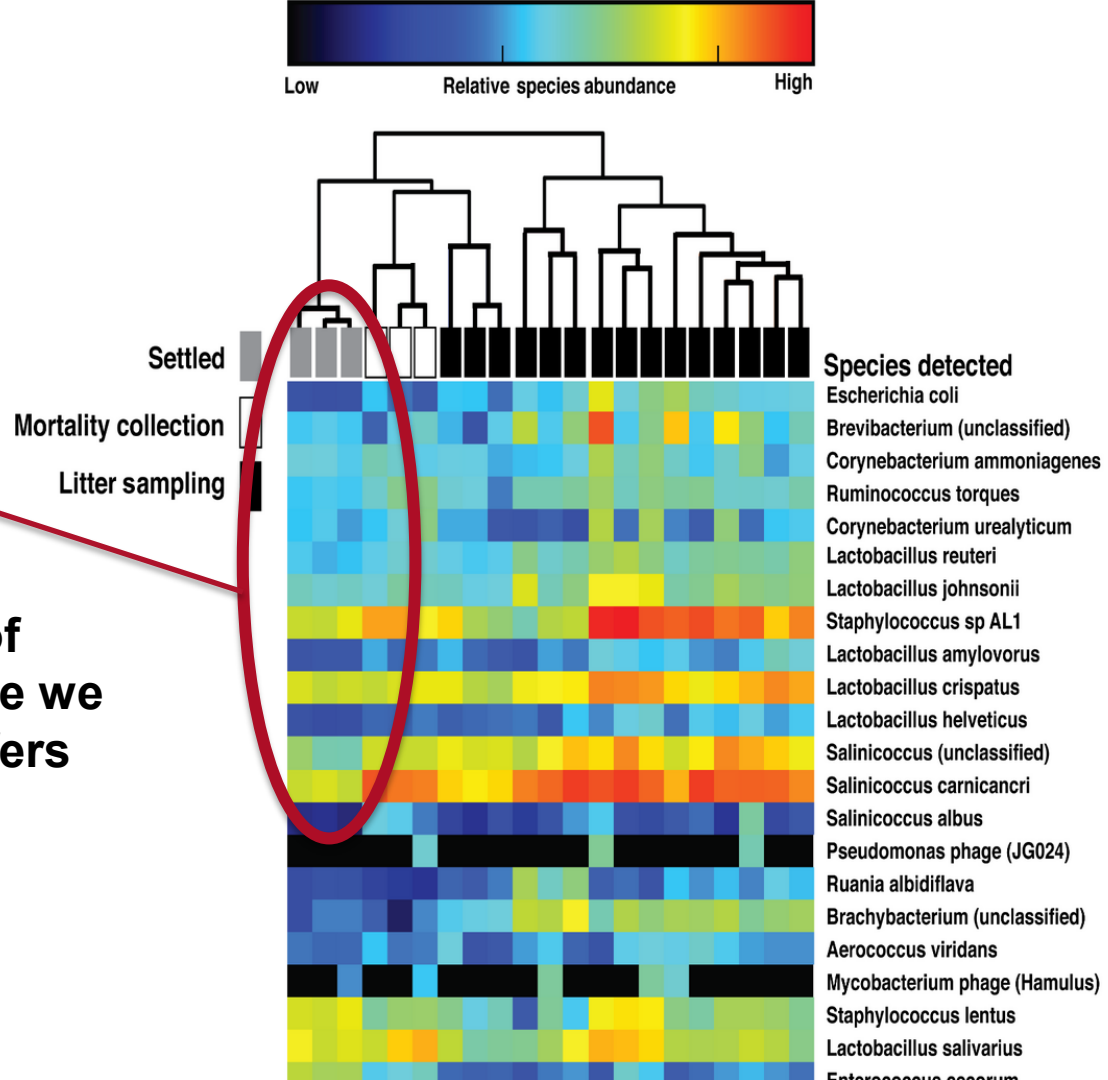
Metagenomics

Tasks



Metagenomics

Dust collected for toxicology studies



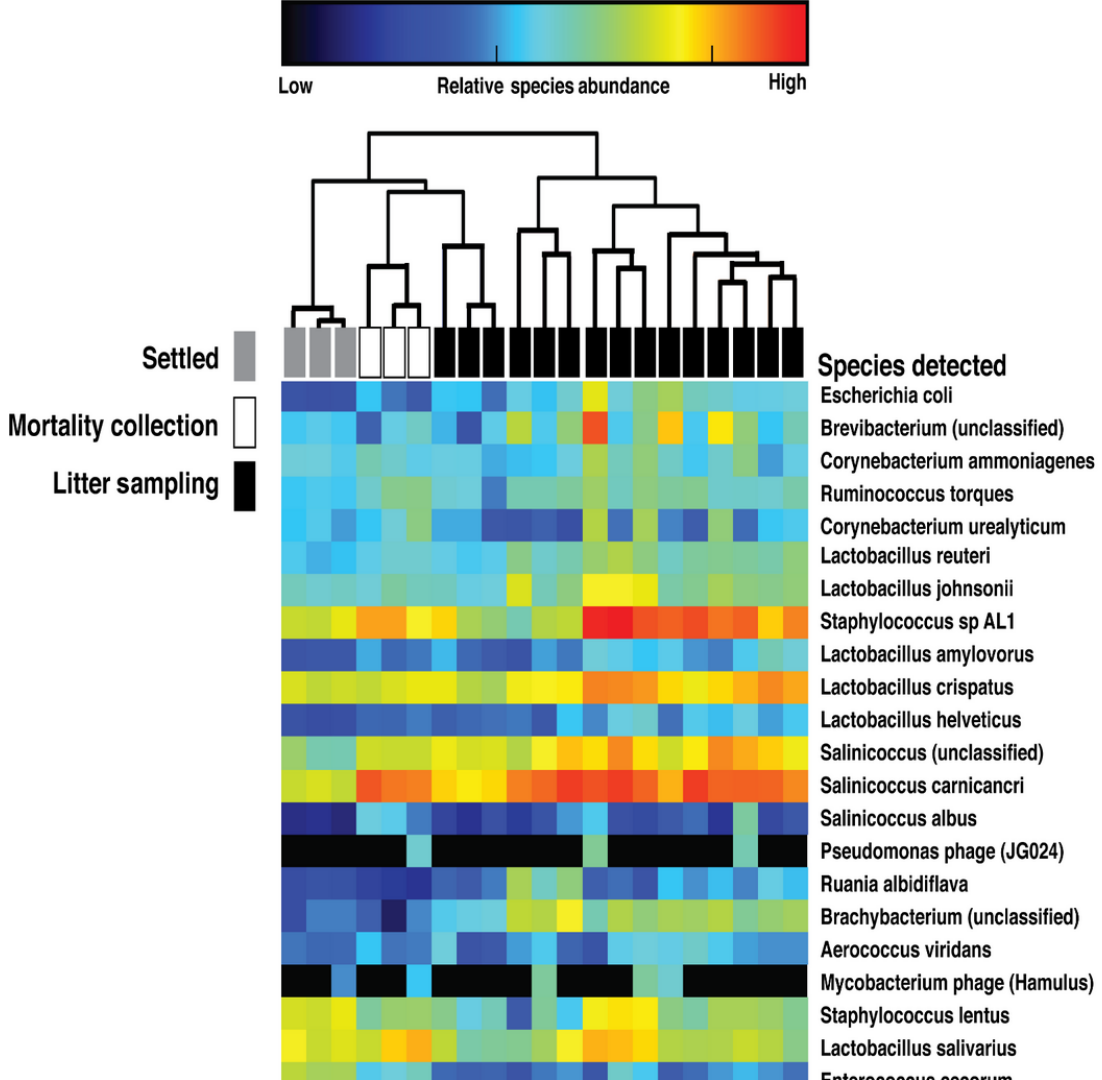
How do we assess the impact of exposure if the dust microbiome we use in toxicological studies differs from the workplace?

Challenge with establishing NOAEL.

Metagenomics

Biases?

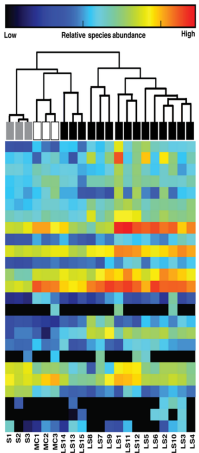
Challenge with establishing NOAEL.



Dynamic, fast paced, work environments: Dairy Parlor

Metagenomic Technology: Biases?

- All DNA sequenced no culture bias – yes!
- Personal inhalation exposure, full shift sampling – yes!
- All organisms that contain DNA – yes!
- Greater specificity - identify many organisms that have not been previously identified – Yes!
- Do we know if the organisms are active – No! ☹
- Can we calculate concentration – No! ☹
    - Tried using 16s technology - Nonnenmann, 2010



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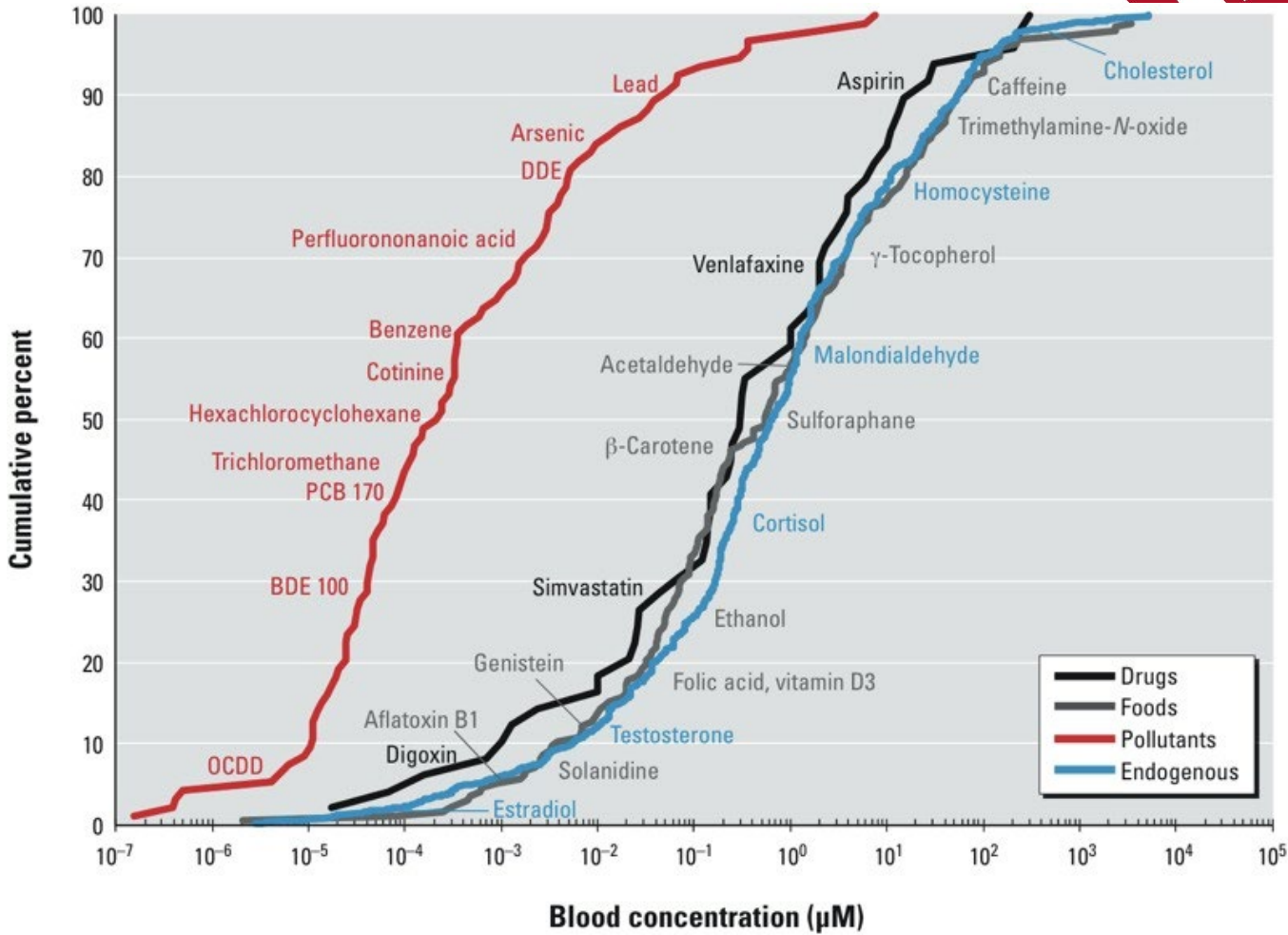
The Future: Microbiome and Exposome

- Single exposure model really doesn't apply



Rappaport, 2014

The Future: Microbiome and Exposome

Exposome:

- High throughput hazard characterization (Dix et al., 2007, Collins et al., 2008)
- High throughput exposure forecasts (Wambaugh et al., 2013)
- High throughput toxicokinetics (i.e., dose-response relationship) linking hazard and exposure (Wetmore et al., 2012)
- Use metagenomic “biome” data to personalize medicine
  - – **Do we know what a normal microbiome is?**

The Future: Microbiome and Exposome

Incorporate microbiome data collection into national health surveys

CDC - National Health and Nutrition Examination Survey (NHANES)

- Ongoing survey representative of the US population
  - demographic, body measures, medical exam, biomonitoring (e.g., health and biomarkers of exposure)
  - reverse dosimetry possible based on biomarkers

Future directions

- microbiome characterizations are not included, but needed for benchmarking (e.g., “normal” microbiome)
- identify *associations* of microbiome patterns with participant characteristics (e.g., diet, sleep, occupational exposures)
- characterize building “biome” data to understand environmental exposures and drive medical decisions

The Future: Microbiome and Exposome

Culturomics

- Advance throughput of microbiological techniques to study the diversity, composition, and function of microbial communities
  - Example: Lung microbiome changes based on exposures
    - Complex bioaerosols – remember 10^6 - 10^9
    - Gases, (e.g., CO_2, irritant gases)
    - Gases, bioaerosol and risk of infectious disease
- Incorporate “representative” microbiomes into animal models for toxicology testing

The Future: Microbiome and Exposome

Artificial Intelligence

- “Big data” analysis
- Machine learning algorithms integrate and analyze data from multiple sources
- Future of AI in IH
  - Example – use AI to integrate data by target organ system, identify exposure duration, “recovery” periods, and personal factors (e.g., age, gender, medication use, comorbidities, etc.)
  - “Brief and Scala 5000” – Ha ha…

The Future: Microbiome and Exposome

Example of Personalized Medicine: Skin Allergy Testing

American Academy of Allergy Asthma and Immunology – skin test recommendations

Standard Panel

1. Alternaria alternata (7)
2. Cladosporium
   herbarum (1), cladosporoides (3), sphaerospermum (10)
3. Penicillium chrysogenum (20)
4. Drechslera/Curvularia or helminthosporium
   bipolaris
5. Epicoccum nigrum (6)
6. Aspergillus fumigatus (30)

Expanded Panel

1. Aspergillus mix (13, 14, 21, 22)
   A flavus (common in indoor settings) (35)
2. Penicillium mix or P. expansum, (28)
3. Fusarium roseum
4. Auerbasidium pullulans (2)
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7. Trichophyton tonsurans: identified as being associated with asthma and nail infections

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Metagenomic data – fungal targets in dust

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Exposure Control and Worker Resiliency Studies:

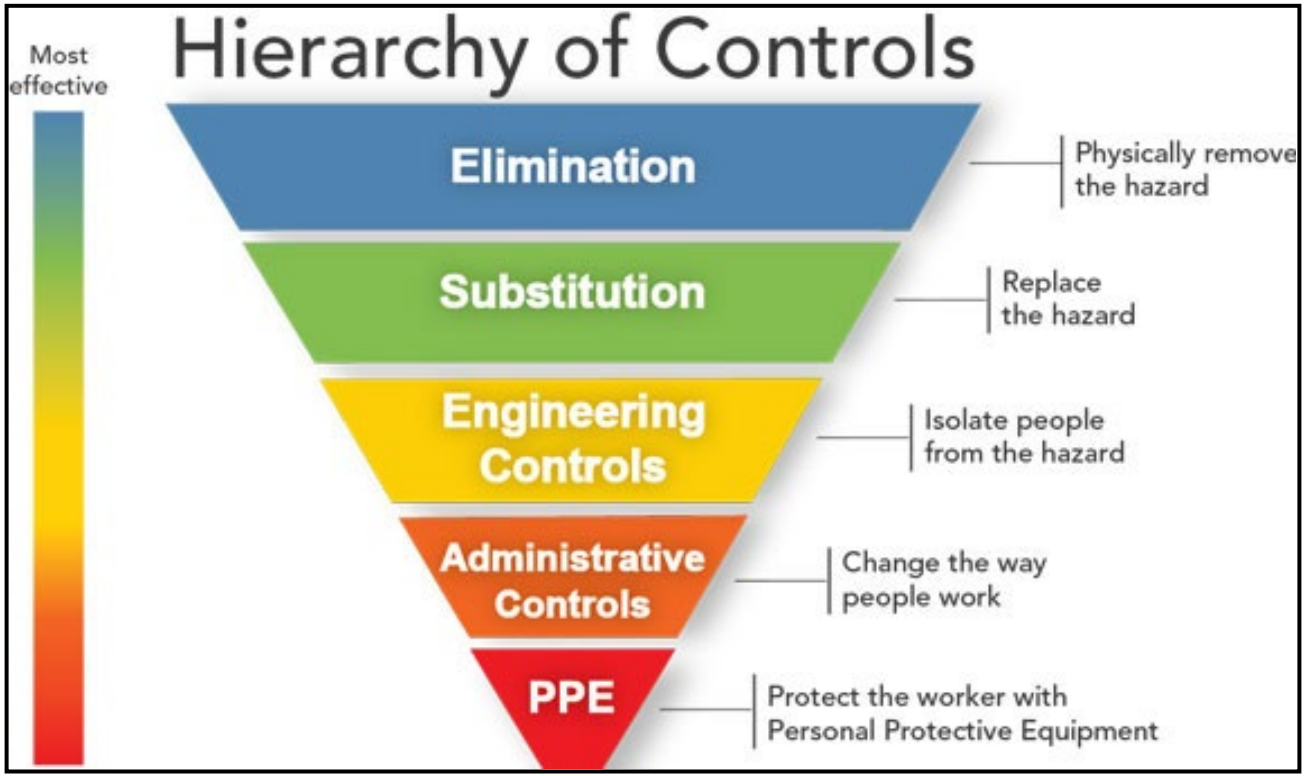
- Do exposure control studies include “baseline” microbiome?
- How does the use of cleaning products impact the worker microbiome?
  - Example: Use of alcohol-based hand sanitizer
- The “kill all the bugs we can” approach – pathway to failure

Exposure Control and Worker Resiliency Studies:

- Therapeutics – probiotic treatments, problematic pathogen treatments (e.g., phage) and nutrition resiliency (e.g., zinc), vaccinations

- Worker wellness – diet, exercise, sleep hygiene effects, Total Worker Health

- How does the use of PPE impact microbiome (?)
  - Barrier clothing and respirators, disposable gloves impact skin microbiome(?)



National Institute for Occupational Safety and Health (CDC)

Conclusions

- The exposome and microbiome overlap
- Methods for measurement we have include many sources of error – one hazard model
- Advancements in exposure science are needed and available
- We need to integrate tools such as AI and use exposure control approaches that are more complex than PPE or the “kill all microbes” method


“If there is one thing about your job you could change, what would it be?”

UNMC COLLEGE OF PUBLIC HEALTH

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AgHealth Central States
Center for Agricultural Safety and Health
www.unmc.edu/publichealth/cscash

University of Nebraska Medical Center

References

- Nonnenmann, M. W., Bextine, B., Dowd, S. E., Gilmore, K., & Levin, J. L. (2010). Culture-Independent Characterization of Bacteria and Fungi in a Poultry Bioaerosol Using Pyrosequencing: A New Approach. Journal of Occupational and Environmental Hygiene, 7(12), 693–699. https://doi.org/10.1080/15459624.2010.526893
- Kate M. O'Brien, Michael S. Chimenti, Morgan Farnell, Tom Tabler, Thomas Bair, Joey L. Bray, Matthew W. Nonnenmann. (2016). High throughput genomic sequencing of bioaerosols in broiler chicken production facilities. Microbial Biotechnology (2016) 9(6), 782–791. https://doi.org/10.1111/1751-7915.12380
- Boles, C., Brown, G., Park, J.H. et al. The Optimization of Methods for the Collection of Aerosolized Murine Norovirus. Food Environ Virol 12, 199–208 (2020). https://doi.org/10.1007/s12560-020-09430-4
- Pratt AA, Brown GD, Perencevich EN, Diekema DJ, Nonnenmann MW. Comparison of virus aerosol concentrations across a face shield worn on a healthcare personnel during a simulated patient cough. Infection Control & Hospital Epidemiology. 2024;45(2):221-226. doi:10.1017/ice.2023.130
- Pratt, A., Eckermann, N., Venugopalan, S.R. et al. Evaluation of aerosols in a simulated orthodontic debanding procedure. Sci Rep 13, 4826 (2023). https://doi.org/10.1038/s41598-023-32082-w
- Knowlton, S.D., Boles, C.L., Perencevich, E.N. *et al.* Bioaerosol concentrations generated from toilet flushing in a hospital-based patient care setting. *Antimicrob Resist Infect Control* **7**, 16 (2018). https://doi.org/10.1186/s13756-018-0301-9
- David J. Dix, Keith A. Houck, Matthew T. Martin, Ann M. Richard, R. Woodrow Setzer, Robert J. Kavlock, The ToxCast Program for Prioritizing Toxicity Testing of Environmental Chemicals, Toxicological Sciences, Volume 95, Issue 1, January 2007, Pages 5–12, https://doi.org/10.1093/toxsci/kfl103
- Francis S. Collins , George M. Gray, and John R. Bucher. Transforming Environmental Health Protection, Science. (2008), Vol 319, Issue 5865 pp. 906-907 DOI: 10.1126/science.1154619
- John F. Wambaugh, R. Woodrow Setzer, David M. Reif, Sumit Gangwal, Jade Mitchell-Blackwood, Jon A. Arnot, Olivier Joliet, Alicia Frame, James Rabinowitz, Thomas B. Knudsen, Richard S. Judson, Peter Egeghy, Daniel Vallero, and Elaine A. Cohen Hubal Environmental Science & Technology 2013 47 (15), 8479-8488, DOI: 10.1021/es400482g
- Barbara A. Wetmore, John F. Wambaugh, Stephen S. Ferguson, Lili Li, Harvey J. Clewell, Richard S. Judson, Kimberly Freeman, Wenjun Bao, Mark A. Sochaski, Tzu-Ming Chu, Michael B. Black, Eric Healy, Brittany Allen, Melvin E. Andersen, Russell D. Wolfinger, Russell S. Thomas, Relative Impact of Incorporating Pharmacokinetics on Predicting In Vivo Hazard and Mode of Action from High-Throughput In Vitro Toxicity Assays, Toxicological Sciences, Volume 132, Issue 2, April 2013, Pages 327–346, https://doi.org/10.1093/toxsci/kft012