Areas of investigation:

1) The microbial ecology of the respiratory tract
   - **What I study:** In the past decade, we have discovered that the lungs – previously considered sterile – harbor diverse and dynamic communities of bacteria. The tools of culture-independent microbiology have revealed a tremendous and unstudied complexity to the microbiota of the respiratory tract. I use the molecular techniques of microbial ecology, including bacterial gene sequencing, to advance our understanding of the relationship between lung bacteria, lung immunity, and respiratory health and disease.
   - **Why it matters:** The lung microbiome is detectable in health, altered in disease, predictive of clinical outcomes, and represents an enormous untapped therapeutic target for the prevention and treatment of respiratory disease.
   - **My key contributions:** I have led the field in defining and determining the ecologic forces that shape the lung microbiome in health and disease, and interrogating how the microbiome informs lung immunity and disease pathogenesis. I have published seminal experimental studies using bronchoscopic sampling to define the bacterial topography of the healthy human respiratory tract. I have published key experimental observations in animals demonstrating the influence of the environment and exposures (e.g. antibiotics) on lung microbiota. I have demonstrated the importance of the lung microbiome in calibrating the “immune tone” of the lungs in health and disease. I have articulated and disseminated novel conceptual models of lung ecology, providing the lung microbiome field with a sound conceptual framework for hypothesis-driven inquiry into the ecology of the respiratory tract.

2) The role of the microbiome in critical illness
   - **What I study:** I study the role of the body’s bacteria, both gastrointestinal and respiratory, on the pathogenesis of critical illness and chronic lung disease. I accomplish this using the techniques of molecular microbiology, including bacterial gene sequencing and DNA quantification. I use an integrative, translational approach, spanning from in vitro and ex vivo assays to small and large animal models of human illness (murine, porcine) to prospective studies of human subjects.
   - **Why it matters:** The common diseases of critical illness – sepsis and the acute respiratory distress syndrome – kill hundreds of thousands of people each year. Yet decades of study have yielded no targeted therapies. I believe this is because the heavily-studied inflammation and tissue injury of critical illness are merely downstream consequences of an upstream source: the disordered bacterial communities of our patients’ gastrointestinal and respiratory tracts. The microbiome has tremendous potential as a diagnostic, prognostic, and therapeutic target in the ICU.
   - **My key contributions:** In a study in *Nature Microbiology*, I demonstrated that the lung microbiome is enriched with gut bacteria both in humans with critical illness and in animal models of sepsis. This publication re-ignited interest in the “gut translocation hypothesis”: in critical illness, a permeable gut epithelial wall permits translocation of bacteria to the lungs, promoting tissue inflammation and dysfunction. I have demonstrated that in critically ill patients, variation in lung microbiota correlates with variation in lung immunity. I have confirmed the causal role of the microbiome by demonstrating that germ-free mice are protected from mortality in a common model of acute lung injury.

3) Bringing the sequencing revolution to bedside diagnostics
   - **What I study:** While the revolution in molecular microbiology has advanced our understanding of the microbiome’s role in health and disease, in our clinics and ICUs we still diagnose respiratory infections using the culture-based techniques of the 19th century. I am using novel sequencing techniques to accelerate our diagnosis of respiratory infections. I accomplish this using a hand-held, USB-powered DNA sequencer (MinION, Oxford Nanopore) to perform real-time metagenomics on patient specimens acquired from University of Michigan patients.
   - **Why it matters:** Pneumonia remains a tremendous cause of morbidity, mortality, and healthcare expense. Current clinical microbiology practices still require 24 hours for species identification and 72 hours for antibiotic susceptibility testing. These are unacceptable delays in critically ill patients, and result in indiscriminate use of empiric broad-spectrum antibiotics. By accelerating time-to-identification and time-to-susceptibility, we can bring precision medicine to our management of respiratory infections, providing tailored antibiotic therapy, improving antimicrobial stewardship.
• *My key contributions:* I published the first demonstration that we can identify respiratory pathogens in patients with pneumonia using real-time metagenomics\(^\text{12}\), identifying pathogens far faster than via conventional clinical microbiologic approaches. I published the first systematic comparison of quantitative culture, qPCR, and 16S-amplified microbiome analysis in the interpretation of bronchoalveolar lavage specimens in pneumonia\(^\text{11}\).

**Accomplishments, honors, and recognitions**

1) **Academic productivity and funding:** I have authored 56 PubMed-indexed manuscripts (39 since 2015). These include first- and senior-author manuscripts in high-impact journals such as *Nature Microbiology*, *Lancet*, and the *American Journal of Respiratory and Critical Care Medicine*. My H-index is 24, with more than 2,300 citations since 2015. I have successfully obtained R01 funding from the NHLBI and R21 funding from NIAID, as well as multiple internal and foundation awards. My first R01 proposal received a perfect impact score (10).

2) **Honors and awards:** My research has been honored with multiple institutional, national, and international awards. I hold the University of Michigan’s Bruce C. Richardson MD Department of Internal Medicine Early Career Endowment Award. I have received both a Young Physician-Scientist Award from the American Society of Clinical Investigation as well as an Early Career Investigator Award from the American Thoracic Society.

3) **International recognition:** I am a member of the Editorial Boards of the three most high-impact journals in my field: *Lancet Respiratory Medicine*, *American Journal of Respiratory and Critical Care Medicine*, and *European Respiratory Journal*. I am an Associate Editor for *Microbiome*, and a Specialist Editor for *European Respiratory Journal*. Since 2015, I have delivered 21 invited talks at international conferences, and 12 invited talks as Visiting Professor to U.S. institutions.

**Collaborations**

I am an active collaborator, providing methodological and clinical expertise to numerous collaborative initiatives. I am a Project Leader on a funded €10 European Commission award (PI Roquilly), an NIH P01 submission (PI Stringer, submitted September 2019) and a $11 million Department of the Defense proposal (PI Najarian, submitted July 2019). I am a Co-Investigator on four funded NIH proposals and six submitted proposals. As an Associate Director of the Michigan Center for Integrative Research in Critical Care, I serve as a “connector,” facilitating productive research collaborations between Critical Care investigators and the rest of the University.

**References cited**


