

Statement of Research Philosophy

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Research facilitates human curiosity by enabling a logically driven investigation to evaluate scientific concepts. It provides refinement in our understanding and fuels the technological advancement required to improve human life. Research is the keystone for a successful university and is critical for enhancing science, technology, and industrial performance. Research is especially crucial for clinical sciences to improve health-care and service-delivery models. Clinical fields, such as audiology, are critically dependent on research.

Hearing Health – A Global Concern:

According to world health organization¹, around 566 million people worldwide have disabling hearing health conditions (e.g., hearing loss, tinnitus – ringing in ears/head). It is estimated that over 900 million people will have disabling hearing loss and related health concerns by 2050. About 1.1 billion youth aged 12-35 years are at risk for permanent hearing loss due to excessive recreational noise. Unaddressed hearing concerns poses an annual global cost of US \$750 billion. Untreated hearing concerns can cause stress, anxiety, depression, cognitive decline, and poor quality of life. About 80% of hearing problems are due to preventable conditions; however, most hearing disorders are not curable once acquired. The lack of clear identification of genetic and molecular architecture of hearing disorders have hindered the development of prevention and individualized treatment strategies.

Philosophical Premise:

My research philosophy is driven by my curiosity to understand the hearing process. After pursuing the graduate degree in clinical audiology, a desire to deepen understanding of hearing disorders led my way to the Ph.D. program at the University of North Carolina at Greensboro. My outstanding mentors equipped me with a wide range of research tools and opened a door for me to the scientific research world. My research program is focused on genomics of hearing disorders, which is an emerging approach for hearing disease treatment and prevention that takes into account individual variability in genetic makeup, environmental factors, and lifestyle for prevention and treatment of hearing disorders. I devised a non-invasive audiological approach for investigating the genetic architecture of hearing disorders. My research targets three key aspects: (1) identifying genetic risk factors, (2) developing individualized prevention and treatment strategies, and (3) developing genetic medicines for patients suffering from tinnitus (*i.e.*, ringing in the ears/head) and hearing loss.

Research Impact:

Research on precision medicine suggests that clinicians armed with the knowledge of genetic predisposition to a health condition can provide better clinical services to their patients. Understanding the genetic and molecular architecture of hearing disorders can revolutionize the clinical practices and service-delivery models in the field of audiology. Currently, no tools are available to identify “susceptible” individuals before they acquire a permanent form of hearing disorders. Besides, no surgical or medical approaches are available for the prevention and

treatment of prevalent hearing disorders, such as age-related hearing loss, noise-induced hearing loss, and tinnitus (*i.e.*, ringing in the ears/head). The genetic risk profiling can empower clinicians by identifying “susceptible” individuals well before they acquire hearing disorders. It can fuel the discovery of individualized pharmaceutical approaches, use of hearing protection devices, dietary changes or supplements, behavior modifications, and hearing-care education programs. My research will continue to benefit all patients with hearing disorders and populations that are at risk for hearing impairment. People exposed to intense sounds, such as industrial workers, military personnel, firefighters, professional musicians, and music lovers, will continue to be benefited by my research. This research program is critical for industrial advances in developing precision prevention and treatment technologies for tinnitus and hearing loss.

Research Agenda – Current and Future Research Directions:

My lab is currently investigating the genetic basis of tinnitus and noise-induced hearing loss. I devised a powerful audiological approach, referred to as “deep phenotyping” to facilitate genetic association to tinnitus and hearing loss. The deep phenotyping approach utilizes existing audiological techniques to quantify clinical heterogeneity and biological processes underlying hearing disorders. This program includes the following research lines:

- **Genetic-Risk Profiling of Tinnitus:** Tinnitus, commonly known as ringing in ears/head, is a highly prevalent hearing disorder in US adults. Over 50 million Americans experience some form of tinnitus, and almost 20 million people struggle with clinical tinnitus, while 2 million have extreme and debilitating cases². I investigated the epidemiology of tinnitus in young college-aged students to document the effects of environmental and health-related risk factors for tinnitus. This research line laid out a theoretical foundation for investigating the genetic influence on tinnitus. My current project, funded by the **National Institute of Health** (National Institute for Deafness and Other Communication Disorders, Early Career Award # 1R21 DC016704-01A1), is investigating the genetic influence on tinnitus in healthy young adults. The study aims to identify clinically useful genetic risk profile for tinnitus.
- **Genetic-Risk Profiling of Noise-Induced Hearing Loss (NIHL):** NIHL is a frequently occurring hearing disorder in individuals exposed to loud noise/music. About 10 million US adults exhibit NIHL³. Patients with NIHL often experience speech perception in noise difficulties (*i.e.*, speech-in-noise deficit). I investigated the genetics of NIHL in young musicians. The deep phenotyping approach was utilized to examine the biological processes underlying NIHL. The research identified novel genetic risk factors for NIHL (Major genes: ESRRB and KCNE1). My subsequent studies evaluated the effects of high noise exposure on the speech-in-noise ability for adults with “normal” hearing sensitivity. These studies revealed that adults with high noise exposure and with “normal” hearing can exhibit speech-in-noise deficit. This research laid out a theoretical groundwork for investigating the genetic architecture of speech-in-noise deficit. I am studying the genetic network underlying NIHL and speech-in-noise deficit that will be crucial to develop individualized prevention and treatment plans for millions of patients suffering from these conditions.
- **Precision Medicine for Noise-Induced Hearing Loss:** My research identified a novel genetic susceptibility locus, rs61742642 Estrogen-Related Receptor Beta (ESRRB), which accounted

for around 25% of the variability in NIHL measures in a sample of young musicians. My study identified a new drug targeted to rs61742642 ESRRB to prevent and treat NIHL in mice. This work laid out a theoretical foundation to design a genetic test and a precision medicine approach for treating NIHL in humans.

Research Effectiveness:			
Grant funding	Article published	Article under review	Presentations
Total: \$631,640	8	5	22

Research Values:

I believe that scientific research is the backbone of clinical audiological services. As a researcher, he values scientific rigor. Scientific research should be conducted in a rigorous manner, which requires great patience, effort, skills, and dedication. He applies appropriate research methods and tools to ensure scientific rigor and data quality. I value an analytical approach/a critical thinking mindset. The analytical approach is necessary to address scientific questions. Researchers should visualize a big picture and utilize tools and techniques to advance science. It is critical to pay careful attention to details throughout the literature review, data collection, data analysis, and communication of the findings. I value interdisciplinary collaboration. It is the most effective way to address hearing health concerns for answering more in-depth questions. I am collaborating with the researchers in the area of genetics, genomics, cell signaling, signal processing, electrical engineering, computer engineering, mathematics, statistics, and informatics. These interdisciplinary collaborations have enriched my research experience and helped me address profound research questions. I value life-long learning. The university environment provides endless opportunities for learning new ideas and skills. Life-long researchers are life-long learners. Acknowledging and addressing our limitations are important for perusing research excellence.

Development of the Next Generation Scientists:

The field of audiology is in **critical shortage**⁴ of Ph.D. level audiologists, that must be addressed systematically to ensure the bright future of the profession. Student engagement in research is an essential component in developing the next generation of clinicians and scientists. My research program provides valuable research-related and leadership opportunities to students across multiple disciplines. I involve students when he develops and identifies the theoretical framework underlying genetic influence on hearing disorders, conducts experiments to evaluate the theoretical foundation, constructs individualized prevention and treatment strategies for audiological diseases, and share my research findings with researchers, clinicians, students, and others.

Major References:

1. Deafness and hearing loss. (2019). Retrieved from <https://www.who.int/news-room/fact-sheets/detail/deafness-and-hearing-loss>
2. Understanding the Facts. (2018, October 31). Retrieved from <https://www.ata.org/understanding-facts>
3. Noise-Induced Hearing Loss. (2019). Retrieved from <https://www.nidcd.nih.gov/health/noise-induced-hearing-loss>
4. Jacobson, G. P., & McCaslin, D. L. (2019). Figures 1 and 2, and Why You Should Worry a Lot More About These Figures Than the One We Showed You in 2014. *Journal of the American Academy of Audiology*, 30(4), 248.