Department of Otolaryngology
Head & Neck Surgery
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

Department of Otolaryngology – Head & Neck Surgery

Department of Otolaryngology – Research Retreat

November 14, 2024

Yuri Agrawal, Professor, Department Chair

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Retreat Agenda

8am-11am: Cluster presentations

11am-12pm: Synthesis of discussion, grouping of cross-cutting themes and priorities across clusters for the Department

12pm-1pm: lunch; Drs. Alan Cheng and Sid Puram will break off into a separate room to discuss their findings & recommendations

Discussion Questions for each Cluster

1. What are the focal points of the cluster's research program?
2. What are the current strengths and weaknesses of the cluster's research program?
3. What are opportunities and threats for the cluster to consider for its research program, and what steps should the cluster take given these opportunities and threats? For both opportunities and threats, consider emerging trends in the research discipline, federal funding patterns and trends, interdisciplinary collaborations, collaborations with clinicians, etc.
4. What recommendations would you make to Department leadership to advance your research cluster and the Department's scientific portfolio?

Research Clusters

1. Hearing and balance physiology: Department leads: **Katie Rennie and Nate Greene**
    a. Affiliated faculty: Sam Gubbels, Steve Cass, Dan Tollin, Achim Klug, Anthony Peng, Tim Benke
2. Clinical Translational: Department leads: **Vinay Manchaiah and Ashley Nassiri**
    a. Affiliated faculty: Yuri Agrawal, Marie Jette, Tina Studts, Liza Creel, Sung-Joon Min, Anu Sharma, Racheal Baiduc, Dan Tollin, Achim Klug, Kristin Uhler, Sean Iwamoto, Micol Rothman, Rita Lee, Dan Loeb
3. Chemical senses: Department leads: **Sue Kinnamon and Conner Massey**
    a. Affiliated faculty: Ashoke Khanwalkar, Diego Restrepo, Tom Finger, Stephen Santoro, Linda Barlow
4. Otolaryngology Omics: Department leads: **Sarah Clark and Regie Santos-Cortez**
    a. Affiliated faculty: Sarah Gitomer, Brian Herrmann, Daniel Frank, Kirk Harris, Eszter Vladar, Edward Janoff, Alexander Horswill, Jenna Guthmiller, Breck Duerkop, Catherine Lozupone, Elan Eisenmesser, Janani Ravi, Bifeng Gao, Nancy Hadley-Miller, Katrina Kechris, Rita Lee, Shay Guetz-Lindahl, Tzu Phang, David A. Schwartz, Stig Somme, Kristin Uhler, Ivana Yang, Sonja Ziniel
5. Head and neck cancer: Department leads: **Shi-Long Lu and Carissa Thomas**
    a. Affiliated faculty: Daniel Frank, Julia Goddard, Brian Cervenka, Eric Clambey, Regie Santos-Cortez, Kristin Kuhn, Dexiang Gao, Charles Robertson, Nichole Reisdorph, Chaitanya Puranik, Katrina Kechris, Mary Rayland, Natalie Serkova, Mohamed Said, Tzu Lip Phang, Zirui Wang, Antonio Jimeno, Leah Novinger

Hearing and balance physiology: Departmental and affiliated faculty

Katie Rennie, PhD, Professor:
The Rennie Lab studies how different cell types in the peripheral vestibular system process sensory information. The lab uses electrophysiological, pharmacological, imaging and modeling techniques to study signaling between vestibular hair cells and their associated afferent fibers.

Nate Greene, PhD, Associate Professor:
Dr. Greene's research focuses on the mechanics and physiology of the auditory system and hearing. His lab focuses on the effects of using hearing restoration devices and hearing protective devices, as well as the mechanisms of hearing loss during high level sound exposure. Studies on hearing restoration devices include investigating the causes of loss of residual acoustic hearing in cochlear implant patients, and transmission of sound via bone conduction. These devices often involve substantial surgical procedures that can cause injurious levels of inner ear stimulation. Likewise, normal use of these devices stimulates the inner ear with indirect, non-ossicular pathways, which can result in unexpected interactions and perceptions. Current studies are focusing on quantifying these effects, investigating their sources, and developing strategies to mitigate their negative effects.

Anna Dondzillo, PhD, Assistant Professor-Research:
My research focuses on understanding the effects of aging on the nervous system, and ultimately, I want to develop therapeutic or preventive strategies for age-related sensory degeneration, particularly in the auditory and vestibular systems. By exploring the specific cellular and synaptic mechanisms that differentiate healthy status from age-related degeneration, I aim to identify key targets for restorative or preventive treatments. Three primary areas of focus drive my work: sensorineural hearing and balance loss, the regenerative potential of the cochlea, and the impact of vestibular schwannoma on human vestibular sensory cells.
In my studies on age-related cochlear degeneration, I discovered a sex-dependent variation in neuronal innervation of sensory cells, emphasizing the importance of sex as a biological variable in auditory research. Additionally, I mentored projects investigating cochlear regeneration, which have demonstrated the potential of murine cochlear cells to proliferate after sensory cell loss, as well as the ability of human pluripotent cells to differentiate into sensory cells in the cochlea. This research holds promise for future therapeutic strategies aimed at restoring hearing. Furthermore, my work on the central auditory system led to the identification of a novel recurrent neuronal connection within the central inhibitory nucleus, contributing to our understanding of sound localization in the brainstem. Additionally, my collaborative efforts have explored the effects of vestibular schwannoma on vestibular cell loss with aging, revealing an accelerated degeneration in patients with this tumor, a finding that has been presented at multiple conferences. Ultimately, my research combines histological, imaging, and electrophysiological approaches to uncover the mechanisms driving age-related changes in the nervous system, intending to develop mitigation strategies.

Hearing and balance physiology: Collaborators and affiliated faculty

The Department of Otolaryngology has several collaborations with faculty in basic science departments that have research interests that relate to otolaryngology. The Department of Physiology and Biophysics has several investigators interested in mechanisms of hearing. These include ***Drs. Dan Tollin*** *(central mechanisms of sound localization),* ***Achim Klug*** *(inhibition in the auditory brain stem), and* ***Anthony Peng*** *(mechanotransduction in the auditory*

and vestibular systems). ***Dr. Tollin*** *collaborates extensively with* ***Dr. Nate Greene****, and also with neurotologists* ***Drs. Steve Cass*** *and* ***Sam Gubbels****. He has mentored several T32 trainees.* ***Dr. Peng*** *currently mentors a T32 trainee and collaborates extensively with* ***Dr. Kennie Rennie****; they have joint NIH grants together from NIDCD and NIA.* ***Dr. Klug*** *has mentored previous T32 trainees and has NIH grant submissions with Dr's Tollin and Rennie.* ***Dr. Tim Benke*** *(Department of Pharmacology) collaborates with Dr. Rennie to study synaptic signaling in the vestibular system and mentors a T32 postdoctoral trainee. These investigators participate in a hearing and vestibular group that meets biweekly on Friday mornings to give research updates and discuss recent publications. Drs Agrawal, Klug, Peng, Rennie and Tollin were recently awarded an internal ASPIRE grant that focuses on synaptopathy as a common etiology underlying hearing and balance disorders with aging. The goal of this funding mechanism is to foster development of interdisciplinary research programs on the Anschutz medical campus.*

Clinical translational: Departmental and affiliated faculty

Vinaya Manchaiah, AuD, PhD, Professor (Audiology):
My primary research goal is to improve accessibility, affordability, and outcomes of hearing healthcare services by promoting self-management and also the use of digital technologies. My current research interests can be summarized along with the following four themes:

1. **eHealth (or Telehealth):** Applications of the internet and modern information technology in the management of hearing-related disorders, in particular, guided behavioral rehabilitation via the internet (i.e., telerehabilitation or digital therapeutics).
2. **Hearing healthcare service delivery model:** Developing evidence-base for new service delivery models (i.e., direct-to-consumer model, community-based rehabilitation) to improve accessibility, affordability, and outcomes of hearing healthcare services.
3. **Consumer Health Informatics (CHI):** The focus is to understand the health communities, as well as patient-generated data and its uses within and outside healthcare systems. In particular, this line of research focuses on understanding the use of information from various digital mediums (e.g., Internet, social media) in self-assessment and self-management of people with communication disorders.
4. **Psychosocial aspects of hearing and balance disorders:** This line of research has three distinct areas, which include: (a) understanding the knowledge, attitudes, and behaviors of adolescents and/or young adults towards music-induced hearing loss and developing preventative strategies; (b) understanding the psychosocial factors related to help-seeking, hearing rehabilitation uptake and use, and to develop appropriate rehabilitative strategies; and (c) understanding the psychosocial consequences of Ménière's disease on the individual affected and their significant others.

Ashley Nassiri, MD, MBA, Assistant Professor (Otology-Neurotology):
The Hearing Health Access Lab, led by Dr. Nassiri, focuses on systematic changes that will improve access to hearing health care in the United States. Prior work has established updated incidence of cochlear implant, metrics for evaluating progress in improving hearing health access, geographic associations in cochlear implant access, and strategies for expanding cochlear implant programs through process efficiencies. Current and future work include establishing a PTA "cut off" for referral for diagnostic testing in adult hearing screening protocol, implementation of adult hearing screening within the UCHealth system and CO community, examining failed newborn hearing screening loss to follow-up and establishing state-based protocols to ensure proper follow-up and intervention when indicated, and identifying and addressing current barriers to care and systemic bottlenecks for cochlear implant candidates nationally.

Yuri Agrawal, MD, MPH, Professor, Department Chair (Otology-Neurotology):
My research program is aimed at understanding the changes in vestibular function that occur with aging and their impacts on physical and cognitive function in older adults. My group was the first to estimate the prevalence of vestibular impairment in the general US population. Our report of a surprisingly high prevalence of 35% vestibular impairment among US adults has been cited >1000 times and has motivated a number of investigators around the world to pursue

vestibular research. Our group was also among the first to rigorously demonstrate the cognitive changes associated with vestibular impairment in older adults. We reported findings from the Baltimore Longitudinal Study of Aging showing a strong relationship between vestibular function and measures of spatial cognitive function in older adults. Moreover, we were among the first to report a significant relationship between vestibular loss and hippocampal atrophy in older adults. My research program is inter-disciplinary and over the years I have worked to cultivate a diverse group of scientists into this research field including neuroscientists, engineers, cognitive psychologists, geriatrics researchers and statisticians.

Marie Jetté, PhD, Assistant Professor (Laryngology):
My research focuses on understanding the biologic and behavioral mechanisms underlying chronic cough and its treatment, with a particular emphasis on the role of laryngeal chemical receptors in initiating and perpetuating cough hypersensitivity. My research collaboration, comprised of researchers at the University of Montana and Emory University, has evaluated survey data, analyzed patient outcomes, helped to develop novel ambulatory monitoring tools, and designed an internet-based treatment, aiming to improve understanding and management of chronic cough. Through translational models and human clinical trials, my research seeks to uncover the mechanisms by which laryngeal afferents contribute to chronic cough and evaluate the efficacy of targeted interventions, ultimately aiming to advance treatment options for patients with chronic cough disorders.

Clinical translational: Collaborators and affiliated faculty

The faculty at the Department of Otolaryngology has extensive collaborations with faculty in at CU SoM and other institutions across the globe. Dr. Manchaiah has ongoing collaboration with ***Dr. Anu Sharma*** *at CU Boulder whose work focuses on how the brain adapts to hearing loss and auditory neurorehabilitation using tools such as EEG, and* ***Drs. Tina Studts*** *(ACCORDS),* ***Liza Creel*** *(healthcare policy research),* ***Sung-Joon Min*** *(healthcare policy) studying the service delivery model of over-the-counter hearing aids (existing R01). Dr. Manchaiah has collaboration with Dr. Nassiri on few projects on cochlear implants and hearing healthcare service delivery model. Dr. Manchaiah also has active collaborations on a range of project with researchers across the globe including* ***Dr. Rachael Baiduc*** *at CU Boulder,* ***Drs. Sumit Dhar and Larry Humes*** *at Northwestern University,* ***Dr. De Wet Swanepoel*** *at the University of Pretoria, South Africa,* ***Dr. Gerhard Andersson*** *at Linkoping University, Sweden.*

Several other researchers have emerging research that may intersect with this theme. These include ***Drs. Dan Tollin*** *(central mechanisms of sound localization in older adults),* ***Achim Klug*** *(drug development to address sound localization and speech-in-noise issues in older adults), and* ***Kristin Uhler*** *(speech and language development in infants and children).*

Dr. Jetté's primary collaborators include ***Drs. Laurie Slovarp*** *and* ***Jane Reynolds*** *at the University of Montana, and* ***Dr. Amanda Gillespie*** *at Emory University, who are all clinician scientists with interest in voice and cough disorders. Dr. Jetté also provides peer mentorship and collaborative support for research projects with* ***Dr. Allison Hilger****, a motor speech disorders researcher at CU Boulder who is investigating speech characteristics in subtypes of motor speech disorders and aerosolization during speech. In addition to her primary research focus, Dr. Jetté also collaborates with clinician-scientists within the Integrated Transgender Program including* ***Drs. Sean Iwamoto****,* ***Micol Rothman****,* ***Rita Lee****, and* ***Dani Loeb****.*

Chemical senses/olfaction: Departmental and affiliated faculty

Sue Kinnamon, PhD, Professor:
The Kinnamon lab is interested in mechanisms of taste transduction and afferent signaling. What are the mechanisms used by taste cells to detect the different taste stimuli and what neurotransmitters are released by the taste cells to activate gustatory afferent nerve fibers? Recent studies have focused on the role of the different cell types in the taste bud-- what taste qualities are transduced by Type II and Type III taste cells and what are the taste receptors and signaling mechanisms utilized? How do the "glial-like" Type I cells support the long-term maintenance of the taste bud and do these cells participate in cell-to-cell signaling within the taste bud? Finally, does intercellular signaling modify the neural output taste signal to the brain? The Kinnamon lab utilizes a variety of approaches to address these questions in transgenic mice, including taste afferent nerve recording, brief access behavioral assays, rt- and single cell PCR, immunocytochemistry, isolation of single taste cells, calcium imaging, and patch clamp recording. Another interest of the lab has been the role of extra-oral bitter taste receptors in the airways and how these receptors initiate a trigeminally-mediated protective airway reflex against bacterial pathogens. These studies utilized both transgenic mice and human tissue obtained from collaborations with Otolaryngology Department rhinologists.

Conner Massey, MD, Assistant Professor (Rhinology, VA):
My research interests include AI applications in rhinology, and environmental exposure and its interaction with rhinologic health, both from air pollution and/or occupational exposures. I completed a T32-trainee program here at CU under the mentorship of Vijay Ramakrishnan. I was awarded AAO-HNS CORE funding for work in validating an AI-based algorithm for sinus CT analysis. During those years, I also collaborated with Diego Restrepo, PhD, performing live *ex vivo* histologic characterization of human olfactory epithelium using 2 photon imaging. My work in fellowship at the University of Utah focused on rhinologic clinical outcomes, validation studies for diagnostics in eosinophilic chronic rhinosinusitis, and environmental exposure in rhinology. Now based primarily at the Rocky Mountain Regional VA, I have access to a unique patient population for measuring occupational toxic exposures, as well as access to critical epidemiologic databases like the national Corporate Data Warehouse and the VA Airborne Hazard and Open Burn Pit Registry. The RMR VA is an Airborne Hazard Center of Excellence, offering many opportunities for clinical research and rich collaborations with occupational exposure experts. Finally, I plan to provide sinonasal and olfactory tissue for ongoing work with Diego Restrepo for his human olfactory tissue projects (R21 grant currently in submission).

Ashoke Khanwalkar, MD, Assistant Professor (Rhinology):
As a fellowship trained rhinologist who treats patients with sinonasal disorders, I have the expertise, training, and motivation necessary to support the studies in this clinical area. I have a particular clinical interest in olfaction. During my residency at Northwestern University, I worked in the basic science lab of NIH-funded physician researcher Dr. Bruce Tan studying local tissue biomarkers to assess the health of a patient's olfactory neuroepithelium. I completed my rhinology fellowship at Stanford University with one of the clinical leaders in the field of olfaction, Dr. Zara Patel, gaining further insight into the current and future treatment paradigms for our patients. Among my studies there, we worked on a randomized controlled trial for the local administration of platelet-rich plasma to enhance olfactory recovery in those with smell loss following infection with COVID-19. I am also a contributing author on the International Consensus Statement on Allergy and Rhinology: Olfaction, authoring sections on congenital and age-related olfactory loss. I look forward to the opportunity to contribute to scholarship based

on my clinical expertise, and to provide the context that will help bridge advances to support improved care for our patients.

Chemical senses/olfaction: Collaborators and affiliated faculty:

Another area of joint interest involves several investigators who are part of the Rocky Mountain Taste and Smell Center. The Center was originally funded by an NIDCD-funded program project grant and later by a NIDCD-funded core facility. Several investigators that comprise the facility are based in the Department of Cell and Developmental Biology. These include ***Drs. Diego Restrepo*** *(role of olfaction in viral disorders and Alzheimer's Disease),* ***Linda Barlow*** *(development and renewal of taste bud cells and role of chemotherapy in taste loss), and* ***Tom Finger*** *(role of cell types and transmitters in taste buds and taste loss after Covid-19).* ***Dr. Stephen Santoro*** *(olfactory development) is a relatively new member of the group in the Dept. of Pediatrics. He is currently mentoring one of our T32 predoc trainees.* ***Dr. Restrepo*** *collaborated extensively with* ***Dr. Ramakrishnan*** *when he was here and now collaborates with* ***Dr. Ash Khanwalkar*** *in mentoring a T32 postdoc.* ***Drs. Finger and Linda Barlow*** *have had collaborations and joint grants with* ***Dr. Sue Kinnamon*** *and have co-mentored trainees.* ***Dr. Barlow*** *also collaborates with head and neck surgeons in Otolaryngology to obtain human taste tissue for developing organoid cultures. The taste and smell center has a bi-weekly journal club where mentors and trainees present.*

Otolaryngology Omics: Departmental and affiliated faculty

Sarah E. Clark, PhD, Assistant Professor:
I am interested in how respiratory tract infections are influenced by interactions between bacteria and the host immune system. My research program is currently divided into two primary project areas, otitis media and bacterial pneumonia. For otitis media, I am interested in the bacterial-host interactions influencing middle ear invasion and infection. Specifically, we are investigating how viral co-infection dysregulates the function of innate immune cells in the middle ear, leading to increased infection with *Streptococcus pneumoniae*. This work uses primarily mouse infection models along with patient sample data from children with recurrent or chronic otitis media. For bacterial pneumonia, I am interested in how exposures to other airway bacteria influence pathogen infection of the lower airway. A large focus of our current work explores the impact of the commensal bacterium *Prevotella*, which we find primes enhanced neutrophil-mediated clearance of *S. pneumoniae* from the lungs. We are also using respiratory tract epithelial models to investigate how pre-exposure and colonization with airway commensal bacteria impairs adherence and cytotoxicity caused by pathogens including *S. pneumoniae* and *Staphylococcus aureus*. The long-term goals of this work are to enhance our understanding of how both beneficial and pathogenic bacteria modulate host responses to improve the prevention and treatment of respiratory tract infections using microbe and host-directed therapies.

Regie Santos-Cortez, MD, PhD, Associate Professor:
Our goal is to identify genetic and epidemiologic factors that influence risk for otolaryngologic diseases, such as otitis media, hearing loss, vestibular disorders and obstructive sleep apnea/sleep-disordered breathing. Our studies are made possible through close collaboration with scientists and clinicians on campus and in multiple institutions within the US and the Americas, Asia, and Europe. Otitis media is an important disease in early childhood and is one of the most common reasons for healthcare visits and antibiotic prescription. It is the leading cause of conductive hearing loss in children, which if not addressed may result in permanent deficits in hearing and auditory processing. Despite the global significance of otitis media as a leading disease of communication, there has been attrition of otitis media researchers over the past decades. This has resulted in less attention to otitis media as a topic of scientific investigation and in the remaining knowledge gaps that could be addressed by basic, translational and clinical research. It also prevents the faster adaptation of new technologies toward improved management of otitis media. To this end, the COMMeND program was created and funded by an NIH R25, to encourage young investigators to get into and stay involved in otitis media research.

Sarah Gitomer, MD, Assistant Professor (Pediatric Otolaryngology):
I am interested in integrating microbiome research into clinical care for chronic pediatric ENT infections, and in studying conductive hearing loss associated with AOM and microtia/atresia.

Brian Herrmann, MD, Associate Professor (Pediatric Otolaryngology):
As someone with hearing loss, my career in Pediatric Otolaryngologist has followed my personal interests to focus on complex ear disease and hearing loss. As a member of the International Working Group on Endoscopic Ear Surgery, I have a keen interest in advancing the capabilities of endoscopic ear techniques in pediatric ear disease. My research focus in otology involves otitis media and microbiome factors related to its development, hearing loss related to meningitis, and outcomes for otologic procedures in children. In addition to multiple publications and previous grant awards related to this work, I also have several manuscripts currently under

review. I am also involved in more traditional clinical research involving pediatric head and neck masses related to familial cancer disorders, otitis and adenotonsillar disease in syndromic children, and complications from pediatric head and neck infections.

Basic science and translational bioengineering otologic research is an important focus for me, and I am currently involved in several projects. Having received a degree in Biomedical Engineering prior to a Doctorate in Medicine, I am also in the unique position of having insight in device design to address surgical instrumentation needs. While in Atlanta, I was a research faculty member for the Pediatric Research Alliance, a collaborative of Children's Healthcare of Atlanta, Georgia Institute of Technology, and Emory University tasked with developing medical device prototypes. During my time at Children's Hospital Colorado, I have developed innovative prototype otosurgical instrumentation, developed tools for surgical aerosol mitigation, and created a prototype device to more accurately assess sites of upper airway obstruction from sleep apnea. All are the process of patent submission or awaiting patent approval. Current projects also include examining acoustic trauma related to surgical procedures, safety aspects of inner ear endoscopy, 3D print modelling of the temporal bone for use in trainee education, and robotic applications for otoendoscopic ear surgery. Leveraging robotic approaches to ear surgery has the potential to advance the field of otologic surgery and create innovative technology that can be more broadly applied in medicine. In addition to the rich potential for IP related to these projects, the preliminary data will create multiple funding opportunities for further research and associated publications.

I currently have had the pleasure of serving as clinical mentor to two NIH T32 trainees in Otolaryngology, and in the past 5 years have also involved ten otolaryngology trainees and six medical and undergraduate students in clinical and translational medical research projects. I also have served as physician mentor/collaborator for three graduate and nearly twenty undergraduate engineering students on bioengineering projects.

Otolaryngology Omics: Collaborators and affiliated faculty:

Several investigators also have intersecting interests in the microbiome of the middle ear and airways. These include ***Dr. Dan Frank*** *in the Dept. of Medicine and* ***Dr. Jonathan (Kirk) Harris*** *in Pediatrics and Pulmonary Medicine, who study the microbiome and collaborate extensively with* ***Drs. Sarah Clark*** *and* ***Sarah Gitomer*** *on how the airway microbiome influences host-pathogen interactions. In addition to* ***Drs. Clark and Gitomer****,* ***Dr. Frank*** *collaborates with* ***Dr. Regie Santos-Cortez*** *on the role of the microbiome in otitis media. In addition to the microbiome,* ***Dr. Clark*** *has several active collaborations with other investigators on campus focused on inflammation and immune modulation by respiratory tract bacterial and viral pathogens with investigators including* ***Dr. Eszter Vladar****, Dept. of Medicine/Pulmonology (pathogen infection of the respiratory tract epithelium),* ***Dr. Edward Janoff****, Dept. of Medicine/Infectious Disease (pneumococcal disease),* ***Dr. Alexander Horswill****, Dept. of Microbiology and Immunology (staphylococcus disease),* ***Dr. Jenna Guthmiller****, Dept. of Microbiology and Immunology (influenza A virus),* ***Dr. Breck Duerkop****, Dept. of Microbiology and Immunology (neutrophil modulation by enteric pathogens),* ***Dr. Catherine Lozupone****, Dept. of Microbiology and Immunology (gut-lung axis and microbiome),* ***Dr. Elan Eisenmesser****, Dept. of Biochemistry and Molecular Genetics (protease activity in respiratory pathogens), and* ***Dr. Janani Ravi****, Biomedical Informatics (computational approaches to pathogenesis research).*

Dr. Regie Santos-Cortez's *laboratory focuses on genetic and multi-omic studies of otolaryngologic diseases, such as hearing loss, otitis media, pediatric vestibular disorders and obstructive sleep-disordered breathing. She mentored one T32 scholar who graduated from the Human Medical Genetics and Genomics Graduate Program. She is also leading an NIDCD-funded R25 program that is expanding a network of otitis media researchers, with a focus on diversity. In addition to the 18 active clinical and 3 basic science otolaryngology faculty that she works with, she has the following collaborators across campus:* ***Dr. Daniel Frank*** *(Medicine/Infectious Diseases);* ***Dr. Bifeng Gao*** *(Medicine/Genomics Core);* ***Dr. Nancy Hadley-Miller*** *(Pediatric Orthopedics/Genetics);* ***Dr. Katerina Kechris*** *(Biostatistics & Informatics);* ***Dr. Rita Lee*** *(Medicine/DEI);* ***Shay Guetz-Lindahl, MS*** *(Pediatrics/Genetic Counseling);* ***Dr. Tzu Phang*** *(Pediatrics/Bioinformatics);* ***Dr. David A. Schwartz*** *(Medicine/Pulmonology);* ***Dr. Stig Somme*** *(Pediatric Surgery);* ***Dr. Kristin Uhler*** *(Physical Medicine and Rehabilitation/Audiology);* ***Dr. Ivana Yang*** *(Biomedical Informatics); and* ***Dr. Sonja Ziniel*** *(Pediatrics/Survey Methodology). At least 6 additional collaborations are being developed for ongoing studies. Lastly, she has multi-disciplinary collaborations with basic science and clinical faculty from 31 institutions within the United States, South America, Europe, Asia and Australia.*

Head and neck cancer: Departmental and affiliated faculty

Shi-Long Lu, MD, PhD, Professor:
I am a Professor of Otolaryngology – Head and Neck Surgery and my research is focused on fundamental and translational aspects of head and neck cancers, including head and neck squamous cell carcinoma (HNSCC) and salivary gland tumors (SGTs). Specifically, my lab works on delineating the roles of PI3K and TGF signaling pathway, cancer stem cell, and oral microbiome in HNSCC pathogenesis, identifying saliva biomarkers for early detection, recurrence, and surveillance of HNSCC, and developing novel therapeutic approaches for HNSCC. Several key discoveries from my lab are: (1) We were among the first to develop multiple genetically engineered mouse models (GEMMs) of HNSCC in both PI3K and TGFβ pathways. In combination with the tobacco carcinogenesis protocol, these models develop HNSCC, which mimic human HNSCC etiologically, pathologically and molecularly. (2) We developed GEMMs for human SGTs and are using these models to study the role of PTEN and Smad4 in SGT pathogenesis. (3) We have identified a panel of methylated genomic loci encoding microRNAs, which can be detected in patient saliva, to serve as biomarkers for early diagnosis, recurrence, and surveillance of HNSCC patients. (4). In collaboration with our colleague, we are among the first to study the functional role of oral microbiome in HNSCC pathogenesis and its impact on immunotherapy and PI3K targeted therapy. (5) In collaboration with our colleague, we developed a novel therapeutic approach using a bivalent EGF immunotoxin-based therapy on HNSCC models my lab has developed. (6) In collaboration with our colleague, we are developing multi-Omics together with optical imaging techniques to predict the risk of malignant transformation of oral lesions.

Carissa Thomas, MD, PhD, Associate Professor (Head and Neck):
Research interests include investigations on an altered oral microbiome that promotes malignant transformation in head and neck cancer, changes in the oral and gut microbiomes that contribute to head and neck cancer-related pain, regulation of PD-L1 expression in the tumor microenvironment by select oral bacteria, the effect of the oral microbiome on tumor associated macrophages and cancer cell metastases, the role of the gut microbiome in head and neck surgical outcomes and cancer cachexia, and clinical outcomes in microvascular reconstruction.

Head and neck: Collaborators and affiliated faculty

Dr. Shi-Long Lu's *laboratory focuses on basic and translation research on head and neck cancer (HNC), including both head and neck squamous cell carcinoma (HNSCC) and salivary gland cancer (SGC). There are several research projects involved in multi-disciplinary collaborations with both basic and clinical faculties in the University of Colorado. 1). Understanding the role and mechanism of oral microbiome in HNSCC. This collaboration occurs with a MPI application with* ***Dr. Daniel Frank*** *(Medicine/Infectious Diseases) and several key personnel including* ***Drs****.* ***Eric Clambey*** *(Anesthesiology/Immunology),* ***Kristi Kuhn*** *(Medicine/Gnotobiotic core),* ***Dexiang Gao*** *(Pediatrics/Biostatistics),* ***Charles Robertson*** *(Medicine/Bioinformatics),* ***Nichole Reisdorph*** *(Pharmacy/Proteomics core),* ***Julia Goddard*** *(Head and neck surgery) and* ***Brian Cervenka*** *(Head and neck surgery). This collaborative study has yielded 4 NIH grants (2 R21 and 1 R56 awarded, and 1 R01 pending). 2). Saliva liquid biopsy for head and neck cancer recurrence. This collaboration includes* ***Drs. John Song*** *(Head and neck surgery),* ***Brian Harry*** *(Pathology),* ***Dexiang Gao*** *(Pediatrics/Biostatistics),*

Julia Goddard *(Head and neck surgery) and* ***Brian Cervenka*** *(Head and neck surgery). The collaboration yielded a NIH UH2/3 grant, multiple institutional/foundation/business grants, and patents. 3). Point of care detection of antibodies against HPV oncoproteins in oropharyngeal cancer. Subcontracting with a Fitzsimmons diagnostic company, we are collaborating with* ***Dr. Carissa Thomas*** *(Head and neck surgery) with a SBIR grant application. 4). Multi-Omics and imaging study for oral precancerous lesions and cholesteatoma. In collaboration with Drs.* ***Regie Santos-Cortez*** *(Otolaryngology),* ***Chaitanya Puranik*** *(Dental School) and* ***Katerina Kechris*** *(Biostatistics & Informatics), we are developing this project for an NIH RM1 grant application. 5). Developing mouse models for saliva gland cancer. This collaboration includes Drs.* ***Mary Reyland*** *(Craniofacial biology),* ***Natalie Serkova*** *(Anesthesiology/animal imaging),* ***Mohamed Said*** *(Pathology), and* ***Tzu Lip Phang*** *(Bioinformatics), and yielded multiple institutional grants and publications. 6). Developing immunotoxin-based therapeutics for HNSCC. This is a collaboration with* ***Dr. Zirui Wang*** *(Surgery/Immunology).*

Dr. Carissa Thomas's *laboratory focuses on translational research on head and neck cancer and the microbiome. Several external multi-disciplinary collaborations exist and new collaborations are being established within the University of Colorado. 1) Understanding the liver-gut-muscle connection in cancer cachexia in head and neck cancer. This is a new collaboration with* ***Dr. Andrea Bonetto*** *(Pathology) and* ***Dr. Leah Novinger*** *(Pathology). An R21 application was submitted in October 2024 to NIAMS. 2) Development of novel prognostic biomarkers for oral squamous cell carcinoma. This is an ongoing collaboration with* ***Dr. Chi Viet*** *(Oralmaxillofacial Surgery) at Loma Linda University. Dr. Thomas is the site PI for Dr. Viet's R01 on the REASON score, which is being transitioned to the University of Colorado. 3) Leveraging artificial intelligence analysis of histology and molecular signatures to prognosticate oral premalignant lesions. This is a second ongoing collaboration with* ***Dr. Chi Viet****, and Dr. Thomas is site PI for Dr. Viet's R01, which is also being transitioned to the University of Colorado. 4) Understanding the interactions between HIV and HPV in oropharyngeal cancer. This is a collaboration with* ***Dr. Anju Bansal*** *(Infectious Disease) and* ***Dr. Sanjib Banerjee*** *(Genetics) at the University of Alabama at Birmingham (UAB). Dr. Thomas is a collaborator on an R01 investigating onco-immunologic factors contributing to oropharyngeal squamous cell carcinoma in people living with HIV. An R21 grant application to understand the role of the microbiome and HIV in oral squamous cell carcinoma is in progress in collaboration with* ***Drs. Bansal*** *and* ***Banerjee.***

NIH Grants

Yuri Agrawal

R01	Clinical trial of vestibular therapy to reduce falls in patients with Alzheimer's disease
R01(MPD/PI)	Impact of vestibular loss on central vestibular pathways in aging adults

Sarah Clark

R01	Airway Prevotella enhance innate immune-mediated protection against lung infection
R21	Host factors influencing early clearance of Streptococcus pneumoniae from the middle ear following invasion from the nasopharynx

Sue Kinnamon

R01(MPD/PI)	Electrophysiological basis of sour taste transduction
T32(MPD/PI)	Institutional Training in Otolaryngology Research
R25(MPD/PI)	Colorado Clinician Scientist Training Program

Shi-Long Lu

UH3	Validation of a saliva test using methylated microRNAs for head and neck cancer recurrence
R21(MPD/PI)	Functional roles of the human microbiome and metabolome in oral cancer

Vinay Manchaiah

R01(MPD/PI)	Emerging Service Delivery Models for Over-the-Counter Hearing Aids: A Hybrid Effectiveness-Implementation Trial

Katie Rennie

R01(MPD/PI)	Aging and Dysfunction in the Peripheral Vestibular System
R01	Ion Channels and Excitability in the Peripheral Vestibular System

Regie Santos-Cortez

R01(MPD/PI)	Genetic and epigenomic determinants of hearing loss in Hispanic populations
R25(MPD/PI)	Development of a diverse workforce through mentoring networks among otitis media researchers

Departmental Clinical Research Core

The Department of Otolaryngology uniquely supports clinical and translational research through a Clinical Research Core, which provides Clinical Research Coordinators (CRCs) who help manage prospective and retrospective projects. We have two CRCs in the Adult Division and two in the Pediatric Division, with one supervisor who oversees this team. Our CRCs manage clinical trials and research studies, ensuring they are conducted according to regulatory requirements and study protocols. Their responsibilities include completing IRB applications and other regulatory work, recruiting and screening participants, obtaining informed consent, coordinating study visits, collecting and managing data, administering questionnaires, and ensuring compliance with ethical guidelines. They work closely with investigators, sponsors, and study participants to safeguard accurate data collection and smooth study operations.

Examples of studies supported by the Clinical Research Core

Gregory Allen (Pediatric Otolaryngology)

- Subcontract clinical site (NIH/University of Utah): A comparative effectiveness study of speech and surgical treatment using a Cleft Palate Registry/Research Outcomes Network
- Subcontract clinical site (NIH/University of Wyoming): Using MRI to Facilitate Precision Medicine for Infants with Cleft Palate

Kenny Chan (Pediatric Otolaryngology)

- Effects of Immersive Virtual Reality Mindfulness Application on Quality of Life, Anxiety and Depression Symptoms in Children with Severe Tinnitus and Misophonia – A Pilot Study

Liz Cuadrado (Speech Language Pathology)

- Colorado Oral Strengthening Device

Daniel Fink (Laryngology)

- Determining Regional Lung Volumes with Electrical Impedance Tomography on Patients Receiving Low-Frequency JET ventilation
- Retrograde Cricopharyngeal Dysfunction Prospective Data Collection

Norman Friedman (Pediatric Otolaryngology)

- Outcome analysis for Children Undergoing Adenotonsillectomy

Anne Getz (Rhinology)

- Sinonasal Cancer Biobank
- Postoperative Pain and Opioid Use in Endoscopic Skull Base Surgery

Sarah Gitomer (Pediatric Otolaryngology)

- Expanded Indications in the Pediatric BONEBRIDGE Population
- Fungal sinus infections in pediatric cystic fibrosis: impact on treatment
- Pediatric Otolaryngology Biobank
- Using Point of Care Ultrasound to Evaluate the Pediatric Airway in intubated patients

Katherine Green (Sleep Medicine)

- Adherence and Outcome of Upper Airway Stimulation (UAS) for OSA International Registry
- Prospective non-randomized post market study collecting clinical data on safety and effectiveness of the remede System

Samuel Gubbels (Otology)

- Department of Otolaryngology Inner Ear Biobank

Brian Herrmann (Pediatric Otolaryngology)

- (AIA/NIH proof of concept): Slumberscope

Marie Jette (Laryngology)

- Investigation of interoceptive awareness in patients with refractory chronic cough

Ashoke Khanwalkar (Rhinology)

- Department of Otolaryngology Biobank

Shi-Long Lu

- Role of human microbiome on head and neck cancer

Jeremy Prager (Pediatric Otolaryngology)

- Subcontract clinical site (CDC/Eastern Virgina Medical School): Monitoring Juvenile Onset Recurrent Respiratory Papillomatosis

Tammy Wang (Pediatric Otolaryngology)

- A 16-Week Randomized, Double-Blind, Placebo Controlled, Parallel-Group, Multicenter Study Evaluating the Efficacy and Safety of OPN-375 186 ìg Twice a Day (BID) in Adolescents with Bilateral Nasal Polyps followed by a 12-Week Open-Label Treatment Phase

Biosketches of Department Faculty Leads

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Clark, Sarah

eRA COMMONS USER NAME (credential, e.g., agency login): seclark

POSITION TITLE: Assistant Professor, Department of Otolaryngology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Colby College, Waterville, ME	BA	05/2008	Biology
University of Pennsylvania, Philadelphia, PA	PHD	05/2013	Microbiology
University of Colorado Denver, Denver, CO	Postdoctoral Fellow	08/2019	Immunology and Microbiology
National Jewish Health, Denver, CO	Postdoctoral Fellow	08/2019	Immunology and Microbiology

A. Personal Statement

I am broadly interested in bacterial-driven mechanisms of immune modulation and the consequences of these responses on infection and inflammation of the respiratory tract. My education and research experience have been divided between the fields of microbiology and immunology to approach this topic from both sides, including graduate training with Dr. Jeffrey N. Weiser focusing on evasion of immune recognition by the respiratory tract bacterial pathogen *Haemophilus influenzae*, and a postdoctoral fellowship with Dr. Laurel L. Lenz investigating how the pathogen *Listeria monocytogenes* suppresses innate immune responses during systemic infection. This cross-disciplinary training leaves me uniquely well-positioned to pursue mechanistic studies evaluating how members of the respiratory tract microbiome interact with each other and the immune system to influence respiratory tract infection and disease. Publications from my lab have identified novel mechanisms by which specific airway bacteria enhance protection against *S. pneumoniae* and how *S. pneumoniae* infection undermines innate immune-mediated clearance. The long-term goal of these studies is to contribute new insights to our understanding of immune responses to bacterial products in the respiratory tract and inform the development of new therapeutic strategies by targeting both (1) pathogen-derived factors and (2) the immune pathways they regulate to address the burden of respiratory tract disease.

Ongoing and recent projects:

1. 1R01AI172958-01 Clark (PI) 03/20/2023-02/29/2028
2. Cystic Fibrosis Foundation Research Grant Clark (PI) 05/01/2023-04/30/2025
3. 1R21DC019169-01A1 Early Career Research Award Clark (PI) 02/01/2022-01/31/2025
4. Boettcher Foundation Webb-Waring Biomedical Research Award Clark (PI) 9/01/2021-8/31/2024
5. American Lung Association Innovation Award Clark (PI) 07/01/2021-06/30/2023
6. American Thoracic Society Research Program Grant Clark (PI) 04/30/2021-04/29/2022
7. 5K22AI143922-02 Career Transition Award Clark (PI) 09/01/2019 – 02/28/2022

Citations:

1. Fulte S, Atto B, McCarty A, Horn KJ, Redzic JS, Eisenmesser E, Yang M, Marsh RL, Tristram S, Clark SE. Heme sequestration by hemophilin from *Haemophilus haemolyticus* reduces respiratory tract colonization and infection with non-typeable *Haemophilus influenzae*. *mSphere*. 2024 Mar 26;9(3):e0000624. PubMed Central PMCID: PMC10964412.

2. Drigot ZG, Clark SE. Insights into the role of the respiratory tract microbiome in defense against bacterial pneumonia. *Curr Opin Microbiol*. 2024 Feb;77:102428. PubMed Central PMCID: PMC10922932.
3. Horn KJ, Fulte S, Yang M, Lorenz BP, Clark SE. Neutrophil responsiveness to IL-10 impairs clearance of *Streptococcus pneumoniae* from the lungs. *J Leukoc Biol*. 2024 Jan 5;115(1):4-15. PubMed Central PMCID: PMC10768920.
4. Horn KJ, Schopper MA, Drigot ZG, Clark SE. Airway *Prevotella* promote TLR2-dependent neutrophil activation and rapid clearance of *Streptococcus pneumoniae* from the lung. *Nat Commun*. 2022 Jun 9;13(1):3321. PubMed Central PMCID: PMC9184549.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2023 - 2023	Study section member, NIH, NIAID BHI/BV Member Conflict Special Emphasis Panel (#IIDA-D02)
2022 - 2023	Study section member, NIGMS COBRE Special Emphasis Panel (#ZGM1 RCB-4-C1), NIH
2021 -	Assistant Professor in the Department of Immunology and Microbiology (secondary appointment), University of Colorado Denver
2021 - 2023	Chair of Advancing Gender Equity and Advocating for Women in Medicine and Science, Junior Faculty Committee , University of Colorado Denver
2021 - 2022	Trainee, Raising Advancement and Parity for Infectious Disease Researchers (RAPID) program (1R25AI147376-01A1), UCSD, NIAID
2021 - 2022	Editorial Review Board Member, Annals of Clinical Microbiology and Antimicrobials (BMC)
2020 -	Member, Central Society for Clinical and Translational Research (CSCTR)
2020 - 2020	Study section member, NIAID Special Emphasis Panel (#ZAI1-ZL-W-S1), NIH
2020 - 2020	Guest editor, Journal of Visualized Experiments
2019 -	Assistant Professor, Department of Otolaryngology, University of Colorado Denver
2019 -	Grant review panel member, Colorado Clinical and Translational Sciences Institute (CCTSI)
2018 -	Reviewer, PLoS Pathogens, Frontiers in Immunology, PLoS ONE, and Scientific Reports
2017 -	Member, American Thoracic Society (ATS)
2017 -	Member, American Association of Immunologists (AAI)
2016 - 2018	Organizer and host for Postdoctoral Invited Speakers, CU Denver Department of Immunology and Microbiology
2015 - 2018	Founder and co-editor, “PhD Post” newsletter focused on career development topics
2015 - 2016	Chair of Communications Committee, The annual Rocky Mountain Biotechnology Symposium (RMBTS)
2014 - 2014	Research Seminar Associate Chair, Microbial Toxins and Pathogenicity Gordan Research Seminar
2013 - 2019	Postdoctoral Fellow, National Jewish Health and the University of Colorado Denver
2008 -	Member, American Society of Microbiology (ASM)

Honors

2014 - 2017	F32 Postdoctoral Fellowship award number F32AI114075, National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH)
2011 - 2012	Microbial Pathogenesis and Genomics T32 program training grant, award number 5T32AI060516-08, National Institutes of Health (NIH)
2009 - 2011	Cell and Molecular Biology (CAMB) training grant, award number 3T32GM007229-37S1 , National Institutes of Health (NIH)
2024	Invited Speaker, Biology of Acute Respiratory Infection Gordan Research Conference
2023	Invited Speaker, STREP-2023 Streptococcal Infections Virtual Conference
2023	Invited Speaker, Annual Colorado Immunology and Microbiology Conference
2023	Student Invited Speaker, Pennsylvania State University, Microbiome Seminar

2022 Early Career Faculty Award, American Association for Immunologists (AAI)
2022 Invited speaker, Streptococcal Biology Gordan Research Conference
2022 Invited speaker, Biology of Acute Respiratory Infection Gordan Research Conference
2021 Featured New Investigator Award, Council of the Central Society for Clinical and Translational Research (CSCTR)
2021 Early Career Faculty Award, American Association for Immunologists (AAI)
2021 Invited speaker, CSCTR Midwest meeting
2021 Invited speaker, Southern Arkansas University Biology Club Seminar Series
2021 Invited speaker, Cell and Molecular Biology Alumni Career Panel, University of Pennsylvania
2020 Invited speaker, Virtual Streptococcal Seminar Series (national and international participants)
2020 Invited speaker, World Immune Regulation Meeting XIV (cancelled due to COVID-19)
2020 Invited speaker, Ultimate Colorado Midwinter Meeting, CU Denver Otolaryngology
2018 AAI Young Investigator Award and invited speaker, Colorado Immunology Conference
2018 Invited speaker, AAI Immunology Conference
2018 CO-Pilot award, Colorado Clinical and Translational Sciences Institute
2016 Translational Research Category Poster Winner, CU Colorado Postdoctoral Research Day
2015 AAI Young Investigator Award and invited speaker, Colorado Immunology Conference
2015 Invited speaker, Keystone Conference “Innate Immunity and Determinants of Microbial Pathogenesis”
2014 American Association of Immunologists (AAI) Young Investigator Award, Colorado Immunology Conference
2011 John Samuel Kanefield Prize for Cystic Fibrosis Research, University of Pennsylvania

C. Contribution to Science

1. **Immune evasion by the respiratory tract bacterium Haemophilus influenzae**
   My graduate work in the lab of Dr. Jeffrey N. Weiser focused on understanding how the opportunistic pathogen *Haemophilus influenzae* evades host recognition during colonization. We found that expression of the phase variable molecule phosphorylcholine (choline phosphate, or ChoP) reduces antibody binding to inner core lipopolysaccharide (LPS) structures on *H. influenzae*. In subsequent studies, we found that human antibody and complement drive selection for ChoP and other phase-variable LPS molecules, which have an additive effect in protecting against antibody recognition. This work demonstrated that *H. influenzae* phase variation of LPS structures contributes to survival during colonization.

   a. Clark SE, Eichelberger KR, Weiser JN. Evasion of killing by human antibody and complement through multiple variations in the surface oligosaccharide of *Haemophilus influenzae*. *Mol Microbiol*. 2013 May;88(3):603-18. PubMed Central PMCID: PMC4550093.
   b. Clark SE, Weiser JN. Microbial modulation of host immunity with the small molecule phosphorylcholine. *Infect Immun*. 2013 Feb;81(2):392-401. PubMed Central PMCID: PMC3553803.
   c. Clark SE, Snow J, Li J, Zola TA, Weiser JN. Phosphorylcholine allows for evasion of bactericidal antibody by *Haemophilus influenzae*. *PLoS Pathog*. 2012;8(3):e1002521. PubMed Central PMCID: PMC3291618.

2. **Activation of immune-suppressive NK cell IL-10 by bacterial pathogens**
   During my Postdoctoral Fellowship in the lab of Dr. Laurel L. Lenz, I investigated how *Listeria monocytogenes* (Lm) modulates the host immune response. We found that a secreted virulence protein, p60, drives natural killer (NK) cell production of IL-10. NK cell-dependent IL-10 impaired host protection by reducing myeloid cell recruitment and activation. This required p60 inflammasome activation in dendritic cells (DCs) and NK cell-intrinsic IL-15 and IL-10 signaling to drive STAT3-dependent IL-10. In contrast, in collaboration with others, we found that NK cell-intrinsic STAT3 induced by IL-15 complex is therapeutic in a model of cerebral malaria. In work continued in my own lab, I used a mouse model of *S. pneumoniae* lung infection to determine the impact of NK cells on host protection in this setting. We found that *S. pneumoniae* induces IL-10, which exacerbates lung infection, and that NK cells are a critical source of immune-suppressive IL-10. Most recently, we found that IL-10 signaling reduces neutrophil-mediated

clearance of *S. pneumoniae* from the lungs. These studies demonstrate a new pathway for immune modulation by a respiratory tract bacterial pathogen.

a. Horn KJ, Fulte S, Yang M, Lorenz BP, Clark SE. Neutrophil responsiveness to IL-10 impairs clearance of *Streptococcus pneumoniae* from the lungs. *J Leukoc Biol*. 2024 Jan 5;115(1):4-15. PubMed Central PMCID: PMC10768920.
b. Clark SE, Schmidt RL, Aguilera ER, Lenz LL. IL-10-producing NK cells exacerbate sublethal *Streptococcus pneumoniae* infection in the lung. *Transl Res*. 2020 Dec;226:70-82. PubMed Central PMCID: PMC7572800.
c. Clark SE, Schmidt RL, McDermott DS, Lenz LL. A Batf3/Nlrp3/IL-18 Axis Promotes Natural Killer Cell IL-10 Production during *Listeria monocytogenes* Infection. *Cell Rep*. 2018 May 29;23(9):2582-2594. PubMed Central PMCID: PMC6170157.
d. Clark SE, Filak HC, Guthrie BS, Schmidt RL, Jamieson A, Merkel P, Knight V, Cole CM, Raulet DH, Lenz LL. Bacterial Manipulation of NK Cell Regulatory Activity Increases Susceptibility *to Listeria monocytogenes* Infection. *PLoS Pathog*. 2016 Jun;12(6):e1005708. PubMed Central PMCID: PMC4905663.

3. **Maternal microbiome influences offspring susceptibility to obesity and non-alcoholic fatty liver disease**
A collaborative effort with Dr. Jed Friedman at CU Denver investigated the impact of maternal obesity on offspring susceptibility to obesity and non-alcoholic fatty liver disease (NAFLD). Dr. Friedman's group found that germ-free mice colonized with stool from human infants born to obese mothers developed NAFLD. I found evidence for intestinal barrier and macrophage dysfunction in these mice, including increased bacterial spread to the liver and reduced macrophage phagocytosis. These results describe a mechanism for the clinical observation that maternal obesity is a risk factor for offspring obesity and NAFLD.

a. Soderborg TK, Clark SE, Mulligan CE, Janssen RC, Babcock L, Ir D, Young B, Krebs N, Lemas DJ, Johnson LK, Weir T, Lenz LL, Frank DN, Hernandez TL, Kuhn KA, D'Alessandro A, Barbour LA, El Kasmi KC, Friedman JE. The gut microbiota in infants of obese mothers increases inflammation and susceptibility to NAFLD. *Nat Commun*. 2018 Oct 26;9(1):4462. PubMed Central PMCID: PMC6203757.

4. **Commensal *Corynebacterium* and *Haemophilus* species in the upper airway mediate improved protection against *S. pneumoniae* colonization and lung infection**
My lab developed new animal models to investigate how airway *Corynebacterium* and *Haemophilus* species impact protection against *S. pneumoniae* infection. In children, increased abundance of *Corynebacterium* species in the upper airway correlates with fewer infections and reduced *S. pneumoniae*. We identified a lipase expressed by *Corynebacterium amycolatum* similar to the previously described lipS1 in *Corynebacterium accolens* which mediates *S. pneumoniae* growth inhibition *in vitro*. Further, we showed that both *C. accolens* and *C. amycolatum* reduced *S. pneumoniae* colonization and lung infection. This protective effect was partially dependent on *C. accolens* expression of lipS1, indicating that both this and other factors contribute to protection. These studies characterize for the first time the mechanisms associated with *Corynebacterium*-mediated protection against *S. pneumoniae in vivo* and provide a new tool to investigate host and pathogen-*Corynebacterium* interactions. In adults, the commensal *Haemophilus haemolyticus* correlates with reduced carriage of the pathogen NTHi, and *H. haemolyticus* produces a heme binding protein called hemophilin which restricts NTHi growth in vitro. In collaboration with the group that originally characterized hemophilin activity, we found that *H. haemolyticus* protected against NTHi colonization and infection in a hemophilin-dependent manner, and that purified hemophilin was sufficient to reduce NTHi infection and adherence to human respiratory tract epithelial cells. These studies demonstrate the beneficial effects of heme sequestration by commensal *Haemophilus* species in the airway.

a. Fulte S, Atto B, McCarty A, Horn KJ, Redzic JS, Eisenmesser E, Yang M, Marsh RL, Tristram S, Clark SE. Heme sequestration by hemophilin from *Haemophilus haemolyticus* reduces respiratory tract colonization and infection with non-typeable *Haemophilus influenzae. mSphere*. 2024 Mar 26;9(3):e0000624. PubMed Central PMCID: PMC10964412.

b. Horn KJ, Jaberi Vivar AC, Arenas V, Andani S, Janoff EN, Clark SE. *Corynebacterium* Species Inhibit *Streptococcus pneumoniae* Colonization and Infection of the Mouse Airway. *Front Microbiol.* 2021;12:804935. PubMed Central PMCID: PMC8784410.

c. Clark SE. Commensal bacteria in the upper respiratory tract regulate susceptibility to infection. *Curr Opin Immunol*. 2020 Oct;66:42-49. PubMed Central PMCID: PMC7665980.

5. **Protective airway *Prevotella* species which enhance neutrophil-mediated clearance of *S. pneumoniae* from the lung**
In recent work, we investigated the impact of airway exposure to *Prevotella*, one of the most abundant bacteria detected in the lung, on susceptibility to infection with *S. pneumoniae*. We found that some species of *Prevotella*, including *P. melaninogenica*, induced a protective immune response associated with improved killing of *S. pneumoniae* by neutrophils recruited to the lung. *Prevotella*-mediated protection required the activation of a limited inflammatory response characterized by neutrophil recruitment and activation by *Prevotella* lipoproteins, which were recognized by host TLR2. This response was regulated by IL-10, which was also required for *Prevotella*-mediated protection and limited *Prevotella*-associated inflammation in mice co-infected with *S. pneumoniae*.

a. Drigot ZG, Clark SE. Insights into the role of the respiratory tract microbiome in defense against bacterial pneumonia. *Curr Opin Microbio*l. 2024 Feb;77:102428. PubMed Central PMCID: PMC10922932.

b. Horn KJ, Schopper MA, Drigot ZG, Clark SE. Airway *Prevotella* promote TLR2-dependent neutrophil activation and rapid clearance of *Streptococcus pneumoniae* from the lung. *Nat Commun*. 2022 Jun 9;13(1):3321. PubMed Central PMCID: PMC9184549.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/10uxXz9PWqHQq/bibliography/public/

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Greene, Nathaniel

eRA COMMONS USER NAME (credential, e.g., agency login): ntgreene

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Wittenberg University, Springfield, OH	BA	05/2004	Physics
University of Rochester, Rochester, NY	MS	03/2009	Biomedical Engineering
University of Rochester, Rochester, NY	PHD	05/2013	Biomedical Engineering
University of Colorado School of Medicine, Aurora, CO	Postdoctoral Fellow	03/2015	Tollin Lab, Dept. of Physiology and Biophysics

A. Personal Statement

My research is driven by an interest in exploring the interactions between the acoustical environment and the mammalian auditory system, and specifically in the mechanisms underlying hearing loss. Sound travels from the environment to the inner ear via the external ear, which introduces location dependent timing, level, and spectral variations to the transmitted sound, and then through vibrations in the bones (the ossicles) of the middle ear, where the geometry and material properties of these and other middle ear components alter the sound transmitted. However, sound may also travel to the inner ear via alternate transmission pathways, including directly to the cochlea via bone conduction. My work has involved several different lines of research investigating the effects of these mechanisms, including several that are directly applicable to the current proposal, including: 1) the hearing ability of humans and animals, and particularly to localize sound sources, 2) surface and single-cell physiology of the auditory brainstem in humans and animals, 3) characterizing normal sound transmission during low frequency and high level sound stimulation (including acoustic blast exposure) in human cadavers and animals, 4) normal sound transmission during bone conducted sound presentation in human cadavers and animals, and 5) the effects on sound transmission with a cochlear implant electrodes inserted in human cadavers. I have broad training in behavioral testing of animal and human hearing ability, and both surface and single-cell brainstem electrophysiological measurements, in addition to specific training in post-mortem human temporal bone preparations and the mechanics of the middle and inner ear. As Principal Investigator, co-Investigator or key-personnel on several university-, NIH-, and DOD-funded grants, I have extensive experience in, and have developed custom software and hardware specifically for, measurements of hearing and sound localization ability of humans, and guinea pig and chinchillas, as illustrated by several publications (below). Similarly, since many of these projects are clinically translatable, and the training conducted during their implementation provides immediate benefit to surgical trainees, I have trained over a dozen Otolaryngology residents in my laboratory, resulting in numerous peer-reviewed publications. Overall, my training uniquely positions me to oversee the present proposal, which encompasses data collection in human cadavers, animals, and human subjects.

1. Anderson DA, Argo TF 4th, Greene NT. Occluded insertion loss from intracochlear pressure measurements during acoustic shock wave exposure. Hear Res. 2023 Feb;428:108669. PubMed PMID: 36565603.
2. Banakis Hartl RM, Greene NT. Measurement and Mitigation of Intracochlear Pressure Transients During Cochlear Implant Electrode Insertion. Otol Neurotol. 2022 Feb 1;43(2):174-182. PubMed

Central PMCID: PMC10260290.

3. Sammeth CA, Greene NT, Brown AD, Tollin DJ. Normative Study of the Binaural Interaction Component of the Human Auditory Brainstem Response as a Function of Interaural Time Differences. Ear Hear. 2021 May/Jun;42(3):629-643. PubMed Central PMCID: PMC8085190.
4. McCullagh EA, Poleg S, Greene NT, Huntsman MM, Tollin DJ, Klug A. Characterization of Auditory and Binaural Spatial Hearing in a Fragile X Syndrome Mouse Model. eNeuro. 2020 Jan/Feb;7(1) PubMed Central PMCID: PMC7031856.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2023 -	Associate Professor, University of Colorado School of Medicine, Department of Otolaryngology, Aurora, CO
2017 - 2023	Assistant Professor, University of Colorado School of Medicine, Department of Otolaryngology, Aurora, CO
2016 - 2017	Hearing Scientist, The Geneva Foundation, The US Army Aeromedical Research Laboratory, Ft Rucker, AL
2015 - 2016	Research Assistant Professor, University of Colorado School of Medicine, Department of Physiology and Biophysics, Aurora, CO
2012 - 2015	Postdoctoral Fellow, University of Colorado School of Medicine, Department of Physiology and Biophysics, Aurora, CO
2004 - 2006	Research Tech, Dartmouth College, Department of Cognitive and Neural Sciences, Hanover, NH

Honors

2002 - 2004	E.O. Weaver Scholarship, Wittenberg University
2000 - 2004	Wittenberg Honors Award, Wittenberg University
2010	ARO Travel Award, Association for Research in Otolaryngology
2009	University of Rochester Graduate Organizing Group Conference Award, University of Rochester

C. Contribution to Science

1. Human and animal hearing ability. Hearing ability varies substantially with listening conditions, and across species. My work has documented the effects on human psychophysical performance of varying the width of the sound source, use of hearing protectors, and physiological status of the middle ear muscles. Additionally, hearing varies dramatically across species, and I have documented the sound localization ability of normal hearing guinea pigs.

    a. Tasko SM, Deiters KK, Flamme GA, Smith MV, Murphy WJ, Jones HG, Greene NT, Ahroon WA. Effects of unilateral eye closure on middle ear muscle contractions. Hear Res. 2022 Oct;424:108594. PubMed PMID: 35964452.

    b. McCullagh EA, Poleg S, Greene NT, Huntsman MM, Tollin DJ, Klug A. Characterization of Auditory and Binaural Spatial Hearing in a Fragile X Syndrome Mouse Model. eNeuro. 2020 Jan/Feb;7(1) PubMed Central PMCID: PMC7031856.

    c. Greene NT, Anbuhl KL, Ferber AT, DeGuzman M, Allen PD, Tollin DJ. Spatial hearing ability of the pigmented Guinea pig (Cavia porcellus): Minimum audible angle and spatial release from masking in azimuth. Hear Res. 2018 Aug;365:62-76. PubMed Central PMCID: PMC6396980.

    d. Brown AD, Beemer BT, Greene NT, Argo T 4th, Meegan GD, Tollin DJ. Effects of Active and Passive Hearing Protection Devices on Sound Source Localization, Speech Recognition, and Tone Detection. PLoS One. 2015;10(8):e0136568. PubMed Central PMCID: PMC4551850.

2. Acoustics and brainstem physiology underlying sound localization ability I have also investigated the acoustics of the head and ears, which introduce the cues to sound source location, as well as the brainstem circuitry that processes these cues. While the anatomical pathways and circuitry are well described up through the first synapse in the brainstem, the cochlear nucleus, the higher order projections in the auditory system are less well understood. My research, and resulting publications, documented the responses and functionally identified projection patterns of the lateral superior olive into the inferior colliculus.

    a. Peacock J, Benson MA, Greene NT, Tollin DJ, Young BA. The acoustical effect of the neck frill of the frill-necked lizard (Chlamydosaurus kingii). J Acoust Soc Am. 2022 Jul;152(1):437. PubMed PMID: 35931550.
    b. Anbuhl KL, Benichoux V, Greene NT, Brown AD, Tollin DJ. Development of the head, pinnae, and acoustical cues to sound location in a precocial species, the guinea pig (Cavia porcellus). Hear Res. 2017 Dec;356:35-50. PubMed Central PMCID: PMC5705338.
    c. Greene NT, Anbuhl KL, Williams W, Tollin DJ. The acoustical cues to sound location in the guinea pig (Cavia porcellus). Hear Res. 2014 Oct;316:1-15. PubMed Central PMCID: PMC4194235.
    d. Greene NT, Lomakin O, Davis KA. Monaural spectral processing differs between the lateral superior olive and the inferior colliculus: physiological evidence for an acoustic chiasm. Hear Res. 2010 Oct 1;269(1-2):134-45. PubMed Central PMCID: PMC2933962.

3. Middle-ear mechanics of bone conduction. Sound transduction to the inner ear can propagate through the external and middle ear (air-conduction), or directly through vibrations of the skull (bone-conduction). I developed methods for measuring the sound transmitted into the cochlea with both air- and bone-conducted stimuli, in a post-mortem human temporal bone preparation. Using these methods, I and collaborators have documented the effects of several hearing assistive devices on middle and inner ear mechanics.

    a. Mattingly JK, Banakis Hartl RM, Jenkins HA, Tollin DJ, Cass SP, Greene NT. A Comparison of Intracochlear Pressures During Ipsilateral and Contralateral Stimulation With a Bone Conduction Implant. Ear Hear. 2020 Mar/Apr;41(2):312-322. PubMed Central PMCID: PMC8043255.
    b. Alhussaini MA, Banakis Hartl RM, Benichoux V, Tollin DJ, Jenkins HA, Greene NT. Intracochlear Pressures in Simulated Otitis Media With Effusion: A Temporal Bone Study. Otol Neurotol. 2018 Aug;39(7):e585-e592. PubMed Central PMCID: PMC6041178.
    c. Banakis Hartl RM, Mattingly JK, Greene NT, Jenkins HA, Cass SP, Tollin DJ. A Preliminary Investigation of the Air-Bone Gap: Changes in Intracochlear Sound Pressure With Air- and Bone-conducted Stimuli After Cochlear Implantation. Otol Neurotol. 2016 Oct;37(9):1291-9. PubMed Central PMCID: PMC5089803.
    d. Mattingly JK, Greene NT, Jenkins HA, Tollin DJ, Easter JR, Cass SP. Effects of Skin Thickness on Cochlear Input Signal Using Transcutaneous Bone Conduction Implants. Otol Neurotol. 2015 Sep;36(8):1403-11. PubMed Central PMCID: PMC4537381.

4. Middle- and inner-ear mechanics of low frequency and high level sound exposures. The relationship between high level impulse noise (such as blast exposure) and hearing loss is not well understood. I have developed methods and procedures to make measurements of middle ear and cochlear mechanics during very low-frequency and very high level sound stimulation using a post-mortem human temporal bone preparation. I have begun to characterize the patterns of stimulation to the cochlea and the semicircular canals during such sound exposures.

    a. Anderson DA, Argo TF 4th, Greene NT. Occluded insertion loss from intracochlear pressure measurements during acoustic shock wave exposure. Hear Res. 2023 Feb;428:108669. PubMed PMID: 36565603.
    b. Greene NT, Alhussaini MA, Easter JR, Argo TF 4th, Walilko T, Tollin DJ. Intracochlear pressure

measurements during acoustic shock wave exposure. Hear Res. 2018 Aug;365:149-164. PubMed Central PMCID: PMC6901182.

c. Maxwell AK, Banakis Hartl RM, Greene NT, Benichoux V, Mattingly JK, Cass SP, Tollin DJ. Semicircular Canal Pressure Changes During High-intensity Acoustic Stimulation. Otol Neurotol. 2017 Aug;38(7):1043-1051. PubMed Central PMCID: PMC6561339.

d. Greene NT, Jenkins HA, Tollin DJ, Easter JR. Stapes displacement and intracochlear pressure in response to very high level, low frequency sounds. Hear Res. 2017 May;348:16-30. PubMed Central PMCID: PMC5759762.

5. Middle ear mechanics during Otologic surgery. Cochlear implants require insertion of an electrode array into the fluid of the cochlea. Recently, cochlear implantation has been investigated as a means of treating hearing loss in subjects with residual low frequency hearing ability. Similar procedures, such as laser stapedotomy and mastoidectomy likewise involve interactions with middle ear structures. I have developed methods, similar to those described above, to measure both air- and bone-conducted stimuli post-insertion of a cochlear implant, in a post-mortem human temporal bone preparation. Using these methods, I and collaborators have documented the effects on the mechanics of the auditory and vestibular periphery of cochlear implant electrode insertion.

   a. Boscoe EF, Banakis Hartl RM, Gubbels SP, Greene NT. Effects of Varying Laser Parameters During Laser Stapedotomy on Intracochlear Pressures. Otolaryngol Head Neck Surg. 2023 Mar;168(3):462-468. PubMed Central PMCID: PMC10097413.

   b. Banakis Hartl RM, Greene NT. Measurement and Mitigation of Intracochlear Pressure Transients During Cochlear Implant Electrode Insertion. Otol Neurotol. 2022 Feb 1;43(2):174-182. PubMed Central PMCID: PMC10260290.

   c. Gonzalez JR, Cass ND, Banakis Hartl RM, Peacock J, Cass SP, Greene NT. Characterizing Insertion Pressure Profiles During Cochlear Implantation: Simultaneous Fluoroscopy and Intracochlear Pressure Measurements. Otol Neurotol. 2020 Jan;41(1):e46-e54. PubMed Central PMCID: PMC10821719.

   d. Banakis Hartl RM, Mattingly JK, Greene NT, Farrell NF, Gubbels SP, Tollin DJ. Drill-induced Cochlear Injury During Otologic Surgery: Intracochlear Pressure Evidence of Acoustic Trauma. Otol Neurotol. 2017 Aug;38(7):938-947. PubMed Central PMCID: PMC5535777.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Kinnamon, Sue C

eRA COMMONS USER NAME (credential, e.g., agency login): SKinnamon

POSITION TITLE: Professor of Otolaryngology and Vice Chair of Research

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
State University College, Potsdam, NY	B.A.	1968	Biology Education
University of Massachusetts, Amherst, MA	M.S.	1971	Zoology
Kansas State University, Manhattan, KS	Ph.D.	1982	Biology/Neurobiology
Univ. Colorado Health Sci. Center, Denver, CO	Postdoc	1983-1985	Neurobiology

A. Personal Statement

My lab has been studying taste transduction and signaling for nearly 40 years. I started my career at Colorado State University in the Dept. of Anatomy and Neurobiology (which became the Dept. of Biomedical Sciences), but 15 years ago I moved to the University of Colorado Anschutz Medical Campus in the Dept. of Otolaryngology. I made the move in order to be in close proximity to collaborators in the chemical senses and to be a participating member of the Rocky Mountain Taste and Smell Center. My recent focus has been to define the role of specific cell types in the taste bud and determine not only how taste stimuli are transduced but how taste information is transmitted to gustatory nerve fibers. What are the taste cell transmitters and their cognate receptors? Our studies utilizing genetic deletion (Finger et al., 2005) and pharmacological blockade (Vandenbeuch et al., 2014) of P2X3-containing receptors indicate that ATP signaling is required for transmission of ALL taste information to the nervous system. While the role of ATP in sweet, bitter and umami taste is well documented, where it is released from Type II cells via a non-vesicular mechanism, questions remain about its role in sour taste, mediated by Type III taste cells. What is the source of the ATP for sour taste and how is it released? What is the role of other transmitters in transmitting sour taste information to the nervous system? In addition to questions about neurotransmitters in Type III cells, we were still unclear about the ion channels that mediate sour taste in these cells. Thus, I began a collaboration with the Liman lab at USC. I provided our PKD2L1-IRES-Cre mice to knock down the KIR2.1 channel in Type III cells and we showed that it mediates the depolarization in response to intracellular acidification (Ye et al. 2016), an important mechanism for transduction of weak acids. More recently, we partnered with the Liman lab to identify a proton channel, OTOP1, as the mammalian sour taste receptor (Teng et al., 2019). Recently we have shown that OTOP1 is also involved in ammonium sensing (Liang, Wilson et al., 2023). I am excited about our continued collaboration and look forward to our proposed experiments. My lab utilizes a variety of approaches to address these questions, including taste afferent nerve recording, brief access behavioral assays, rt- and single cell PCR, immunocytochemistry, isolation of single taste cells, calcium imaging, and patch clamp recording.

Ongoing and recently completed research projects that I would like to highlight include: (Trainee publications indicated by *)

R01 DC012555
Kinnamon (PI)
7/1/12-6/30/23
Neurotransmission in taste buds

R01 DC017679
Kinnamon (PI)
12/1/18-11/30/24 (NCE)
Illuminating the structure and function of Type I taste cells

R01 DC013741-06
Liman & Kinnamon (MPIs)
6/01/19-5/31/24 (NCE)
Electrophysiological basis of sour taste transduction-- the renewal/resubmission of this grant was submitted July 2024.

Citations:

1. Wilson CE*, Vandenbeuch A*, **Kinnamon SC**. (2019). Physiological and Behavioral Responses to Optogenetic Stimulation of PKD2L1+ Type III Taste Cells. ENeuro 6(2). doi: 10.1523/ENEURO.0107-19. * These authors contributed equally.
2. Teng B, Wilson CE, Tu YH, Joshi NR, **Kinnamon SC**, Liman ER. (2019). Cellular and Neural Responses to Sour Stimuli Require the Proton Channel Otop1. Curr Biol. 29:3647-3656.
3. Larson ED*, Vandenbeuch A*, Anderson CB, **Kinnamon SC.** (2020). Function, innervation, and neurotransmitter signaling in mice lacking Type II taste cells. eNeuro. 2020 Feb 3;7(1):ENEURO.0339-19.2020. doi: 10.1523/ENEURO.0339-19.2020. Print 2020 Jan/Feb. *These authors contributed equally.
4. Liang Z*, Wilson CE*, Teng B, **Kinnamon SC**, Liman ER (2023). The proton channel Otop1 is a sensor for the taste of ammonium chloride. Nat Commun. 2023 Oct 5;14(1):6194. *These authors contributed equally.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2018-present. Vice Chair of Research, Dept. of Otolaryngology,
2009- present. Professor, Dept. of Otolaryngology, Univ. of Colorado Anschutz Medical Campus, Aurora, CO
2009- present. Professor, Dept. of Physiology and Biophysics, Univ. of Colorado Anschutz Medical Campus, Aurora, CO (joint appt.)
2009- present. Professor, Dept. of Cell and Developmental Biology, Univ. of Colorado Anschutz Medical Campus, Aurora, CO (joint appt.)
2001-2008. Professor of Anatomy and Neurobiology, (currently Biomedical Sci.) Colo. St. Univ., Ft. Collins, CO
1994-2001. Associate Professor of Anatomy and Neurobiology, Colo. St. Univ., Ft. Collins, CO
1989-1994. Assistant Professor of Anatomy and Neurobiology, (tenure track), Colo. St. Univ., Ft.Collins, CO
1986-1989. Assistant Professor (Special Track), Anatomy and Neurobiology, Colo. St. Univ., Ft. Collins, CO
1985-1986. Research Associate, Anatomy, Univ. Colorado Med. Sch., Denver, CO
1981-1984 Postdoctoral Fellow, Physiology, Univ. Colorado Med. Sch., Denver, CO

Scientific Appointments

NIDCD Advisory Council, 2015-2021
Study section to review NIDCD T32 training grants. 2022-2023
NIH Director's Pioneer Award review panel, 2011-2014
NIH Director's New Innovator Award review panel, 2009
College of CSR Reviewers- 2009-2014
Member of several NIH Special Emphasis Panels, 2006-present
Member of NIH study section SCS, 2005
Ad-hoc member of NIH study section IFCN-4, 2000, 2002-2004
AChemS Advisory Committee, 2003-2005
Achems Program Co-Chair, 2001
Editorial Boards: Chemical Senses, 2001-2005 and 2014-present; BMC Neuroscience, 2003-2013. Pflugers Archiv, 2006-2013
Member of the special NIH study section, "Phenotyping the mouse nervous system", July 1999
Sensory Systems Panel, National Science Foundation, 1994-1998
NIDCD Strategic Planning Committee, 1992, 2016

Honors

Faculty of 1000, 2005- present
AChemS Award for Outstanding Achievement, 2001
Grass Fellowship to take Single Channel Methods, Cold Spring Harbor, 1985
N.I.H. Individual Postdoctoral Fellowship, 1983-84
Stipend to take Developmental Neurobiology, Cold Spring Harbor, 1982
H.H. Haymaker Award, excellence in graduate research, Div. of Biol., Kansas St. U., 1980
Phi Kappa Phi, 1980
Best Student Paper Award, 2nd place, Amer. Soc. Zool. annual meeting, 1980

C. Contributions to Science

1. Voltage-gated currents in mudpuppy taste cells. My early publications used whole cell and loose patch clamp recording to describe the membrane currents and electrical excitability of taste cells. These studies were begun while I was a postdoc in S. Roper's laboratory and continued in my own laboratory at Colorado State University. At that time patch clamp was a relatively new approach and had not yet been applied to taste cells. I took a course at Cold Spring Laboratory to learn the technique and then published the first reports of voltage gated currents in taste cells, utilizing the large, isolated taste cells of the mudpuppy. These studies documented that taste cells have voltage-gated sodium, potassium, and calcium currents, and that the potassium currents are restricted to the apical membrane of the cells, where they provide the basis for sour and bitter taste transduction in this species.

    a. **Kinnamon SC**, & Roper SD (1987). Passive and active membrane properties of mudpuppy taste receptor cells. J Physiol 383:601-614, PMC1183092
    b. **Kinnamon SC**, & Roper SD. (1988). Membrane properties of isolated mudpuppy taste cells. J Gen Physiol 91:351-371, PMC2216137.
    c. **Kinnamon SC**, Dionne VE, & Beam KG (1988). Apical localization of K+ channels in taste cells provides the basis for sour taste transduction. Proc Natl Acad Sci U S A 85:7023-7027, PMC2219208.
    d. Cummings, T. A., and. **Kinnamon S C**. (1992). Apical K+ channels in Necturus taste cells. Modulation by intracellular factors and taste stimuli. J Gen Physiol 99:591-613, PMC2219208.

2. Transduction elements in mammalian taste cells. Although the mudpuppy has large cells that are easily isolated and accessible for recording, it is not an ideal model for studying taste since the animal responds only to sour and bitter stimuli and lacks an appetitive taste response to sugars, NaCl, and amino acids. Thus, I began studying taste cells in rodent models. In early studies we used whole cell patch clamp, loose patch recording, calcium imaging, and anatomical methods to identify several key

transduction elements in rodent taste cells. The main findings are identification and characterization of ENaC as a taste receptor for NaCl; identification of the Type III IP3 receptor as the target of PLC signaling in taste transduction; defining the physiological role of α-gustducin in taste, defining the role of cAMP and protein kinases in sweet taste, and demonstrating that umami taste involves multiple receptors and mechanisms, and role of the proton channel Otop1 in sour and ammonium transduction. Examples are shown below.

a. Gilbertson TA, Roper SD & **Kinnamon SC** (1993). Proton currents through amiloride-sensitive Na+ channels in isolated hamster taste cells: enhancement by vasopressin and cAMP. Neuron 10:931-942.
b. Varkevisser B, & **Kinnamon SC**. (2000). Sweet taste transduction in hamster: role of protein kinases. J Neurophysiol 83:2526-2532.
c. Teng B, Wilson CE, Tu YH, Joshi NR, **Kinnamon SC**, Liman ER. (2019). Cellular and neural responses to sour stimuli require the proton channel Otop1. Curr Biol. 29: 3647-3656.
d. Liang Z*, Wilson CE*, Teng B, **Kinnamon SC**, Liman ER (2023). The proton channel Otop1 is a sensor for the taste of ammonium chloride. Nat Commun. 2023, 14(1):6194. *These authors contributed equally.

3. Role of identified taste cell types in mice. Once taste receptors and signaling effectors were molecularly identified, markers became available to characterize the different taste cell types functionally. Using transgenic mice expressing GFP in defined subsets of taste cells, we used whole cell recording, calcium imaging, and capacitance measurements to characterize the membrane properties of the different cell types. A principal finding is that Type II taste cells, those that express the taste receptors and downstream effectors for bitter, sweet, and umami tastes, lack voltage-gated calcium channels and presynaptic specializations for classical vesicular release of transmitter. Only Type III cells, those that respond to sour and salty stimuli, have voltage-gated calcium channels and exhibit calcium and voltage-dependent exocytosis of transmitter. We also showed that Type I cells, the glial-like cells, lack voltage-gated sodium and calcium channels, but may express ENaC, the epithelial sodium channel involved in amiloride-sensitive salt taste.

    a. Medler K, Margolskee RF, & **Kinnamon SC**. (2003). Electrophysiological characterization of voltage-gated currents in defined taste cell types of mice. J Neurosci 23:2608-2617.
    b. Clapp TR, Medler KF, Damak S, Margolskee R, & **Kinnamon SC** (2006). Mouse taste cells with G protein-coupled taste receptors lack voltage-gated calcium channels and SNAP-25. BMC Biol 4:7, PMC1444931.
    c. Vandenbeuch A, Clapp TR, & **Kinnamon SC** (2008). Amiloride-sensitive channels in type I fungiform taste cells in mouse. BMC Neurosci 9:1-13, PMC2235881.
    d. Vandenbeuch A, Zorec R, & **Kinnamon SC** (2010). Capacitance measurements of regulated exocytosis in mouse taste cells. J. Neuroscience, 30(44):14695-701, PMC3064517.

4. Neurotransmitters in taste buds. Because Type II cells lack the synaptic machinery to release transmitter in a conventional matter, we suspected that an unusual transmitter may link Type II cells to afferent nerve fibers. In collaboration with Tom Finger's laboratory, we established that ATP meets all the criteria required for a taste transmitter: presence in the taste cells, release in response to taste stimuli, postsynaptic P2X receptors on afferent nerve fibers, and a mechanism for breaking down the released ATP (NTPDase2, located on the membranes of the Type I glial-like cells). We found that double knockout of the purinergic receptors P2X2 and P2X3, or pharmacological inhibition by a membrane permeable P2X3 antagonist abolishes responses to all taste qualities. Interestingly, we expected that only the Type II cell qualities, i.e., bitter, sweet, and umami, would be affected, but all qualities, including sour and salty are abolished. Thus ATP release is required for transmission of all tastes to the nervous system. Since Type III cells are not known to release ATP, we are currently examining the source of ATP for sour and salty tastes, and the role of other neurotransmitters in the transmission process. We also showed that glutamate may serve as an efferent transmitter that is released as an axon reflex when afferent fibers are activated by ATP. The glutamate then binds to ionotropic glutamate receptors on Type III taste cells.

a. Finger TE, Danilova, Barrows J, Bartel DL, Vigers AJ, Stone L, Hellekant G., and **Kinnamon SC** (2005). ATP signaling is crucial for communication from taste buds to gustatory nerves. Science 310:1495-1499.
b. Vandenbeuch A, Anderson CB, Parnes J, Enjyoji K, Robson SC, Finger TE, **Kinnamon SC**. (2013). Role of the ectonucleotidase NTPDase2 in taste bud function. Proc Natl Acad Sci U S A. 2013 Sep 3;110(36):14789-94, PMC3767538.
c. Vandenbeuch A, Larson, ED. Anderson, CB, Smith, SA, Ford, AP, Finger, TE, **Kinnamon SC** (2015). Postsynaptic P2X3-containing receptors mediate responses to all taste qualities in mice. J. Physiol. 2015 Mar 1;593(5):1113-25, PMC4358674.
d. Larson, ED*, Vandenbeuch A*, Voigt A., Meyerhof W, **Kinnamon SC**, & Finger TE (2015). The role of 5-HT3 receptors in signaling from taste buds to nerves. J. Neurosci. 35:15984-95, PMC4666921. *Co-1st authors

5. Solitary chemosensory cells in airway epithelium. We have identified a population of scattered chemosensory cells in the epithelium of the upper airway that utilize taste receptor molecules to signal the presence of irritant substances that enter the nose and trachea. These airway chemosensory cells utilize bitter taste receptors and signaling effectors similar to those in taste buds. Yet this airway system does not give rise to taste sensations despite using a transduction cascade similar to taste buds. Bitter compounds activate the airway chemosensory cells which relay this information to pain fibers of the trigeminal nerve which activate protective airway responses (e.g. coughing, apnea, inflammation), presumably to rid the airways of noxious substances. In collaboration with Tom Finger, we have used transgenic mice expressing GFP in solitary chemoreceptor cells to determine the types of compounds that are detected by these cells and how these cells participate in protective airway reflexes. Recently, we have been collaborating with Rhinologists in the Otolaryngology Department to investigate the role of these cells in humans and to determine if they play a role in sinus diseases such as chronic rhinosinusitis.

   a. Gulbransen B, Clapp T, Finger TE, & **Kinnamon SC** (2008). Nasal solitary chemoreceptor cell responses to bitter and trigeminal stimulants *in vitro*. J. Neurophysiol., 99:2929-37, PMC2765583.

   b. Tizzano M, Gulbransen, BD, Vandenbeuch A, Clapp TR, Herman JP, Sibhatu HM, Churchill MEA, Silver WL, **Kinnamon SC**, & Finger TE (2009). Nasal chemosensory cells utilize bitter taste signalling to detect irritants and pathogenic Bacteria. PNAS 107:3210-5, PMC2840287.

   c. Barham HP, Cooper SE, Anderson CB, Tizzano M, Kingdom TT, Finger TE, **Kinnamon SC**, & Ramakrishnan VR (2013). Solitary chemosensory cells and bitter taste receptor signaling in human sinonasal mucosa. Int Forum Allergy Rhinol. 2013 Jun;3(6):450-7, PMC3655139.

Complete S. Kinnamon bibliography

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Lu, Shi-Long

eRA COMMONS USER NAME (credential, e.g., agency login): LUSHIL

POSITION TITLE: Professor of Otolaryngology - Head and Neck Surgery

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
China Medical University, Shenyang, China	MD	07/1982	07/1987	Medicine
China Medical University, Shenyang, China	Resident/Fellow	07/1987	07/1992	Medical Oncology
Tokyo Medical & Dental University, Tokyo	PhD (Mentor: Yasuhito Yuasa)	04/1995	04/1999	Molecular Oncology
HHMI, Case Western Reserve University, Cleveland, OH	Post-doc (Mentor: Sanford Markowitz)	04/1999	02/2003	Translational Oncology

A. Personal Statement

I am a Professor of Otolaryngology – Head and Neck Surgery and my research is focused on fundamental and translational aspects of head and neck cancers, including head and neck squamous cell carcinoma (HNSCC) and salivary gland tumors (SGTs). Specifically, my lab works on delineating the roles of PI3K and TGFβ signaling pathway, cancer stem cell, and oral microbiome in HNSCC pathogenesis, identifying saliva biomarkers for early detection, recurrence, and surveillance of HNSCC, and developing novel therapeutic approaches for HNSCC. Several key discoveries from my lab are: (1) We were among the first to develop multiple genetically engineered mouse models (GEMMs) of HNSCC in both PI3K and TGFβ pathways. In combination with the tobacco carcinogenesis protocol, these models develop HNSCC, which mimic human HNSCC etiologically, pathologically and molecularly. (2) We developed GEMMs for human SGTs and are using these models to study the role of PTEN and Smad4 in SGT pathogenesis. (3) We have identified a panel of methylated genomic loci encoding microRNAs, which can be detected in patient saliva, to serve as biomarkers for early diagnosis, recurrence, and surveillance of HNSCC patients. (4). In collaboration with our colleague, we are among the first to study the functional role of oral microbiome in HNSCC pathogenesis and its impact on immunotherapy and PI3K targeted therapy. (5) In collaboration with our colleague, we developed a novel therapeutic approach using a bivalent EGF immunotoxin-based therapy on HNSCC models my lab has developed. (6) In collaboration with our colleague, we are developing multi-Omics together with optical imaging techniques to predict the risk of malignant transformation of oral lesions.

Ongoing and recently completed projects and publications that I would like to highlight include:

UH2/UH3 CA262045 (PI: Lu) 9/1/2021-8/31/2026
NIH/NCI
Validation of a saliva testing using methylated microRNAs for head and neck cancer recurrence
The goal is to analytically validate “HNKlear”, the saliva test for head and neck cancer, in UH2 phase, and to clinically validate HNKlear in early detection of head and neck cancer recurrence in UH3 phase.

R21DE033826 (MPI: Lu & Frank) 9/1/2024-8/31/2026
NIH/NIDCR
Functional roles of human microbiome and metabolome in oral cancer
and Toll-like Receptor Pathways in Head and Neck Cancer

The goal is to perform metagenomics and metabolomics studies on saliva of human oral cancer and test the functional role of oral microbiome in oral cancer mouse models.

R21DE029262 (MPI: Lu & Frank) 7/1/2020-6/30/2023
NIH/NIDCR
Oral Microbiota and Toll-like Receptor Pathways in Head and Neck Cancer
The goal is to understand the role of Toll-like receptor pathways in mediating oral dysbiosis in head and neck cancer, and their effects on PI3K targeted therapy.

R56DE028959 (MPI: Lu & Frank) 8/1/2019-7/31/2022
NIH/NIDCR
Modulation of tumor microenvironment by microbiome in head and neck cancer
The goal is to understand oral and gut microbiome in local and systemic immune modulation through AHR/IDO pathway and potential translational applications to immunotherapy.

Citations:

1). Du L, Chen X, Cao Y, Lu L, Zhang F, Bornstein S, Li Y, Owens P, Malkoski S, Said S, Kulesz-Martin M, Gross N, Wang XJ, **Lu SL** (2016): Overexpression of PIK3CA in head and neck epithelium drives tumor invasion and metastasis through PDK1 and enhanced TGFbeta signaling. *Oncogene* 35: 4641-4652. PMCID: PMC4985507

2). Cao Y, Liu H, Gao L, Lu L, Du L, Bai H, Li J, Said S, Wang X, Song J, Serkova N, Wei M, Xiao J, **Lu SL** (2018): Cooperation between Pten and Smad4 in mouse salivary gland tumor formation and progression. *Neoplasia* 20: 764-774. PMCID: PMC6031150

3) Chen X, Cao Y, Sedhom W, Lu L, Liu Y, Wang H, Oka M, Bornstein S, Said S, Song J, **Lu SL** (2020): Distinct roles of PIK3CA in enriching and maintaining of cancer stem cells in head and neck squamous cell carcinoma. *Molecular Oncology* 14: 139-158. PMCID: PMC6944113

4) **Frank DN,** Qiu Y, Cao Y, Zhang S, **Lu L, Kofonow JM, Robertson CE,** Liu Y, Wang H, Levens CL, **Kuhn KA,** Song J, Ramakrishnan VR**, Lu SL**. (2022): A Dysbiotic Microbiome Promotes Head and Neck Squamous Cell Carcinoma. *Oncogene.* 41: 1269-1280. PMID: 35087236

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2021-Present	Professor, Department of Otolaryngology – Head and Neck Surgery (Primary), Dermatology and Pathology (Secondary), University of Colorado School of Medicine, Aurora, CO
2013-2021	Associate Professor, Department of Otolaryngology – Head and Neck Surgery (Primary), Dermatology and Pathology (Secondary), University of Colorado School of Medicine, Aurora, CO
2008-2013	Assistant Professor, Department of Otolaryngology – Head and Neck Surgery (Primary), Dermatology and Pathology (Secondary), University of Colorado School of Medicine, Aurora, CO
2003-2008	Research Assistant Professor, Department of Otolaryngology – Head and Neck Surgery (Primary), and Dermatology (Secondary), Oregon Health & Science University, Portland, OR
1994-1995	Molecular Oncology Research Fellow, Department of Molecular Oncology, Tokyo Medical and Dental University, Tokyo, Japan
1992-1994	Attending Physician, Medical Oncology, The First University Hospital of China Medical University, Shenyang, China

Other Experience and Professional Memberships

2024	*Ad hoc reviewer,* NCI Small Business Innovation Research Solicitation: Topic 458.
2024	*Ad Hoc* reviewer, NIH Oncological Sciences F09C fellowship review panel. (2024)
2023	*Ad Hoc* reviewer, NIDCR RFA study section "Understanding Persistent Oral Human Papillomavirus and Human Immunodeficiency Virus Co-infection and Its Role with Oropharyngeal Cancer Induction."
2023	Invited Speaker, NCI workshop on ctDNA in Cancer Treatment and Clinical Care
2021-2023	*Ad Hoc* reviewer, NCI R21 Clinical and Translational Cancer Research Studies Review Panel
2021	*Ad Hoc* reviewer, NCI Specialized Program of Research Excellence (SPORE) for Brain, Lung, Head and Neck Cancers
2020	*Ad Hoc* reviewer, NCI SPORE for Brain, Lung, Head and Neck Cancers
2020	*Ad Hoc* reviewer, NCI SPORE for Head and Neck, Brain cancers and Leukemia
2020-	Member, American Association of Dental Research (AADR)-Diagnostic Sciences Group

2020- Member, International Association of Dental Research (ICDR)-Salivary Research Group
2019- Member, American Society of Clinical Oncology (ASCO)
2018 Invited Speaker, *NIH SPORE Head and Neck Cancer workshop*
2018 Founder & CSO, Summit Biolabs, Inc
2015 *Ad Hoc* reviewer, NIH Patterns of Interaction in Peer Review Meetings
2014 Invited Speaker, *FASEB meeting on lipid and lipid regulated kinases in cancer*
2012- Editorial Board, *International Journal of Oncology*
2011- *Ad Hoc* reviewers for Medical Research Council of United Kingdom, UK-Malaysia Newton Fund, Israel Science Foundation, Research Grant Council of Hong Kong, National Natural Science Foundation of China
2008 Invited Speaker, *Thyroid Head and Neck Cancer (THANC) Foundation,* New York City
2005- Peer reviewers: *Journal of Clinical Investigation, Nature Communications*, *iScience*, *Cancer Research*, *Clinical Cancer Research, Molecular Cancer Research*, *Molecular Cancer Therapeutics, Oncogene, Molecular Carcinogenesis, Molecular Medicine, Oncotarget, PloS One*, *Head and Neck, Laryngoscope, International Journal of Cancer, Cancer Letters, Clinical Epigenetics, Genes, Chromosomes and Cancer, Gene, Journal of Investigative Dermatology, BBA-Reviews on Cancer, Expert Opinion on Therapeutic Targets*, etc
2003- Member, Society of Investigative Dermatology (SID)
2000- Member, American Association for Cancer Research (AACR)

Honors and Awards:

2021 Entrepreneur of the Year, Finalist-ColoradoBiz magazine
2020 Highlight on Annual Report of CU Innovations
2019 BioScience Profile on Annual magazine of Colorado BioSciences Association
2019 Chancellors Discovery Innovation Award, University of Colorado
2018 CU Innovations SPARK Award
2015 Whedon Cancer Detection Foundation Award
2011 Co-Chair, Head, Neck, Nasopharyngeal, Oral Cavity and Thyroid Cancers, 4th Word Cancer Congress, Dalian, China
2009 Research on Smad4 head and neck cancer model was highlighted in Journal of Clinical Investigation by accompanying editorial
2008 Young Investigator Award, from THANC (Thyroid, Head and Neck Cancer) Foundation, NY
2007-2010 Career Development Award, Dermatology Foundation, IL
2005 Albert M. Kligman Travel Award, the Dermatology Foundation, IL
2005 OHSU Certificate of Appreciation for Mentoring Next Generation of Scientists
2004 Oregon Medical Research Foundation Award
2004 Best Poster Award, the 6th International Head and Neck Cancer Conference
1999 PhD Graduation Speech, Tokyo Medical and Dental University
1995-1999 The Japanese Government (Monbusho) Scholarship for PhD Degree
1994-1995 The Japanese Government (Monbusho) Fellowship

C. Contributions to Science

1. Role of TGFβ signaling in colorectal cancer. During my PhD and postdoctoral training, I focused on studying the role of TGFβ signaling in colorectal cancer. Under the mentoring of Drs. Yashuhito Yuasa, and Kohei Miyazono, I reported the genomic structure of TGFβ type II receptor, and somatic and germline mutations, in hereditary nonpolyposis colorectal cancers. I also functionally characterized the mutations in the TGFβ signaling pathway. Working in Dr. Sanford Markowitz lab as a postdoctoral fellow, I contributed to identifying a TGFβ-induced tumor suppressor, 15-Hydroxyprostaglandin dehydrogenase, in colorectal cancer. These studies were innovative, and I was among the first to report that the TGFβ type II receptor mutation in the poly(A) tracts due to DNA mismatch repair defect, and I was among the first to describe the role of the TGFβ signaling pathway in human cancers.

a) **Lu SL**, Zhang WC, Akiyama Y, Nomizu T, Yuasa Y: Genomic structure of the transforming growth factor-beta type II receptor gene and its mutations in hereditary nonpolyposis colorectal cancers. ***Cancer Research*** 56: 4595-4598, 1996 (PMID: 8840968)
b) **Lu SL**, Kawabata M, Imamura T, Akiyama Y, Nomizu T, Miyazono K, Yuasa Y: HNPCC associated with germline mutation in the TGF-beta type II receptor gene. ***Nature Genetics*** 19: 17-18, 1998 (PMID: 9590282)

c) **Lu SL**, Kawabata M, Imamura T, Miyazono K, Yuasa Y: Two divergent signaling pathways for TGF-beta separated by a mutation of its type II receptor gene. ***Biochemical Biophysical Research Communications*** 259: 385-390, 1999 (PMID: 10362519)
d) Yan M, Rerko R, Platzer P, Dawson D, Willis J, Tong M, Lawrence E, Lutterbaugh J, **Lu SL**, Willson JK, Luo G, Hensold J, Tai, H, Wilson K, Markowitz SD: 15-Hydroxyprostaglandin dehydrogenase, a COX-2 oncogene antagonist, is a TGF-beta-induced suppressor of human gastrointestinal cancers. ***Proceedings of the National Academy of Sciences*** 101: 17468-17473, 2004 (PMCID: PMC536023)

2. Role of TGFβ signaling in skin cancer and development. During the transition to my independent lab, I worked in Dr. Xiao-Jing Wang's lab as a Research Assistant Professor. I obtained further in-depth training on developing genetically engineered mouse models (GEMMs) and using GEMMs to study the in vivo role of TGFβ signaling in skin cancer and development. The work was innovative, and the results opened new avenues of research on Smads in skin cancer and development.

a) Li AG, **Lu SL**, Zhang MX, Deng C, Wang XJ: Smad3 knockout mice exhibit a resistance to skin chemical carcinogenesis. ***Cancer Research*** 64: 7836-7845, 2004 (PMID: 15520189)
b) Han G, **Lu SL**, Li AG, He W, Corless CL, Kulesz-Martin M, Wang XJ: Distinct mechanisms of TGFbeta1-mediated epithelial-mesenchymal transition and metastasis during skin carcinogenesis. ***Journal of Clinical Investigation*** 115: 1714-1723, 2005 (PMCID: PMC1142114)
c) Han G, Li AG, Liang YY, Owens P, He W, **Lu SL**, Yoshimatsu Y, Wang D, Lin X, Wang XJ: Smad7-induced beta-catenin degradation alters epidermal stem cell differentiation. ***Developmental Cell,*** 11: 301-12, 2006 (PMID: 16950122)
d) Hoot K, Lighthall J, Han G, **Lu SL**, Han G, Li A, Ju W, Kulesz-Martin M, Bottinger E, Wang XJ: Keratinocyte-specific Smad2 ablation results in increased epithelial-mesenchymal transition during skin cancer formation and progression. ***Journal of Clinical Investigation*** 118:2722-32, 2008 (PMCID: PMC2447925)

3. In vivo modeling of head and neck squamous cell carcinoma. In collaboration with Dr. Xiao-Jing Wang, I developed the first GEMMs for HNSCC. Prior to generation of these mice, there were no relevant in vivo disease models available for HNSCC. Using a head and neck-specific inducible system, we were able to either overexpress or knock down genes relevant to HNSCC tumorigenesis, which enabled our studies describing the molecular mechanisms of HNSCC. These studies also helped us to identify novel targets for development of HNSCC diagnosis and therapies.

a) **Lu SL**, Reh D, Li AG, Woods J, Corless CL, Kulesz-Martin M, Wang XJ: Overexpression of transforming growth factor beta1 in head and neck epithelia results in inflammation, angiogenesis, and epithelial hyperproliferation. ***Cancer Research*** 64: 4405-4410, 2004 (PMID: 15231647)
b) **Lu SL**, Herrington H, Reh D, Weber S, Bernstein S, Wang D, Tang CF, Siddiqui Y, Nord J, Andersen P, Corless C, Wang XJ: Loss of transforming growth factor-beta type II receptor promotes metastatic head-and-neck squamous cell carcinoma. ***Genes & Development*** 20: 1331-1342, 2006 (PMCID: PMC1472907)
c) Bornstein S, White R, Malkoski S, Reh D, Anderson P, Gross N, Olson S, Deng CX, **Lu SL*,** Wang XJ: Smad4 loss in mice causes spontaneous head and neck cancer with increased genomic instability and inflammation. ***Journal of Clinical Investigation*** 119: 3408-3419, 2009 (PMCID: PMC2769185) *Co-corresponding author
[Commentary by Korc M: Smad4: gatekeeper gene in head and neck squamous cell carcinoma. *Journal of Clinical Investigation* 119: 3208-321, 2009]
d) **Lu SL*,** Herrington H, Wang XJ: Mouse models for human head and neck squamous cell carcinomas. ***Head & Neck*** 28: 945-54, 2006 (PMID: 16721744) *Co-corresponding author

4. Role of the PI3K/PTEN/AKT pathway in human cancers. In addition to the contributions described above, my lab has investigated the role of the PI3K/PTEN/AKT pathway and its interplay with the TGFβ pathway in head and neck cancer initiation, progression, and metastasis. We generated an inducible PIK3CA transgenic mouse model, which promotes tumor invasion and metastasis. Our work was innovative, and we found that PDK1 and TGFβ1 were two major mediators contributing to HNSCC invasion and progression. Moreover, overexpression of PIK3CA drives epithelial-mesenchymal transition, and enriches cancer stem cell-like properties. We also found that AKT activation acts as an early molecular event upon tobacco exposure in HNSCC. In collaboration with Dr. Malkoski, we studied the role of PTEN in a murine lung cancer model. Currently, we have modified the inducible system into a salivary gland-specific GEMM, and have used this model for studying of molecular mechanisms of PTEN and Smad4 in salivary gland tumors. These studies are applicable to the development of novel strategies for therapy in salivary gland tumors. The work is innovative and has resulted in development of the only well-established SGT-GEMM in the field.

a) Weber S, Bornstein S, Li, Y, Malkoski S, Wang D, Rustgi A, Kulesz-Martin M, Wang XJ, **Lu SL**: Tobacco-specific carcinogen nitrosamine 4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone induces AKT activation in head and neck epithelia. ***International Journal of Oncology*** 39:1193-1198, 2011 (PMCID: PMC3249931)
b) Du L, Chen X, Cao Y, Lu L, Zhang F, Bornstein S, Li Y, Owens P, Malkoski S, Said S, Kulesz-Martin M, Gross N, Wang XJ, **Lu SL**: Overexpression of PIK3CA in head and neck epithelium drives tumor invasion and metastasis through PDK1 and enhanced TGFbeta signaling. ***Oncogene*** 35: 4641-4652, 2016 (PMCID: PMC4985507)
c) Cao Y, Liu H, Gao L, Lu L, Du L, Bai H, Li J, Said S, Wang X, Song J, Serkova N, Wei M, Xiao J, **Lu SL**: Cooperation between Pten and Smad4 in mouse salivary gland tumor formation and progression. ***Neoplasia*** 20: 764-774, 2018 (PMCID: PMC6031150)
d) Chen X, Cao Y, Sedhom W, Lu L, Liu Y, Wang H, Oka M, Bornstein S, Said S, Song J, **Lu SL:** Distinct roles of PIK3CA in enriching and maintaining of cancer stem cells in head and neck squamous cell carcinoma. ***Molecular Oncology*** 14: 139-158, 2020 (PMCID: PMC6944113)

5. DNA methylation and microRNA in human cancer. As a postdoctoral fellow in Dr. Sanford Markowitz's lab, I initiated a study using Vimentin DNA methylation as a biomarker for colorectal cancer detection using fecal DNA. The expertise gained from this study has led to one of the important research projects currently going on in my lab, i.e., the development of methylated microRNAs as biomarkers for head and neck cancers. In addition, in collaboration with Dr. Xiao-Jing Wang, we also investigated the role of microRNAs in head and neck cancer stem cells, particularly with respect to metastasis. These innovative studies have impacted the field and resulted in a patent of "Biomarkers for head and neck cancer and methods of their use" issued by the USPTO.

a) Minor J, Wang X, Zhang F, Song J, Jimeno A, Wang XJ, Lu X, Gross N, Kulesz-Martin M, Wang D, **Lu SL**: Methylation of microRNA-9 is a specific and sensitive biomarker for oral and oropharyngeal squamous cell carcinomas. ***Oral Oncology*** 48: 73-8, 2012 (PMCID: PMC3291120)
b) White R, Neiman J, Reddi A, Han G, Birlea S, Mitra D, Dionne L, Fernandez P, Murao K, Bian L, Keysar S, Goldstein N, Song N, Bornstein S, Han Z, Lu X, Wisell J, Li F, Song J, **Lu SL**, Roop D, Wang X: Epithelial stem cell mutations that promote squamous cell carcinoma metastasis. ***Journal of Clinical Investigation*** 123: 4390-4404, 2013 (PMCID: PMC3784525)
c) Cao Y, Green K, Quattlebaum S, Milam B, Lu L, Gao D, HE H, Li N, Gao L, Hall F, Whinery M, Handley E, Ma Y, Jin F, Xiao J, Wei M, Smith D, Bornstein S, Gross N, Pyeon D, Song J, **Lu SL**: Methylated genomic loci encoding microRNAs in saliva as a biomarker panel in tissue and saliva for head and neck squamous cell carcinoma. ***Clinical Epigenetics*** 10:43, 2018 (PMCID: PMC5883341)
d) Yang CX, Seldom W, Song JI, **Lu SL**: The role of microRNAs in recurrence and metastasis of head and neck squamous cell carcinoma. ***Cancers*** 11: 395, 2019 (PMCID: PMC6468798)

6. Oral microbiome and head and neck cancer. In collaboration with Dr. Daniel Frank, we are among the first to study the functional role of oral microbiome in HNSCC pathogenesis and its impact on immunotherapy and PI3K targeted therapy.

a) Frank DN, Qiu Y, Cao Y, Zhang S, Lu L, Kofonow JM, Robertson CE, Liu Y, Wang H, Levens CL, Kuhn KA, Song J, Ramakrishnan VR, **Lu SL**. (2022): A Dysbiotic Microbiome Promotes Head and Neck Squamous Cell Carcinoma. ***Oncogene***. 41: 1269-1280. PMID: 35087236

7. Saliva diagnostics for infectious diseases: During the pandemic, we leveraged our expertise in saliva diagnostics for head and neck cancer and developed an extraction-free fast and high throughput saliva diagnostics for COVID. The technology was licensed to a commercial diagnostic company, which provided almost a third of all COVID testing for the state of Colorado.

a) Qiu Y, Lu L, Halven A, Terrio R, Yuldelson S, Dougal N, Galbo F, Lu A, Gao D, Blomquist B, Zevallos J, **Lu SL***, Yao X, Harry B: Extraction-free testing for SARS-CoV-2 in nasal swab and saliva samples on a single high-throughput platform. ***Journal of Biotechnology and Biomedicine***, 7: 214-220 (2024) *=co-corresponding author
b) Qiu Y, Lu L, Lu A, Gao D, McGrath P, Han C, Kogut I, Blomquist B, Yao X, Zevallos J, **Lu SL***, Harry B: SARS-Cov-2 Viral Load in Nasal Swab and Raw Saliva Samples from COVID-19 Patients. ***Archives of Microbiology and Immunology***. 8: 280-289 (2024). *=co-corresponding author

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/shi-long.lu.1/bibliography/public/

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Manchaiah, Vinaya

eRA COMMONS USER NAME (credential, e.g., agency login): VINAYAMAANCHAIAH

POSITION TITLE: Professor, Director of Audiology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Mysore, India	BSc	05/2005	Speech and Hearing Sciences
University of Southampton, UK	MSc	10/2006	Audiology
Nova Southeastern University, USA	AuD	06/2010	Audiology
Swansea University, UK	PGCtHE	07/2011	Teaching and Learning
Swansea University, UK	MBA	10/2013	Business Administration
Linköping University, Sweden	PhD	10/2013	Disability Research

A. Personal Statement

As Professor at the University of Colorado School of Medicine and Director of Audiology at the University of Colorado Hospital (UCHealth), I have wide ranging experience in clinical, teaching, research, and administrative roles in hearing healthcare. My primary training is in audiology and hearing healthcare; however, I also have substantial experience in healthcare business administration and disability research. I co-lead the Virtual Hearing Lab (collaborative initiative between the University of Colorado School of Medicine and the University of Pretoria) together with Dr. Swanepoel.

My research focus is on the development of eHealth solutions to improve accessibility, affordability, and outcomes of rehabilitation for people with hearing and balance disorders mainly by promoting self-management. In addition to access and adherence to hearing health services, some of the main barriers my work addresses include the availability of trained hearing healthcare professionals, the time and cost associated with professional consultations, and the cost of hearing instruments. Clinical care alone is insufficient to achieve optimal outcomes in the management of chronic conditions such as hearing loss. For all these reasons, the promotion of self-management of chronic conditions has become popular in healthcare. Self-management support goes beyond traditional knowledge-based patient education to include processes that develop patient problem-solving skills, improving patient self-efficacy, and support for the application of knowledge in patient's day-to-day, real-life situations. Patient involvement, leadership, and ownership of care can help prevent and/or prolong the occurrences of health conditions, can help improve accessibility and affordability, and can result in improved health outcomes.

I have led or participated in 6 randomized controlled trials including to evaluate the efficacy of Internet-based cognitive behavioral therapy (ICBT) for tinnitus, as well as a recent effectiveness trial on over-the-counter (OTC) hearing aids. Since joining University of Colorado in 2022, I have developed a strong collaboration with MPI, Dr. Anu Sharma resulting in two co-authored publications and two funded grants on the topic of OTC hearing aids. I also have strong and active collaborations with other professionals including otolaryngologists, computer scientists, statisticians, sociologists, and psychologists at the University of Colorado and other sites. I believe I have the skills, experience, discipline and drive necessary to successfully complete this project.

Ongoing and recently completed projects that I would like to highlight include:

NIDCD R21DC020561 2024-2026
Assessment of cochlear dysfunction in Black and White adults with stage 2 hypertension using high-frequency distortion product otoacoustic emissions
PI: Baiduc, R.R., Co-Is: **Manchaiah, V.,** Goodman, S.S., & Vance, E.

William Demant Foundation 2023-2025
Sound advice for delivering hearing health care: Outcome evaluation and patient profiles for current and emerging service delivery models for hearing aids
MPIs: Sharma, A. & **Manchaiah, V.;** OSC: Ng, E.

University of Colorado AB Nexus 2022-2024
Sound advice for delivering hearing health care: Evaluation of current and emerging service delivery models for hearing aids
MPIs: Sharma, A. & **Manchaiah, V.**

Sonova Holding AG 2021-2024
The emotions behind writing: Using natural language to understand hearing aid benefit and satisfaction
MPIs: Swanepoel, D.W. & **Manchaiah, V.**

NIDCD R21DC017214 2018-2023
Cognitive Behavior Therapy based self-help delivered via the Internet for tinnitus suffers: Efficacy trial in the U.S. population
PI: **Manchaiah, V.**

Citations:

1. **Manchaiah, V.**, Swanepoel, D.W., & Sharma, A. (2023). Prioritizing research on Over the Counter (OTC) hearing aids for age-related hearing loss. *Frontiers in Aging*, 4, 1105879. doi: 10.3389/fragi.2023.1105879
2. De Sousa, K., **Manchaiah, V.**, Moore, D.R., Graham, M., & Swanepoel, D.W. (2023). Effectiveness of over-the-counter self-fitting hearing aid compared to an audiologist-fitted hearing aid: A randomized clinical trial. *JAMA Otolaryngology – Head & Neck Surgery,* Published Online. doi: 10.1001/jamaoto.2023.0376
3. Swanepoel, D.W., Oosthuizen, I., Graham, M., & **Manchaiah, V.** *(*2023). Comparing hearing aid outcomes in adults using over-the-counter and hearing care professional service delivery models. *American Journal of Audiology,* Published Online. doi: 10.1044/2022_AJA-22-00130
4. Tran, N. & **Manchaiah, V.** (2018). Outcomes of direct-to-consumer hearing devices for people with hearing loss: A review. *Journal of Audiology and Otology,* 22(4), 178-188. doi: 10.7874/jao.2018.00248

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022-	P*rofessor*, Department of Otolaryngology-Head and Neck Surgery, University of Colorado School of Medicine, Aurora, Colorado, USA
2022-	*Director of Audiology*, UCHealth Hearing and Balance, University of Colorado Hospital, Aurora, Colorado, USA
2021-	*Extraordinary Professor,* Department of Speech-Language Pathology and Audiology, University of Pretoria, South Africa
2016-	*Adjunct Faculty*, Department of Speech and Hearing, Manipal University of Higher Education, India
2019-2022	*Professor of Speech and Hearing Sciences,* Department of Speech and Hearing Sciences, Lamar University, Beaumont, Texas, USA
2015-2022	*Jo Mayo Endowed Professor,* Department of Speech and Hearing Sciences, Lamar University, Beaumont, Texas, USA

2015-2019 *Associate Professor of Audiology,* Department of Speech and Hearing Sciences, Lamar University, Beaumont, Texas, USA
2013-2015 *Senior Lecturer in Audiology and Course Leader for Foundation Degree in Hearing Aid Audiology*, Department of Vision and Hearing Sciences, Anglia Ruskin University, Cambridge, UK
2009 *Visiting Research Fellow,* University of Essex, UK
2007-2013 *Lecturer and Program Manager - Audiology*, College of Human and Health Sciences, Swansea University, Swansea, UK
2006-2017 *Senior Audiologist*, NHS Lothian University Hospital Division, Edinburgh, UK
2005 *Research Audiologist*, All India Institute of Speech and Hearing, Mysore, India

Honors

2017-19 Shapiro Prize, British Tinnitus Association (BTA), UK
2017 Bharat Samman Award, NRI Institute, India
2016 Jerger Future Leaders of Audiology (JFLAC), American Academy of Audiology, USA
2013 Fast and efficient PhD award, Linköping University, Sweden
2013 Distinction in Executive MBA program, Swansea University, UK
2010 Highest honors in Doctor of Audiology (AuD) program, Nova Southeastern University, USA
2004 Best poster presentation award, Indian Speech and Hearing Association Conference, India

C. Contributions to Science

1. Hearing healthcare service delivery model with emphasis on over-the-counter (OTC) hearing aids: This line of research focuses on developing the evidence base for new service delivery models (i.e., direct-to-consumer model, community-based rehabilitation) to improve accessibility, affordability, and outcomes of hearing healthcare services. More specifically, this research theme is focused on developing evidence on the efficacy of OTC hearing aids for individuals with mild-to-moderate hearing loss.

a) De Sousa, K., **Manchaiah, V.**, Moore, D.R., Graham, M., & Swanepoel, D.W. (2023). Effectiveness of over-the-counter self-fitting hearing aid compared to an audiologist-fitted hearing aid: A randomized clinical trial. *JAMA Otolaryngology – Head & Neck Surgery,* Published Online. doi: 10.1001/jamaoto.2023.0376
b) Swanepoel, D.W., Oosthuizen, I., Graham, M., & **Manchaiah, V.** *(*2023). Comparing hearing aid outcomes in adults using over-the-counter and hearing care professional service delivery models. *American Journal of Audiology,* Published Online. doi: 10.1044/2022_AJA-22-00130
c) **Manchaiah, V.**, Sharma, A., Rodrigo, H., Bailey, A., De Sousa, K., & Swanepoel, D.W. (2023). Hearing healthcare professionals' views about Over-the-Counter (OTC) hearing aids: Analysis of retrospective survey data. *Audiology Research*, 13, 185-195. doi: 10.3390/audiolres13020018
d) **Manchaiah, V.**, Taylor, B., Dockens, A.L., Tran, N.R., Lane, N., Castle, M. & Grover, V. (2017). Applications of direct-to-consumer hearing devices for adults with hearing loss: A review. *Clinical Interventions in Aging*, 12:859-871. doi: 10.2147/CIA.S135390

2. Hearing aid outcomes: This line of research focuses on examining the hearing aid outcomes (i.e., benefit and satisfaction), potential adverse effects as well as factors that contribute to success with hearing aids.

a) Bannon, L., Picou, E., Bailey, A., & **Manchaiah, V.** (2023). Consumer survey on hearing aid benefit and satisfaction. *Journal of Speech, Language and Hearing Research*, 66(4), 1410-1427. doi: 10.1044/2022_JSLHR-22-00066
b) **Manchaiah, V.,** Picou, E.M., Bailey, A., & Rodrigo, H. (2021). Consumer ratings of the most desirable hearing aid attributes. *Journal of the American Academy of Audiology,* 32(8), 537-546. doi: 10.1055/s-0041-1732442
c) **Manchaiah, V.**, Amlani, A.M., Bricker, C.M., Whitfield, C.T. & Ratinaud, P. (2019). Benefits and shortcomings of direct-to-consumer hearing devices: Analysis of large secondary data generated from Amazon customer reviews. *Journal of Speech, Language, and Hearing Research,* 62(5), 1506-1516. doi: 10.1044/2018_JSLHR-H-18-0370
d) **Manchaiah, V.**, Abrams, H., Bailey, A. & Andersson, G. (2019). Negative side effects of hearing aids in adult hearing aid users. *Journal of the American Academy of Audiology*, 30(6), 472-481. doi: 10.3766/jaaa.17118

3. Consumer Health Informatics (CHI) of hearing healthcare services*:* The focus of this line of research is to understand the patient-generated online hearing health information about hearing loss and hearing aids. More specifically, this research seeks to understand the perspectives of individuals with hearing loss and hearing aid users using a large-secondary data. This line of exploratory research serves as hypothesis generating research supplementing the two key areas discussed above on hearing healthcare service delivery model as well as factors influencing the hearing aid outcomes.

a) Heselton, T., Bennett, R.J., **Manchaiah, V.** & Swanepoel, D.W. (2022). Online consumer reviews of hearing aid acquisition and use: A qualitative thematic analysis. *American Journal of Audiology,* 31(2), 284-298. doi: 10.1044/2021_AJA-21-00172
b) Bennett, R., Swanepoel, D.W., Ratinaud, P., Bailey, A., Pennebaker, J.W., & **Manchaiah, V.** (2021). Hearing aid acquisition and ownership: What can we learn from online consumer reviews? *International Journal of Audiology,* 60(11, 917-926. doi: 10.1080/14992027.2021.1931487
c) **Manchaiah, V.**, Swanepoel, D.W., Bailey, A., Pennebaker, J.W., & Bennett, R. (2021). Hearing aid consumer reviews: A linguistic analysis in relation benefit and satisfaction ratings. *American Journal of Audiology,* 30(3), 761-768. doi: 10.1044/2021_AJA-21-00061
d) **Manchaiah, V.,** Swanepoel, W., & Bennett, R. J. (2021). Online Consumer Reviews on Hearing Health Care Services: A Textual Analysis Approach to Examine Psychologically Meaningful Language Dimensions. *American journal of audiology*, *30*(3), 669–675. doi: 10.1044/2021_AJA-20-00223

4. Internet-based interventions for hearing and balance disorders*:* This line of research focuses on developing and evaluating self-help internet interventions for individuals with hearing and balance disorders to improve accessibility, affordability, and outcomes.

a) Beukes, E.W., Andersson, G., Fagelson, M.A., & **Manchaiah, V.** (2021). Dismantling internet-based cognitive behavioral therapy for tinnitus. The contribution of applied relaxation: A randomized controlled trial. *Internet Interventions*, 25, 100402. doi: 10.1016/j.invent.2021.100402
b) Beukes, E.W., Andersson, G.A., Allen, P.A., **Manchaiah, V.** & Baguley, D.M. (2018). Effectiveness of guided Internet-based Cognitive Behavioral Therapy vs face-to-face clinical care for treatment of tinnitus: A randomised clinical trial. *JAMA Otolaryngology – Head & Neck Surgery,* 144(12), 1126-1133. doi: 10.1001/jamaoto.2018.2238
c) Beukes, E.W., Baguley, D.M., Allen, P.M., **Manchaiah, V.** & Andersson, G. (2018). Audiologist-guided Internet-based cognitive behaviour therapy for adults with tinnitus in the United Kingdom: A randomised controlled trial. *Ear and Hearing*, 39(3), 423-433. doi: 10.1097/AUD.0000000000000505
d) **Manchaiah, V.**, Rönnberg, J., Andersson, G. & Lunner, T. (2014). Use of the 'patient journey' model in the internet-based pre-fitting counseling of a person with hearing disability: Lessons from a failed clinical trial. *BMJ Ear, Nose and Throat Disorders,* 14, 3. doi: 10.1186/1472-6815-14-3

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/51855865/.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Conner Joseph Massey

eRA COMMONS USER NAME (credential, e.g., agency login): COMASSEY

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Brandeis University	BS	06/2011	Biology
Tufts University School of Medicine	MD	05/2015	Medicine
George Washington University School of Medicine	Research Fellow	06/2016	Rhinology
University of Colorado School of Medicine	Resident	06/2023	Otolaryngology Residency
University of Utah School of Medicine	Fellow	06/2024	Rhinology & Anterior Skull Base Surgery

A. Personal Statement

Improving clinical outcomes in rhinology has been the main focus of my research activities for the past decade. This interest started as a Postdoctoral Clinical Research Fellow in Rhinology, where I gained valuable experience in understanding and executing clinical outcomes studies, both retrospective and prospective in design. During residency, I completed a two-year NIDCD T32 training program in rhinology research. I had a broad exposure to both translational and clinical outcomes research that culminated in the award of an AAO-HNSF CORE resident research grant for clinical validation of an AI-enabled sinus CT diagnostic platform. My research efforts since that time have largely focused on analysis of rhinology clinical outcomes using multi-institutional datasets.

My research and clinical interests currently lie in the interaction between our environment and inflammatory conditions of the upper airway, namely chronic rhinosinusitis (CRS). This is an issue of critical importance due to ever-increasing effects of global climate change on human health. Air pollution has a number of detrimental effects on our health, and these are only beginning to be understood in a rhinologic context.

B. Positions and Honors

Positions and Employment

2024-Present Assistant Professor, University of Colorado School of Medicine, Department of Otolaryngology - Head & Neck Surgery, Aurora, CO
2024-2026 Editorial Board Member, *Otolaryngology – Head & Neck Surgery*
2024 Reviewer, AAO-HNSF CORE Grant Study Section, General Section
2023-2024 Neurorhinology and Advanced Sinus Surgery Fellow, University of Utah, Department of Otolaryngology – Head & Neck Surgery, Salt Lake City, UT
2023-Present Mentor, Resident Reviewer Development Program, *Otolaryngology – Head & Neck Surgery*

2022-Present Peer Reviewer, *Otolaryngology – Head & Neck Surgery*
2022-Present Peer Reviewer, *OTO Open*
2016-2023 Resident Physician/NIDCD T32 Trainee, University of Colorado School of Medicine, Department of Otolaryngology – Head & Neck Surgery, Aurora, CO
2015-2016 Clinical Research Fellow, George Washington University School of Medicine, Division of Otolaryngology, Washington, DC

Honors and Professional Memberships

2024 "Star Reviewer," *Otolaryngology – Head & Neck Surgery*
2024 "Top Clinical Abstracts," ARS at COSM, Chicago, IL
2020 "Best of Orals," AAO-HNSF Annual Meeting, held virtually
2019-2020 AAO-HNSF CORE Resident Research Grant, *Principal Investigator*
2019-Present Member, American Rhinologic Society
2012 Shader Family Summer Research Fellowship, Tufts University School of Medicine
2011 *Summa cum laude*, Brandeis University
2007-2011 Leonard Bernstein Scholarship, Brandeis University

C. Contributions to Science

A. My graduate and pre-graduate work was largely basic science and translational in nature, focusing on the development of microfluidic biotechnology as a point-of-care diagnostic device, as well as studying the effects of novel bioactive peptides on impaired cutaneous wound healing models.

Relevant Publications
1. Jia Y, Mak PI, **Massey CJ**, Martins RP, Wangh LJ. Construction of a microfluidic chip, using dried-down reagents, for LATE-PCR amplification and detection of single-stranded DNA. Lab on a chip. 2013; 13(23):4635-41.
2. Sheets AR, **Massey CJ**, Cronk SM, Iafrati MD, Herman IM. Matrix- and plasma-derived peptides promote tissue-specific injury responses and wound healing in diabetic swine. Journal of Translational Medicine. 2016; 14(1):197.

B. My post-graduate research work has focused exclusively on rhinologic clinical outcomes and validation studies. These efforts have examined the utility of new technologies, such as AI, and diagnostic modalities. Much of this work utilizes large database analysis or is multi-center in nature.

Relevant Publications
1. Tullis B, Mace J, Hagedorn R, Nguyen C, Stockard R, **Massey C**, et al. "The impact of acute peri-operative particulate matter exposure on endoscopic sinus surgery outcomes: a preliminary multi-site investigation." *Am J Rhinol Allergy*. 2024; 38(4): 237-44.
2. Ramos L, **Massey C**, Asokan A, Rice JD, Kroehl M, Ramakrishnan VR. "Examination of sex differences in a chronic rhinosinusitis surgical cohort." *Otolaryngol – Head Neck Surg*. 2022; Sep 167(3): 583-9.
3. Schlosser R, Smith T, Mace J, Alt J, Beswick D, Mattos J, Ramakrishnan V, **Massey C**, Soler Z. The Olfactory Cleft Endoscopy Scale: A multi-institutional validation study in chronic rhinosinusitis. *Rhinology*. 2021 Apr 59(2): 181-90.
4. **Massey C**, Humphries S, Mace J, Smith T, Soler Z, Ramakrishnan V. "Multi-institutional validation of an AI-based sinus CT analytic platform with olfactory assessments." *Int Forum Allergy Rhinol*. 2024 Jul 12.

A complete list of publications can be found at https://orcid.org/0000-0002-6558-4559

D. Research Support

None

BIOGRAPHICAL SKETCH

NAME: Ashley M. Nassiri, MD, MBA

eRA COMMONS USER NAME (credential, e.g., agency login): ANASSIRI

POSITION TITLE: Assistant Professor of Otolaryngology - Head & Neck Surgery at the University of Colorado Anschutz School of Medicine in Aurora, CO.

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
University of California, Berkeley; Berkeley, CA	BS	08/2006	05/2010	Molecular Biology
University of Chicago, Pritzker School of Medicine; Chicago, IL	MD	08/2010	06/2015	Medicine
University of Chicago, Booth School of Business; Chicago, IL	MBA	09/2013	06/2015	Entrepreneurship & Management
Vanderbilt University Medical Center; Nashville TN	Residency	07/2015	06/2020	Otolaryngology - Head & Neck Surgery
Mayo Clinic; Rochester, MN	Fellowship	07/2020	06/2022	Neurotology

A. Personal Statement

I am actively an Assistant Professor of Otolaryngology with sub-specialization in otology and neurotology. My practice focuses on managing disorders of the ear and skull base, namely those that impact hearing and balance as well as skull base tumor pathology such as vestibular schwannomas (acoustic neuromas) and meningiomas, among others. I have experience in operations and behavioral management, entrepreneurship and clinical outcomes research, which have directed my research efforts to date. My practical experience in developing a protocolized clinical care pathway for cochlear implant and vestibular schwannoma patients has informed my work in both developing and executing new healthcare models. On a broader level, my work has focused on identifying and implementing innovations to address barriers to care in hearing healthcare. Specifically, we have defined current metrics for penetrance of cochlear implants within the candidate population on national and locoregional scales, identified methods to measure progress in expansion of programs, and identified "watershed" areas in access to care. Moving forward, we will be working on a more granular study that reveals the specifics of barriers to care, with the aim to develop and implement regional, socio-economic, and culturally-specific systems to increase rates of hearing health care utilization including hearing amplification and cochlear implantation.

B. Positions, Scientific Appointments and Honors

ACADEMIC RANK AND POSITION

1/2023-present	Assistant Professor of Otolaryngology, University of Colorado Anschutz Medical Center, Aurora, CO
12/2020-6/2022	Assistant Professor of Otolaryngology, Mayo Clinic College of Medicine and Science; Rochester, MN

SCIENTIFIC APPOINTMENTS

1. *Associate Editor,* Otology & Neurotology Open, 2020 – present
    - Inaugural editorial board for new, open-access journal
2. Conference Track Co-Chair: Lateral Skull Base/Neurotology. North American Skull Base Society 2024 Scientific Program Committee, 2023-2024.
    - Lead scientific program development for the lateral skull base program (vestibular schwannoma, meningioma, and hearing rehabilitation).
    - Invite and coordinate with speakers and panelists.
    - Abstract selection and educational content development.
3. Co-Leader, Countermeasure 1: Establishing a Vital Sign for Hearing Health. Hearing Health Collaborative, 2021-present.

- Identification subgroup: design roadmap for implementation of national adult hearing screening.
- Pinpoint and contribute to insufficient data required for US Preventive Services Task Force approval for adult hearing screening on next review.
- Publish A3 process, Rationale for Development of a Hearing Vital Sign

4. Committee Member, StrategyShare2020 Conference. Vanderbilt University Medical Center, Nashville, TN, 2019 – 2020.
    - Amplify Innovation Committee: vetting and selection of presentations for hospital-wide program for dissemination of research and funding opportunities.
5. Member, Value-based Healthcare Group, Vanderbilt University, Nashville, TN, 2017-2020.
    - Implemented internal survey system for the evaluation of quality and cost outcomes in facial plastics surgery (functional rhinoplasty), with plans to implement in neurotology (chronic ear surgery).
    - Partnered with Vanderbilt Operations Management to address bottlenecks in the skull base patient referral and treatment pathways.

PROFESSIONAL ORGANIZATIONS

1. 2021-present Member, North American Skull Base Society (NASBS)
2. 2021-present Member, AAO-HNS Hearing Committee
3. 2018-present Trainee Member, American Neurotology Society
4. 2015-present American Academy of Otolaryngology-Head & Neck Surgery (AAO-HNS)

HONORS AND AWARDS

1. Best Abstract Award, American Cochlear Implant Alliance (ACIA) Meeting, 2021
2. 2nd Place, 27th Annual Resident Research Competition, Vanderbilt University, 2019
3. 3rd Place Oral ePoster Presentation, World Congress on Endoscopic Ear Surgery 3.0, 2019
4. Original Study Selected for Podcast, *Otolaryngology–Head and Neck Surgery* Journal, May 2019
5. 2nd place, Vanderbilt Bill Wilkerson Center Annual Poster Competition, 2019
6. American Neurotology Society (ANS) Trainee Award, 2018
7. 1st place, 25th Annual Resident Research Poster Competition, Vanderbilt University, 2017
8. 1st place, Building the New Venture, Booth School of Business, 2015
9. Entrepreneurial Design Select Few (top 10% selected), 2014
10. New Venture Challenge (25 of >100 applicants selected), 2014
11. Booth Leadership Challenge (top 20% of class selected), 2013

C. Contributions to Science

Peer-Reviewed Publications

1. **Nassiri AM**, Messina SA, Benson JC, Lane JI, McGee KP, Trzasko JD, Carlson ML. Magnetic Resonance Imaging Artifact Associated with Transcutaneous Bone Conduction Implants: Cholesteatoma and Vestibular Schwannoma Surveillance. Otolaryngology-Head and Neck Surgery. 2023. (Accepted; PMID: pending)
2. **Nassiri AM**, Randall Nicolas, Johnson BJ, Carlson ML. Hearing device coil placement lateral to the temporalis: an alternative to flap thinning for cochlear and transcutaneous bone-anchored implants. Otology & Neurotology. 2023. (Accepted; PMID: pending)
3. **Nassiri AM**, Marinelli JP, Lohse CM, Carlson ML. Age and incidence of cochlear implantation in the pediatric population with congenital bilateral profound hearing loss. Otology & Neurotology. 2023. (PMID: 37367698)
4. Marinelli JP, Schnurman Z, Killeen DE, **Nassiri AM**, Hunter JB, Lees KA, Lohse CM, Roland JT Jr, Golfinos JG, Konziolka D, Link MJ, Carlson ML. Stratifying risk of future growth among sporadic vestibular schwannoma. Otology & Neurotology. 2023. (PMID: 37367632)
5. **Nassiri AM**, Marinelli JP, Lohse CM, Carlson ML. Incidence of cochlear implantation among adult candidates in the United States. Otology & Neurotology. 2023. (PMID: 37205861)
6. Farnsworth PJ, Benson JC, **Nassiri AM**, Carlson ML, Larson NB, Lane JI. Improved cochlear implant localization using co-registration of pre- and post-operative CT. Journal of Neuroimaging. 2023. (PMID: 36811338)
7. Marinelli JP, **Nassiri AM**, Lohse CM, Carlson ML. Effect of a global pandemic on adult and pediatric cochlear implantation across the United States. Otology & Neurotology. 2023. (PMID: 36624592)

8. Burkett BJ, Burkett BJ, Oien MP, Benson JC, **Nassiri AM**, Carlson ML, Lane JI. Absent stapedial tendon: Imaging features of an underrecognized entity: Clinic neuroradiology. Clinical Neuroradiology. 2023. (PMID: **36593357**)
9. Xie K, Antezana LA, Gottlich HC, Yaekel S, **Nassiri AM**, Moore EJ, Carlson ML. Experience with telemedicine in a tertiary academic otologic clinic during the COVID-19 pandemic. Otology & Neurotology. 2023. (PMID: 36509445)
10. Vakharia K, Mikula A, **Nassiri AM**, Driscoll CLW, Link MJ. Right medium-sized vestibular schwannoma with trigeminal neuralgia post-fractionated radiosurgery (video). Neurosurgical Focus: Video. 2021. (PMID: 36285235)
11. Vakharia K, Naylor R, Hasegawa H, **Nassiri AM**, Driscoll CL, Link MJ. Right posterior petrosectomy for resection of petroclival meningioma. Neurosurgical Focus: Video. 2022. (PMID: 36285001)
12. **Nassiri AM**, Lohse CM, Link MJ, Carlson ML. Comparing patient satisfaction after upfront treatment versus wait-and-scan for small sporadic vestibular schwannoma. Otology & Neurotology. 2023. (PMID: 36240733)
13. Goates AJ, **Nassiri AM**, Carlson ML. Cochlear implantation after intralabyrinthine schwannoma microsurgical resection. Otology & Neurotology. 2022. (PMID: 36167026)
14. Goates AJ, **Nassiri AM**, Carlson ML. Cochlear implantation after intralabyrinthine schwannoma microsurgical resection. Otology & Neurotology. 2023. (PMID: 36167026)
15. Rinaldo L, Flanigan PM, **Nassiri AM**, Neff BA, Van Gompel JJ. Combined Middle Fossa and Transmastoid Approach for Resection of Petrous Temporal Meningioma with Facial Nerve Reanimation via Interposition Grafting. Operative Neurosurgery. 2022. (PMID: 36103350)
16. Xie K, Antezana LA, Yin LX, Bowen AJ, Yaekel S, **Nassiri AM**, Moore EJ. Telemedicine evaluation of new head and neck patients at a tertiary academic clinic during the COVID-19 pandemic. Journal of Telemedicine and Telecare. 2022. (Accepted, PMID: pending)
17. Marinelli JP, Killeen DE, Schnurman Z, **Nassiri AM**, Hunter JB, Lees KA, Lohse CM, Roland TJ, Golfinos JG, Kondziolka D, Link MJ, Carlson ML. Spontaneous volumetric tumor regression during wait-and-scan management of 952 sporadic vestibular schwannomas. Otology & Neurotology. 2022. (PMID: 36001695)
18. Benson JC, **Nassiri AM**, Saoji AA, Carlson ML, Lane JI. Co-registration of pre- and post-operative images after cochlear implantation: a proposed technique to improve cochlear visualization and localization of cochlear electrodes. Neuroradiology Journal. 2022. (PMID: 35985649)
19. Spear JA, Bauman MM, Graffeo CS, **Nassiri AM**, Carlson ML, Van Gompel JJ. Retrosigmoid approach using suboccipital osteoplastic craniotomy for resection of vestibular schwannoma. Operative Neurosurgery. 2022. (PMID: 35972099)
20. **Nassiri AM**, Saoji AA, DeJong MD, Tombers NM, Driscoll CLW, Neff BA, Haynes DS, Carlson ML. Implementation strategy for highly-coordinated cochlear implant care with remote programming: the Complete Cochlear Implant Care (CCIC) model. Otology & Neurotology. 2022. (PMID: 35870171)
21. Saoji AA, Graham MK, Adkins WJ, **Nassiri AM**, Neff BA, Carlson ML, Driscoll CLW. Relationship between intraoperative electrocochleography (ECochG) responses and immediate postoperative bone conduction thresholds in cochlear implantation. Otology & Neurotology. 2022. (PMID: 35970166)
22. Benson JC, Trejo-Lopez JA, **Nassiri AM**, Eschbacher KL, Link MJ, Driscoll CL, Tiegs RD, Sfier J, DeLone DR. Phosphaturic Mesenchymal Tumor. American Journal of Neuroradiology. 2022. (PMID: 35589138)
23. Antezana LA, Xie K, Yin LX, Bowen AJ, Yaekel S, **Nassiri AM**, Moore EJ. Performing parotid postoperative follow-ups via telemedicine: experience at a single tertiary care center. Journal of Telemedicine and Telecare. 2022. (PMID: 35549759)
24. **Nassiri AM**, Sorkin DL, Carlson ML. Current estimates of cochlear implant utilization in the United States. Otology & Neurotology. 2022. (PMID: 35261379)
25. Adkins WJ, Henrie T, **Nassiri AM**, Neff BA, Carlson ML, Driscoll CLW, Saoji AA. Preoperative imaging of temporoparital scalp thickness predicts off-the-ear sound processor retention in cochlear implants with diametric magnets. Otology & Neurotology. 2022. (PMID: 35195570)
26. Kocharyan A, Daher GS, **Nassiri AM**, Khandalavala KR, Saoji AS, Van Gompel J, Carlson ML. Intraoperative use of electrical stapedius reflex testing for cochlear nerve monitoring during simultaneous translabyrinthine resection of vestibular schwannoma and cochlear implantation. Otology & Neurotology. 2022. (PMID: 35195569)
27. Manzoor NF, **Nassiri AM**, Sherry AD, Dang S, Yancey KL, Monsour M, Perkins EL, Khattab MH, Thompson RC, O'Malley MR, Bennet ML, Rivas AC, Haynes DS. Predictors of recurrence after sub-total or near-total resection of vestibular schwannoma: importance of tumor volume and ventral extension. Otology & Neurotology. 2022. (PMID: 35184072)

28. Macielak R, **Nassiri AM**, Fillmore WJ, Lane JI, Driscoll CLW, Carlson ML. Persistent foramen of Huschke: presentation, evaluation and management. Laryngoscope Investigative Otolaryngology. 2022. (PMID: 35155803)
29. Carlson ML, **Nassiri AM**, Marinelli JP, Lohse CL, Sydlowski S. Awareness, perceptions, and literacy surrounding hearing loss and hearing rehabilitation among the adult population in the United States. Otology & Neurotology. 2022. (PMID: 35061637)
30. **Nassiri AM**, Holcomb MA, Perkins EL, Bucker AL, Prentiss SM, Welch CM, Andresen NS, Valenzuela CV, Wick CC, Angeli SI, Sun DQ, Bowditch SP, Brown KD, Zwolan TA, Haynes DS, Saoji AA, Carlson ML. Catchment profile of large cochlear implant centers in the United States. Otolaryngology-Head and Neck Surgery. 2022. (PMID: 35041546)
31. Kocharyan A, Daher GS, **Nassiri AM**, Molligan J, Link MJ, Carlson ML, Driscoll CLW. Jugular foramen capillary hemangioma masquerading as paraganglioma. American Journal of Otolaryngology. 2021. (PMID: 34973661)
32. Marinelli JP, Schnurman Z, Killeen DE, **Nassiri AM**, Hunter JB, Lees KA, Lohse CM, Roland JT, Golfinos JG, Kondziolka D, Link MJ, Carlson ML. Long-term natural history and patterns of sporadic vestibular schwannoma growth: a multi-institutional volumetric analysis of 952 patients. Neuro-Oncology. 2021. (PMID: 34964894)
33. **Nassiri AM**, Marinelli JP, Sorkin DL, Carlson ML. Barriers to adult cochlear implant care in the United States: an analysis of health care delivery. Seminars in Hearing. 2021. (PMID: 34912159)
34. McMillan RA, **Nassiri AM**, Leonel LC, Rezende NC, Peris Celda M, Sweeney AD, Carlson ML. The posterior ligament of the incus ("white dot"): A reliable surgical landmark for the facial recess. American Journal of Otolaryngology. 2021. (PMID: 34896938).
35. Gordon SA, **Nassiri AM**, Driscoll CLW, Carlson ML, Patel NS. Auricular cartilage resection for treatment-refractory idiopathic chondritis: a case series. Otology & Neurotology. 2021. (PMID: 34889844)
36. **Nassiri AM,** Wallerius KP, Lohse CM, Marinelli JP, Saoji AA, Driscoll CLW, Neff BA, Carlson ML. Speech perception performance growth and benchmark score achievement after cochlear implant for single-sided deafness. Otology & Neurotology. 2021. (PMID: 34889843)
37. **Nassiri AM**, Wallerius KP, Saoji AA, Neff BA, Driscoll CLW, Carlson ML. Impact of duration of deafness on speech perception in single-sided deafness. Otology & Neurotology. 2021. (PMID: 34889841)
38. Vakharia K, Naylor RM, **Nassiri AM**, Driscoll CLW, Link MJ. Microsurgical resection of a petroclival epidermoid cyst using an anterior petrosectomy approach: 2-dimensional operative video. Operative Neurosurgery. 2021. (PMID: 34560780)
39. Daher GS, **Nassiri AM**, Vanichkachorn G, Carlson ML, Neff BA, Driscoll CLW. New onset tinnitus in the absence of hearing changes following COVID-19 infection. American Journal of Otolaryngology. 2021. (PMID: 34536917)
40. **Nassiri AM**, Haynes DS, Carlson ML. The business of medicine: gaps in medical education can be addressed through asynchronous learning. ENT Today. 2021.
41. **Nassiri AM**, Benson JC, Doerfer KW, Perkins EL, Sweeney AD, Patel NE, Babu SC, Rivas A, Lane JI, Carlson ML. Absent pyramidal eminence and stapedial tendon associated with congenital stapes footplate fixation: Intraoperative and radiographic findings. American Journal of Otolaryngology. 2021. (PMID: 34171699)
42. **Nassiri AM**, Ricketts TA, Carlson ML. Current estimate of hearing aid utilization in the United States. Otology & Neurotology Open. 2021. (DOI: 10.1097/ONO.0000000000000001)
43. Marinelli JP, Carlson ML, Hunter JB, **Nassiri AM**, Haynes DS, Link ML, Lohse CM, Reznitsky M, Stangerup S, Caye-Thomasen P. Natural history of growing sporadic vestibular schwannoma during observation: an international multi-institutional study. Otology & Neurotology. 2021. (PMID: 34121081)
44. Marinelli JP, **Nassiri AM**, Habermann EB, Lohse CM, Holton SJ, Carlson ML. Underreporting of vestibular schwannoma incidence within national brain tumor and cancer registries in the United States. Otology & Neurotology. 2021. (PMID: 34111053)
45. Carlson ML, Barnes JH, **Nassiri A**, Patel NS, Tombers NM, Lohse CM, Van Gompel JJ, Neff BA, Driscoll CLW, Link MJ. Prospective study of disease-specific quality-of-life in sporadic vestibular schwannoma comparing observation, radiosurgery, and microsurgery. Otology & Neurotology. 2021. (PMID: 33177408)
46. Yawn RJ, **Nassiri AM**, Harris JE, Manzoor NF, Godil S, Haynes DS, Bennett ML, Weaver SM. Reducing ICU Length of Stay: The impact of a multidisciplinary perioperative pathway in vestibular schwannoma. Journal of Neurological Surgery Part B Skull Base. 2021. (PMID: 35832972)
47. Manzoor NF, **Nassiri AM**, Rivas A. Trans-canal endoscopic repair of cerebrospinal fluid (CSF) leak following vestibular schwannoma resection (video case report). Otology & Neurotology. 2020. (PMID: 33492802)
48. Kimura KS, O'Connell BO, **Nassiri AM**, Dedmon MD, Haynes HS, Bennett ML. Outcomes of revision cochlear implantation. Otology & Neurotology. 2020. (PMID: 32472921)

49. Jayawardena ADL, **Nassiri AM**, Levy DA, Valeriani V, Kemph AJ, Kahue CN, Segaren N, Labadie RF, Bennett ML, Elisee CL, Netterville JL. Community health worker-based hearing screening on a mobile platform: a scalable protocol piloted in Haiti. Laryngoscope Investigative Otolaryngology. 2020. (PMID: 32337362)
50. **Nassiri AM**, Garrett CG, Tiwari V, Dail TL, Haynes DS, Rivas A, Langerman A. Should I buy this? A decision-making tool for value-based purchasing. Otolaryngology-Head and Neck Surgery. 2020. (PMID: 32284008)
51. **Nassiri AM**, Stephan SJ, Du L, Ries WR, Eavey RD. Factors associated with patient satisfaction after nasal breathing surgery. JAMA Network Open. 2020. (PMID: 32202642)
52. **Nassiri AM**, Yawn RJ, Holder JT, Dwyer RT, O'Malley MR, Bennett ML, Labadie RF, Rivas A. Hearing preservation outcomes using a precurved electrode array inserted with an external sheath. Otology & Neurotology. 2019. (PMID: 31746820)
53. **Nassiri AM**, Yawn RJ, Gifford RH, Holder JT, Stimson CJ, Eavey RD, Haynes DS. Same-day patient consultation and cochlear implantation: innovations in patient-centered health care delivery. Otology & Neurotology. 2019. (PMID: 31664000)
54. Holder JT, Yawn RJ, **Nassiri AM**, Dwyer RT, Rivas A, Labadie RF, Gifford RH. Matched cohort comparison indicated superiority of precurved electrode arrays. Otology & Neurotology. 2019. (PMID: 31469799)
55. **Nassiri AM**, Yawn RJ, Gifford RH, Roberts JB, Haynes DS, Gilbane, MS, Murfee J, Roberts J, Bennett ML. Intraoperative electrically evoked compound action potential (ECAP) levels in traditional and hearing preservation cochlear implantation. Journal of the American Academy of Audiology. 2019. (PMID: 31274070)
56. Tolisano AM, Fontenot MR, **Nassiri AM**, Hunter JB, Kutz JW Jr, Rivas A, Isaacson B. Pediatric stapes surgery: Hearing and surgical outcomes in endoscopic vs. microscopic approaches. Otolaryngology-Head and Neck Surgery. 2019. (PMID: 30857467)
57. Tittman SM, **Nassiri AM**, Manzoor NF, Yawn RJ, Mobley BC, Wellons JC 3rd, Rivas A. Juvenile xanthogranuloma of the cerebellopontine angle: a case report and review of the literature. Otolaryngology Case Reports. 2019. (DOI: 10.1016/j.xocr.2019.100124)
58. **Nassiri AM**, Pichert JW, Domenico HJ, Galloway MB, Cooper WO, Bennett, ML. Unsolicited patient complaints among otolaryngologists. Otolaryngology-Head and Neck Surgery. 2019. (PMID: 30642235)
    ***Selected for OHNS Podcast with Editor-in-Chief, Dr. John Krouse (May 2019).**
59. **Nassiri AM**, Yawn RJ, Dedmon MM, Hunter JB, Tolisano AM, Isaacson B, Rivas A. Audiologic and surgical outcomes in revision endoscopic stapes surgery. Laryngoscope. 2019. (PMID: 30623430)
60. **Nassiri AM**, Campbell B, Mannion K, Sinard RJ, Rohde SL. Survival outcomes in T4aN0M0 mandibular gingival squamous cell carcinoma treated with surgery alone. Otolaryngology-Head and Neck Surgery. 2019. (PMID: 30598048)
61. **Nassiri AM**, Owen SR, Ries WR, Stephan SJ. Sculpting porous polyethylene in microtia reconstruction: novel techniques and the effects on the microscopic pore structure of the implant. Journal of Reconstructive Surgery & Anaplastology. 2019. (DOI: 10.29011/JRSA-104. 000004)
62. **Nassiri AM**, Yawn RJ, Dedmon MM, O'Connell BP, Holder JT, Haynes DS, Rivas A. Facial nerve stimulation patterns associated with cochlear implantation in labyrinthitis ossificans. Otology & Neurotology. 2018. (PMID: 30444844)
63. **Nassiri AM**, Yawn RJ, Brown CL, O'Malley MR, Bennett ML, Labadie RF, Haynes DS, Rivas A. Unilateral versus bilateral cochlear implantation in children with auditory neuropathy spectrum disorder (ANSD). Otology & Neurotology. 2018. (PMID: 30199499)
64. **Nassiri AM**, Yawn RJ, Dedmon MM, Hunter JB, Tolisano AM, Isaacson B, Rivas A. Primary endoscopic stapes surgery: audiologic and surgical outcomes. Otology & Neurotology. 2018. (PMID: 30124621)
65. Mhlaba JM, Christianson LW, Davidson SJ, Graves SN, Still BR, Silas MR, Fong AJ, **Nassiri AM**, Pariser JJ, Langerman AJ. Field research in the operating room. Ergonomics in Design. 2016. (DOI: 10.1177/1064804616642916)
66. Voce D, Schmitt A, Uppal A, McNerney M, Wahlstrom J, Bernal G, **Nassiri A**, Yu X, Crawley, C, White K, Weichselbaum R, Yamini B. Nfkb1 is a haploinsufficient DNA damage-specific tumor suppressor. Oncogene. 2015. (PMID: 25043302)
67. Fan W, **Nassiri A**, Zhong Q. Autophagosome targeting and membrane curvature sensing by Barkor/Atg12(L). Proceedings of the National Academy of Sciences. 2011. (PMID: 21518905)

Chapters and Invited Publications

1. **Nassiri AM**, Driscoll CLW. Cerebellopontine angle pathology. In: Essential Otology and Neurotology. (With publisher)

2. **Nassiri AM**, Carlson ML. Radiosurgery of the jugular foramen. In: Radiosurgery of the Skull Base. (With publisher)
3. Marinelli JP, **Nassiri AM**, Carlson ML. Vestibular schwannoma. In: Glasscock-Schambaugh Surgery of the Ear, 7th Ed. (With publisher)
4. **Nassiri AM**, Carlson ML, Haynes DS. Canal-wall-up mastoidectomy. In: Glasscock-Schambaugh Surgery of the Ear, 7th Ed. (With publisher)
5. **Nassiri AM**, Rivas A. Endoscopic tympanoplasty. In: Brackmann D, Otologic Surgery, 5th Ed. Philadelphia, PA: Elsevier, Inc; 2023.
6. Manzoor NF, **Nassiri AM**, Rivas A. Endoscopic ossiculoplasty. Current Otorhinolaryngology Reports. 2019. (DOI: 10.1007/s40136-019-00252-y)
7. **Nassiri AM**, Kuhs KA, Langerman A. Management of carcinoma of the lateral pharynx and soft palate. In: Genden EM, Head and Neck Cancer: Management and Reconstruction, 2nd Ed. New York, NY: Thieme Medical Publishers, Inc; 2020.
8. Yawn RJ**, Nassiri AM**, Rivas A. Auditory neuropathy spectrum disorder: bridging the gap between hearing aid and cochlear implant. Otolaryngology Clinics of North America. 2019. (PMID: 30765091)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Rennie, Katherine J.

eRA COMMONS USER NAME (credential, e.g., agency login): KJRENNIE

POSITION TITLE: Professor of Otolaryngology, Resident Research Director

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Leeds, U.K.	B.Sc.	06/1987	Physiology
University of Bristol, Bristol, U.K.	Ph.D.	04/1991	Physiology
University of Texas Medical Branch at Galveston	Postdoctoral	08/1996	Vestibular Neuroscience

A. Personal Statement

I am interested in how cells in the peripheral vestibular system process sensory information and my lab uses electrophysiological, imaging and modeling techniques to study signaling between vestibular hair cells and their associated afferent dendrites. In my early work I characterized a highly unusual low-voltage activated K^+ current in type I hair cells that confers a low input resistance on these cells and I investigated the membrane properties of type I and type II vestibular hair cells in a variety of species (for review see Meredith and Rennie, 2016). To probe the type I hair cell/calyx synapse, I subsequently developed a mammalian isolated vestibular calyx preparation, where calyx terminals are dissociated along with type I hair cells. We showed using whole cell patch clamp recordings that glutamatergic quantal transmission occurs at the unique synapse between mammalian type I hair cells and their calyx terminals and that isolated calyces express a variety of conductances. Recently my lab has developed procedures to study cells in vestibular slices and wholemounts. Our findings show that mature afferent terminals are electrically heterogeneous and that their ion channel expression profiles vary with position in the sensory epithelium. These variations have important implications for how vestibular afferent signals are conveyed as action potentials to the central nervous system.

My current research is funded by R01 grants from the NIDCD (PI) and NIA (MPI with Peng) and encompasses the neurophysiology of hair cells and afferents across the lifespan. I collaborate with investigators in the department of Physiology & Biophysics (Klug, Peng and Tollin) and Pediatrics (Benke) to investigate inner ear mechanisms such as synaptopathy. Identifying synaptic transmission mechanisms between hair cells and afferents and changes associated with ototoxicity and ageing will identify potential strategies to combat changes associated with hearing and balance loss. The Hearing and Balance labs of PI's Greene, Klug, Peng, Rennie and Tollin labs meet biweekly on Friday mornings to discuss scientific papers in our field and present and discuss new research findings. These ongoing meetings are extremely valuable for providing feedback and generating new ideas and research directions within our group. In addition, I am a member of the training faculty and chair of the training committee on the department of Otolaryngology's NIDCD T32 and R25 training grants. I serve on the department of Otolaryngology-Head & Neck Surgery's Diversity, Equity and Inclusion (DEI) committee. I have experience with and am deeply committed to mentoring and training individuals from diverse backgrounds and have undergone upstander and unconscious bias training.

Ongoing and recently completed projects that I would like to highlight include:

NIDCD R01 DC018786 04/01/2021-03/30/2026
Ion Channels and Excitability in the Peripheral Vestibular System
Rennie (PI)
Total Costs $2,371,163

The goal is to investigate ionic mechanisms underlying differences in firing in different regions of vestibular neuroepithelia.

NIA R01 AG073997 09/05/2021-05/31/2026
Aging and Dysfunction in the Peripheral Vestibular System
Rennie/Peng (Multi PI)
Total Costs $3,199,125

The goal is to study changes associated with aging in the rodent vestibular periphery using a combination of electrophysiological, immunohistochemical and behaviorial approaches. Identifying impairments of the vestibular signaling pathway in aging has important implications for developing new therapies for patients with vestibular dysfunction.

ASPIRE, University of Colorado SOM Programmatic Incubator for Research 07/01/2024-06/30/2026

Synaptopathy as a common etiology underlying hearing and balance disorders with aging and noise exposure.
Tollin, D (PI), Rennie (Co-I)
Total Costs $100,000

The goal of this internal award to Dr's Agrawal, Klug, Peng, Rennie and Tollin (PI) is to investigate synaptic mechanisms contributing to hearing and balance dysfunction with age and insult.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2024- Professor (without tenure), Department of Otolaryngology, University of Colorado AMC, Aurora, CO
2019- External Relations Committee, Association for Research in Otolaryngology
2018- Chair of Training Committee, University of Colorado Department of Otolaryngology T32 Institutional Training in Otolaryngology Research.
2009- Associate Professor, Department of Otolaryngology, University of Colorado Denver, Aurora, CO
2004- Resident Research Director, Department of Otolaryngology, University of Colorado
2004- Neuroscience Graduate Program Faculty (Chair of Admissions/Recruitment Committee 2009-2011, Graduate Training Committee member 2015-2020, Membership Committee member 2021-2024)
2003- Joint appointment, Department of Physiology & Biophysics, UCDHSC, Denver, CO.
2002 Assistant Professor, Department of Otolaryngology, UCDHSC, Denver, CO.

Other Experience and Professional Memberships

2023 Regular Member AUD (NIDCD)
Reviewer ZDC1 SRB-X (NIDCD) Hearing and Balance Fellowships
2022 Reviewer AUD and NIA ZAG1
2020 Reviewer and Meeting Co-chair, ZRG1 IFCN-U
2019 Reviewer ZRG1 IFCN-E
2017 Reviewer, ZRG1 HCN-M (NIDCD)

2016	Reviewer, Action on Hearing Loss
2014-2015	Reviewer, Italian Ministry of Health
2014	Reviewer, NSBRI
2013-2018	Reviewer, NIDCD ZDC1 Hearing and Balance Fellowships
2012	Reviewer, Hearing Health Foundation & ZRG1 IFCN-B (NIDCD)
2010-11	Reviewer AUD Study Section (NIDCD)
2010	Reviewer, RNID
2009	Reviewer ZRG-IFCN-B (IAR) Study Section (NIDCD)
	CSR/NIH/Italian Ministry of Health reviewer
2006-09,2011	Reviewer, Deafness Research Foundation Study Section
2003	Reviewer, Special Emphasis Panel Study Section (NIDCD)
2001-	Member, Society for Neuroscience
2000-	Member, American Physiological Society
1995-	Member, Association for Research in Otolaryngology
1994-	Member, Biophysical Society
1993-	Member, Sigma Xi Scientific Research Society (elected)

Reviewer for:
Acta Pharmacologica Sinica, American Journal of Physiology-Cell Physiology, American Journal of Physiology-Heart and Circulatory Physiology, Annals of Otology, Rhinology & Laryngology, Biomedicine & Pharmacotherapy, Biophysical Journal, Current Medical Imaging Reviews, eLife, Experimental Neurology, FASEB Journal, Frontiers in Cellular Neuroscience, Frontiers in Neurology, Hearing Research, JARO, Journal of Comparative Neurology, Journal of Neurophysiology, Journal of Neuroscience, Journal of Neuroscience Research, Journal of Physiology, Journal of Experimental Zoology Part A: Ecological Genetics and Physiology, Journal of Vestibular Research, Journal of Visualized Experiments, Neurochemical Research, Neuropharmacology PLoSOne and Purinergic Signalling.

Honors

2007	James A. Shannon Director's Award (NIDCD R55).
2003	American Physiological Society Research Career Enhancement Award.
1996	NASA-NSF-Gordon Res. Conference Young Investigator Award.
1994-1997	NIH NIDCD F32 individual Post-doctoral Fellowship
1988	Dale and Rushton Fund (Physiological Society) award
1988	NATO travel award, Biophysics of Sensory Transduction

C. Contributions to Science

1. My early work focused on developing a procedure for isolating sensory cells from mammalian and avian vestibular organs and investigating differences in membrane properties between type I and type II vestibular hair cells. Previous work on vestibular hair cells had been carried out on vestibular organs from frogs and fishes, which contain only type II hair cells. I described a low voltage-activated K^+ current in rodent, reptilian and avian type I hair cells that confers a low input resistance on these cells. Type II vestibular hair cells were found to have a much higher input resistance than type I hair cells and different types of K^+ channels conferring different filtering characteristics.

a. Rennie, K. J. and Correia, M. J. Potassium currents in mammalian and avian isolated type I semicircular canal hair cells. *J. Neurophysiol.* 71: 317-329, 1994.
b. Rennie, K. J., Ricci, A. J. and Correia, M. J. Electrical filtering in gerbil isolated type I semicircular canal hair cells. *J. Neurophysiol.* 75: 2117-2123, 1996.

c. Correia, M. J., Wood T. G., Prusak, D., Weng, T. X., Rennie, K. J. and Wang, H-Q. Molecular characterization of an inward rectifier channel (IKir) found in avian vestibular hair cells: cloning and expression of pKir 2.1. *Physiol. Genomics* 19:155-169, 2004.
d. Meredith F.L, Rennie K. J. Channeling your inner ear potassium: K^+ channels in vestibular hair cells. *Hearing Res* 338:40-51, 2016.

2. The low voltage-activated K^+ current was uniquely associated with type I hair cells but was found in type I hair cells in diverse vestibular end organs (semicircular canal crista, utricle, saccule and lagena). Unlike most K^+ channels, I found that this conductance increased rather than decreased under raised K^+ conditions. Initial immunohistochemical data from other labs suggested that KCNQ4 channels mediated the low voltage-activated K^+ current, however we found that KCNQ channel blockers were ineffective in adult type I hair cells.

a. Ricci, A. J., Rennie, K. J. and Correia, M. J. The delayed rectifier, I_{KI}, is the major conductance in type I vestibular hair cells across vestibular end organs. *Pflügers Arch.* 432:34-42, 1996.
b. Ricci, A. J., Rennie, K. J. and Correia, M. J. A delayed rectifier conductance shapes the voltage response of type I hair cells. In: New Frontiers of Vestibular Research. B. Cohen and S. Highstein Eds. *Ann. N. Y. Acad. Sci.* 781:690-692, 1996.
c. Rennie, K. J. and Correia, M. J. Effects of cationic substitutions on delayed rectifier current in type I vestibular hair cells. *J. Membr. Biol.* 173:139-148, 2000.
d. Rennie, K. J., Weng, T. X., and Correia, M. J. Effects of KCNQ channel blockers on K^+ currents in vestibular hair cells. *Am. J. Physiol. Cell Physiol.* 280:C473-C480, 2001.

3. Vestibular hair cells show a robust regeneration in birds following damage due to ototoxic drugs. In collaboration with Dr. Manning Correia I studied vestibular hair cell regeneration following streptomycin-induced hair cell death in adult pigeons. Type II hair cells with mature complements of K^+ channels were observed after 3 weeks after streptomycin treatment, whereas the low voltage activated K^+ conductance characteristic of mature type I hair cells returned 10 weeks post treatment. Prior to this the ionic currents in type I hair cells were typical of those in type II hair cells, suggesting type II hair cells may transform into type I hair cells during regeneration. In postnatal development studies a similar sequence was established and at birth rodent vestibular hair cells showed a type II hair cell phenotype. The low voltage activated K^+ conductance first appeared in type I hair cells towards the end of the first postnatal week and reached mature levels by the third postnatal week. A Na^+ conductance was transiently expressed in both hair cell types, but its expression declined drastically by the end of the first postnatal month. In addition, we have characterized tetrodotoxin-sensitive and -insensitive Na^+ currents in developing calyces and immature type I hair cells. We identified transient, persistent and resurgent components of the Na^+ current in vestibular calyces and concluded that Nav1.6 channels contribute to afferent firing properties. This body of work helped elucidate electrophysiological mechanisms underlying vestibular hair cell and afferent fiber maturation and re-growth and may help inform future strategies for regenerative therapies in the inner ear.

a. Correia, M. J, Rennie, K. J. and Koo, P. Return of potassium ion channels in regenerated hair cells: Possible pathways and the role of intracellular calcium signalling. *Ann. N. Y. Acad. Sci. Vol. 942:*228-240, 2001.
b. Li, G., Meredith, F. L. and Rennie, K. J. Development of K^+ and Na^+ conductances in rodent postnatal semicircular canal type I hair cells *Am. J. Physiol*. *Regul. Integr. Comp. Physiol.* 298:R351-R358, 2010. PMCID: PMC2828173.
c. Meredith, F. L. Li, G., and Rennie, K. J. Postnatal expression of an apamin-sensitive K(Ca) current in vestibular calyx terminals. *J. Membr. Biol.* 244:81-91, 2011. PMCID: PMC3242503.
d. Meredith F.L, Rennie K. J. Regional and developmental differences in Na^+ currents in vestibular primary afferent neurons. *Front Cell. Neurosci.* 12: 423, 2018. PMCID: PMC6246661.

4. Type I hair cells are surrounded by a calyx afferent terminal that covers most of the basolateral surface of the type I hair cell. Synaptic transmission at this synapse is not well understood. To address this, I developed an isolated vestibular calyx preparation, where calyx terminals are dissociated along with type I hair cells. Using this preparation, I recorded excitatory postsynaptic events confirming that quantal chemical transmission occurs at this unusually large synapse. The isolated vestibular calyx preparation proved extremely useful for studying ion channels at the synaptic terminal, but a more intact preparation of the vestibular epithelia was needed to study zonal variations in signaling. My lab therefore developed mammalian crista and utricle slice preparations to study regional variations *in vitro.* We utilize thin slices to study ion channels and synaptic signaling across different neuroepithelial zones in the young adult and aging vestibular periphery.

a. Dhawan, R., Mann, S. E., Meredith, F. L. and Rennie, K. J. K^+ currents in isolated vestibular afferent calyx terminals. *J Assoc Res Otolaryngol* 11:463-476, 2010. PMCID: PMC2914245.
b. Meredith F.L., Rennie K. J. Zonal variations in K^+ currents in vestibular crista calyx terminals. *J. Neurophysiol.* 113:264-76, 2015. PMCID: PMC5005277.
c. Meredith F.L., Rennie K. J. Persistent and resurgent Na^+ currents in vestibular calyx afferents. *J. Neurophysiol*. 124: 510-524, 2020. PMCID: PMC5491709
d. Mohamed, N. M. M., Meredith, F. L. Rennie, K. J. Inhibition of ionic currents by fluoxetine in vestibular calyces in different epithelial loci. *Int. J. Mol. Sci. 25(16)*, 8801, 2024 doi.org/10.3390/ijms25168801.

5. To better understand the transformation of mechanical signals by the type I hair cell and calyx synapse we have studied mechano-transduction currents in hair cells and afferent and efferent synaptic transmission mechanisms in vestibular calyces. We developed mathematical models of the calyx incorporating our electrophysiological ion channel data. I have collaborated with Dr. Benke (University of Colorado) and Dr. Tony Ricci (Stanford University) on this work.

a. Rennie, K. J., Manning K. C. and Ricci, A. J. Mechano-electrical transduction in the turtle utricle. *Biomed. Sci. Instrum.* 40 *(ISA Volume 449):*441-446, 2004.
b. Meredith F.L., Benke T.A., Rennie K. J. Hyperpolarization-activated current (I_h) in vestibular calyx terminals: characterization and role in shaping postsynaptic events *J Assoc Res Otolaryngol,* 13:745-758, 2012. PMCID: PMC3505587.
c. Kirk M. E, Meredith F.L., Benke T.A., Rennie K. J. AMPA receptor-mediated rapid EPSCs in vestibular calyx afferents. *J. Neurophysiol.*117:2312-2323, 2017. PMCID: PMC5491709.
d. Meredith F.L., Vu T. A., Gehrke B., Benke, T.A., Dondzillo A., Rennie KJ. Expression of hyperpolarization-activated currents in zonally-identified vestibular calyx terminals of the crista. *J Neurophysiol.* 129: 1468-1481, 2023. PMCID: PMC10259860.

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/katie.rennie.1/bibliography/public/

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Santos-Cortez, Regie Lyn Pastor

eRA COMMONS USER NAME (credential, e.g., agency login): SANTOSCO

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of the Philippines (UP) Manila	B.S., B.M.S.	04/1994	Liberal Arts and Medicine
UP Manila College of Medicine (UPCM)	M.D.	04/1997	Medicine
UPCM – Philippine General Hospital (PGH)	Residency	12/2001	Otorhinolaryngology
Erasmus Medical Centre (MC), Rotterdam, Netherlands Institute for Health Sciences (NIHES)	M.Sc.	06/2003	Genetic Epidemiology
Erasmus MC Rotterdam, NIHES	D.Sc.	06/2004	Genetic Epidemiology
Erasmus University Rotterdam	Ph.D.	09/2006	Genetic Epidemiology

A. Personal Statement

Since my lab was established at the University of Colorado Anschutz Medical Campus (CU-AMC) in 2016, my group and our collaborators have been working on genetic and multi-omic studies that seek to fine-tune knowledge of etiology and pathophysiology of several otolaryngologic diseases, including otitis media, hearing loss, vestibular disorders, and obstructive sleep-disordered breathing. Our main motivation is to discover disease-specific mechanisms that will be targeted for improved diagnosis, treatment, and prevention.

During the conduct of these studies, I have had the pleasure of working with many trainees at various levels, while using these projects as a teaching tool for basic research methods, including analysis of genomic and transcriptomic data. Since 2016, I have trained the following in the lab: 4 undergraduate summer interns; 3 PRAs (one is now a radiologist); 3 medical student summer rotators; 1 predoctoral trainee as rotation student; 1 MD PhD student; 2 predoctoral students in genetics; and 5 otolaryngology T32 residents. All trainees are assigned projects within their scope of interest, which are usually collaborative and allow them to earn co-authorship in publications and, for first authors, presentation of talks or posters in national and international meetings, with several lab members obtaining Travel Awards. Additionally, in 2016 I was awarded a travel grant by the Philippine Council for Health and Research Development for conducting otitis media studies at two sites in the Philippines. Over several years I worked closely with three MSc genetic counseling students and eight otorhinolaryngology residents from the Philippine General Hospital (PGH). After graduation three previous PGH trainees now work as surgeon-researchers and collaborators in our projects and also perform their own independent academic and clinical activities. I have also conducted courses/lecture series on research methodology and genetic epidemiology, and I am developing new basic lectures and computer exercises for trainees. Finally, I served as faculty mentor to Sarah Clark, an assistant professor in our department, through the UC San Diego Raising Advancement and Parity for Infectious Disease Researchers (RAPID) program, and who recently obtained her first R01 funding and is submitting her second R01 application on otitis media.

I am pleased to serve as co-mentor to Sarah Gitomer for her K22 application. Using my training in otolaryngology and genetic epidemiology and almost two decades of experience in otitis media research, I can help guide her with the design and implementation of her clinical-microbiome study and share my group's

experiences with successes and failures, which I believe will aid in streamlining efforts in establishing her own research trajectory. I also look forward to collaborating with her on multiple NIH-funded projects.

Publications with trainees as first authors (trainee names in bold italics – also see sections C.1-C.5):

1. ***Hirsch SD, Elling CL, Bootpetch TC,*** Scholes MA, Hafrén L, Streubel SO, Pine HS, Wine TM, Szeremeta W, Prager JD, Einarsdottir E, Yousaf A, Baschal EE, Rehman S, Bamshad MJ, Nickerson DA, Riazuddin S, Leal SM, Ahmed ZM, Yoon PJ, Kere J, Chan KH, Mattila PS, Friedman NR, Chonmaitree T, Frank DN, Ryan AF, Santos-Cortez RLP. The role of *CDHR3* in susceptibility to otitis media. J Mol Med (Berl) 2021; 99:1571-1583. PMCID: PMC8541908
2. ***Elling CL,*** Scholes MA, Streubel SO, Larson ED, Wine TM, ***Bootpetch TC,*** Yoon PJ, Kofonow JM, Gubbels SP, Cass SP, Robertson CE, Jenkins HA, Prager JD, Frank DN, Chan KH, Friedman NR, Ryan AF, Santos-Cortez RLP. The *FUT2* variant c.461G>A (p.Trp154*) variant is associated with differentially expressed genes and nasopharyngeal microbial shifts in patients with otitis media. Front Cell Infect Microbiol 2022; 11:798246. PMCID: PMC8798324
3. ***Lee NK,*** Cass SP, Gubbels SP, ***Gomez HZ,*** Scholes MA, Jenkins HA, Santos-Cortez RLP. Novel candidate genes for cholesteatoma formation. Front Genet 2023; 13:1033965.
4. ***Sumalde AAM,*** Scholes MA, ***Kalmanson OA,*** Terhune E, Frejo L, Wethey C, Roman-Naranjo P, Carry P, Gubbels SP, Lopez-Escamez JA, Hadley-Miller N, Santos-Cortez RLP. Rare coding variants in patients with non-syndromic vestibular dysfunction. Genes 2023; 14:831.

Past project:

R01 DC015004 Santos-Cortez (PI) NIH-NIDCD 02/10/16-01/31/22
Otitis Media Susceptibility and Middle Ear Microbial Shifts due to Gene Variants
The aim of this project was to identify novel variants that contribute to otitis media susceptibility and induce changes in the middle ear microbiome.

Ongoing projects:

R01 DC019642 Santos-Cortez (contact MPI), Yang NIH-NIDCD 07/01/21-06/30/26
Genetic and epigenomic determinants of hearing loss in Hispanic populations
The aims of this study are to identify novel genes and variants and also genome-wide differentially methylated regions in Hispanic children with sensorineural hearing loss.

R25 DC020697 Preciado, Ryan, Santos-Cortez (contact MPI) NIH-NIDCD Pending
Development of a diverse workforce through mentoring networks among otitis media researchers
The main objective is to promote the recruitment and retention of early-stage and new investigators and individuals and trainees from various disciplines and backgrounds in otitis media research.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2016-present Associate Professor, Department of Otolaryngology - Head and Neck Surgery, CU-AMC
2017-present Member with PhD Training Status, Human Medical Genetics and Genomics Program, CU-AMC
2023-present Visiting Professor, Department of Pediatrics, College of Medicine, UP Manila
2016-2023 Member, Center for Children's Surgery, Children's Hospital Colorado
2017-2019 Adjunct Research Associate Professor, Philippine National Ear Institute, NIH-UP Manila
2009-2016 Assistant Professor, Center for Statistical Genetics, Department of Molecular and Human Genetics, Baylor College of Medicine
2009 Visiting Scholar in Audiology/Otology, Department of Otolaryngology and the Marion Downs Hearing Center, University of Colorado Denver
2007-2009 Consultant, Pediatric Otorhinolaryngology, Department of Surgery, Philippine Children's Medical Center
2007-2009 Visiting Consultant, ENT Section, Department of Surgery, Capitol Medical Center, Philippines
2006-2009 Research Associate Professor, Philippine National Ear Institute, UP Manila–NIH
2006-2009 Clinical Associate Professor, Department of Otorhinolaryngology, UPCM–PGH

Other Experience and Professional Memberships

2024 Reviewer, NIH Study Section, Genetics of Health and Disease (GHD)
2023 Reviewer, NIH Environmental Influences on Child Health Outcomes (ECHO) SEP
2022-23 Reviewer, NIH-NIDCD SEP
2021 Reviewer, NIH Small Business: Aging, Auditory, Vision and Low Vision Technologies SEP
2021 Reviewer, NIH Study Section, Neurological Aging and Musculoskeletal Epidemiology (NAME)
2014-present Grant Reviewer, Action on Hearing Loss (multiple mechanisms)
2020 Invited Member, NIH-NIDCD Workshop on Otitis Media in Early Childhood (Chair, Workforce Training)
2018-19 Cohort Member, CCTSI Leadership for Innovative Team Science (LITeS), CU-AMC
2007-09 Trainor and facilitator for various grantsmanship, GCP, faculty development and bioethics training workshops at UP Manila
2022-present Member, Philippine Academy of Neurotology, Otology and Related Sciences
2018-present Member, Collegium Oto-Rhino-Laryngologicum Amicitiae Sacrum (CORLAS)
2014-present Member, International Society for Otitis Media (current Treasurer/Board Member)
2012-present Member, Association for Research in Otolaryngology (Program Committee, 2023-2025)
2012-present Member, American Society of Human Genetics
2023-present Review Editor, Editorial Board in Molecular and Genetic Auditory Diagnosis and Therapies, Frontiers in Audiology and Otology
2022-present Review Editor, Editorial Board, Microbial Vaccines, Frontiers in Cellular and Infection Microbiology
2021-present Editorial Board, Genes
2019-present Academic Editor, PLoS One
2018-2023 Editorial Board/Senior Associate Editor, Genetic Testing and Molecular Biomarkers

Honors

2022 The University of the Philippines Medical Alumni Society in America (UPMASA) National Awardee for Research
2019 Honorary Fellow, Philippine Society of Otolaryngology Head and Neck Surgery
2018 Elected Member, CORLAS (inducted 2019)
2016 Balik-Scientist Awardee, Department of Science and Technology-Philippine Council of Health Research and Development (DOST-PCHRD)
2012 Collette Ramsey Baker Research Award
2009 Recipient, A. Charles Holland Foundation scholarship
2003 Recipient, Netherlands institute for health sciences (Nihes) scholarship
2002 Recipient, University Fellowships Program, Netherlands organization for international cooperation in higher education (Nuffic) scholarship

C. Contributions to Science (total 101 publications)

1. As coordinating PI of a multi-institutional, multinational collaborative effort on otitis media genetics, our group was the first to identify rare variants in a novel gene *A2ML1* as being involved in predisposition to nonsyndromic otitis media in humans. Since this discovery, we identified additional novel genes with common or rare variants and also replicated novel loci (*SPINK5, FUT2, ABO, PLG, CDHR3,* etc.) for otitis media susceptibility. We also identified novel otitis media-gene-microbiota associations for *A2ML1, SPINK5, FUT2* and *CDHR3,* as well as differences in microbiota according to sampling site (outer ear, nasopharynx, oral cavity; for middle ear: cholesteatoma, discharge, mucosa, granulation tissue). These studies were made possible through close coordination with collaborators from 12 US and international institutions.
   a. Santos-Cortez RLP, Chiong CM, Reyes-Quintos MRT, Tantoco MLC, Wang X, Acharya A, Abbe I, Giese AP, Smith JD, Allen EK, Li B, Cutiongco-de la Paz EM, ***Garcia MC,*** Llanes EGdV, Labra PJ, Gloria-Cruz TL, Chan AL, Wang GT, Daly KA, Shendure J, Bamshad MJ, Nickerson DA, Patel JA, Riazuddin S, Sale MM, University of Washington Center for Mendelian Genomics, Chonmaitree T, Ahmed ZM, Abes GT, Leal SM. Rare *A2ML1* variants confer susceptibility to otitis media. Nat Genet 2015; 47:917-920. PMCID: PMC4528370
   b. Santos-Cortez RLP, Chiong CM, Frank DN, Ryan AF, Giese APJ, ***Bootpetch Roberts T,*** Daly KA, ***Steritz MJ,*** Szeremeta W, Pedro M, Pine H, Yarza TKL, Scholes MA, Llanes EGdV, Yousaf S, Friedman N, Tantoco MLC, Wine TM, ***Labra PJ,*** Benoit J, Ruiz AG, ***de la Cruz RAR,*** Greenlee C, Yousaf A, Cardwell J, ***Nonato RMA,*** Ray D, ***Ong KMC,*** So E, Robertson CE, Dinwiddie J, Lagrana-Villagracia SM,

University of Washington Center for Mendelian Genomics, Gubbels SP, Shaikh RS, Cass SP, Einarsdottir E, Lee NR, Schwartz DA, Gloria-Cruz TLI, Bamshad MJ, Yang IV, Kere J, Abes GT, Prager JD, Riazuddin S, Chan AL, Yoon PJ, Nickerson DA, Cutiongco-de la Paz EMC, Streubel SO, Reyes-Quintos MRT, Jenkins HA, Mattila P, Chan KH, Mohlke KL, Leal SM, Hafrén L, Chonmaitree T, Sale MM, Ahmed ZM. *FUT2* variants confer susceptibility to familial otitis media. Am J Hum Genet 2018; 103:679-690. PMCID: PMC6217759

c. ***Wiesen BM,*** Hafrén L, Einarsdottir E, Kere J, Mattila PS, Santos-Cortez RLP. *ABO* genotype and blood type are associated with otitis media. Genet Test Mol Biomarkers 2019; 23:823-827. PMCID: PMC6857544

d. Frank DN, Giese APJ, Hafrén L, ***Bootpetch TC,*** Yarza TKL, ***Steritz MJ,*** Pedro M, ***Labra PJ,*** Daly KA, Tantoco MLC, Szeremeta W, Reyes-Quintos MRT, ***Ahankoob N,*** Llanes EGdV, Pine HS, Yousaf S, Ir D, Einarsdottir E, ***de la Cruz RAR,*** Lee NR, ***Nonato RMA,*** Robertson CE, ***Ong KMC, Magno JPM, Chiong ANE,*** Espiritu-Chiong MC, San Agustin ML, Cruz TLG, Abes GT, Bamshad MJ, Cutiongco-de la Paz EM, Kere J, Nickerson DA, Mohlke KL, Riazuddin S, Chan AL, Mattila PS, Leal SM, Ryan AF, Ahmed ZM, Chonmaitree T, Sale MM, Chiong CM, Santos-Cortez RLP. Otitis media susceptibility and shifs in the head and neck microbiome due to *SPINK5* variants. J Med Genet 2020; 58:442-452. PMCID: PMC8218788

2. In addition to identification of novel genes for otitis media, our group determined tissue-specific expression changes in individuals with otitis media and changes in the middle ear microbiota. Through follow-up studies, we showed that genetic variants have a strong effect on otitis media susceptibility and hearing, which is in some cases stronger than other known environmental risk factors.

   a. Cutiongco-de la Paz EM, Pedro M, Yarza TKL, Lagrana-Villagracia SM, ***Amoranto AJP, Jover EJM, Domine MTB,*** Chiong CM, Santos-Cortez RLP. Genetic counseling in an indigenous Filipino community with a high prevalence of *A2ML1*-related otitis media. J Community Genet 2018; 10:143-151. PMCID: PMC6325045

   b. Larson ED, ***Magno JPM, Steritz MJ,*** Llanes EGdV, Cardwell J, Pedro M, ***Bootpetch Roberts T,*** Einarsdottir E, Rosanes RAQ, Greenlee C, Santos RAP, Yousaf A, Streubel SO, Santos ATR, Ruiz AG, Lagrana-Villagracia SM, Ray D, Yarza TKL, Scholes MA, Anderson CB, Acharya A, University of Washington Center for Mendelian Genomics, Gubbels SP, Bamshad MJ, Cass SP, Lee NR, Shaikh RS, Nickerson DA, Mohlke KL, Prager JD, Cruz TLG, Yoon PJ, Abes GT, Schwartz DA, Chan AL, Wine TM, Cutiongco-de la Paz EM, Friedman N, Kechris K, Kere J, Leal SM, Yang IV, Patel JA, Tantoco MLC, Riazuddin S, Chan KH, Mattila PS, Reyes-Quintos MRT, Ahmed ZM, Jenkins HA, Hafrén L, Chiong CM, Santos-Cortez RLP. *A2ML1* and otitis media: novel variants, differential expression, and relevant pathways. Hum Mutat 2019; 40:1156-1171. PMCID: PMC6711784

   c. Frank DN, Magno JPM, Velasco KJS, ***Bootpetch TC,*** Salud JED, David KJV, Miller AL, Yee EC, Dulnuan HP,Pyles RB, Lacuata JAC, Arbizo JL,Kofonow JM, Guce B, Mendoza MD, Robertson CE, Ilustre GMS, Chiong ANE, Lu SL, Tongol EA, Sacayan ND, Yarza TKL, Chiong CM, Santos-Cortez RLP. Microbiota associated with cholesteatoma tissue in chronic suppurative otitis media. Front Cell Infect Microbiol 2022; 12:746428. PMCID: PMC9063009 – *PGH residents are underlined*

   d. Santos-Cortez RLP, ***Ong KMC, Carlos-Hiceta A,*** Tantoco MLC, Yarza TKL, San Agustin ML, Pedro M, Cruz TLG, Cutiongco-de la Paz EM, Abes GT, Llanes EGdV, Chan AL, Chiong CM, Reyes-Quintos MRT. Audiologic measures in an indigenous community with *A2ML1*- and *FUT2*-related otitis media. Genet Test Mol Biomarkers 2023; 27:12-17. PMCID: PMC9902046

3. Collaborative work on otitis media studies have led to expert reviews that summarize current state-of-the-field in otitis media research. The comprehensive review of genomic loci and expression studies have added to the knowledge base on otitis media-related pathways, including genes and pathways that overlap with other respiratory tract disorders such as chronic rhinosinusitis and chronic bronchitis.

   a. Baschal EE, Larson ED, ***Bootpetch Roberts TC, Pathak S,*** Frank G, Handley E, Dinwiddie J, Moloney M, Yoon PJ, Gubbels SP, Scholes MA, Cass SP, Jenkins HA, Frank DN, Yang IV, Schwartz DA, Ramakrishnan VR, Santos-Cortez RLP. Identification of novel genes and biological pathways that overlap in infectious and nonallergic diseases of the upper and lower airways using network analyses. Front Genet 2019; 10:1352. PMCID: PMC6979043

b. Santos-Cortez RLP, Bhutta MF, Earl JP, Hafrén L, Jennings M, Mell JC, Pichichero ME, Ryan AF, Tateossian H, Ehrlich GD. Panel 3: Genomics, Precision Medicine and Targeted Therapies. Int J Pediatr Otorhinolaryngol 2020; 130 Suppl 1:109835. PMCID: PMC7155947
c. Santos-Cortez RLP, Ehrlich GD, Ryan AF. Editorial: Otitis media genomics and the middle ear microbiome. Front Genet 2021; 12:763688. PMCID: PMC8546293
d. ***Lee NK,*** Santos-Cortez RLP. An overview of the genetic determinants of otitis media susceptibility. In: Goycoolea MV, Selaimen da Costa S, De Souza C, Paparella MM, eds. Otitis media: The basics, further and beyond. Cham, Switzerland: Springer Nature Switzerland AG, 2023.

4. Since 2002, I have worked on the genetics of hearing loss. My work has included mapping of novel loci, identification of variants in known and novel genes, and genotype-phenotype correlation using audiologic data. I have analyzed exome sequence data from families with hearing loss, a large majority of which were consanguineous families from Pakistan. From the exome data I identified *KARS, TBC1D24, ADCY1, S1PR2, ADAMTS1, MVD* and *SEZ6* as novel genes for hearing loss. I also recently identified novel genes and variants for hearing loss within the Filipino population.
   a. Santos-Cortez RLP, Lee K, Azeem Z, Antonellis PJ, Pollock LM, Khan S, Irfanullah, Andrade-Elizondo PB, Chiu I, Adams MD, Basit S, Smith JD, University of Washington Center for Mendelian Genomics, Nickerson DA, McDermott BM Jr, Ahmad W, Leal SM. Mutations in *KARS*, encoding lysyl-tRNA synthetase, cause autosomal recessive nonsyndromic hearing impairment DFNB89. Am J Hum Genet 2013; 93:132-140. PMCID: PMC3710764
   b. ***Truong BT,*** Yarza TKL, ***Bootpetch Roberts T, Roberts S, Xu J, Steritz MJ,*** Tobias-Grasso CAM, Azamian M, Lalani SR, Mohlke KL, Lee NR, Cutiongco-de la Paz EM, Reyes-Quintos MRT, Santos-Cortez RLP, Chiong CM. Exome sequencing reveals novel variants and unique allelic spectrum for hearing impairment in Filipino cochlear implantees. Clin Genet 2019; 95:634-636. PMCID: PMC6499369
   c. Santos-Cortez RLP, Yarza TKL, ***Bootpetch TC,*** Tantoco MLC, Mohlke KL, Cruz TLG, Chiong Perez ME, Chan AL, Lee NR, Tobias-Grasso CAM, Reyes-Quintos MRT, Cutiongco-de la Paz EM, Chiong CM. Identification of novel candidate genes and variants for hearing loss and temporal bone anomalies. Genes 2021; 12. PMCID: PMC8069784
   d. Bharadwaj T, Schrauwen I, Rehman S, Liaqat K, Acharya A, Giese APJ, Nouel-Saied LM, Nasir A, Everard JL, Pollock LM, Zhu S, Bamshad MJ, Nickerson DA, Ali RH, Ullah A, Wali A, Ali G, Santos-Cortez RLP, Ahmed ZM, McDermott BM Jr, Ansar M, Riazuddin S, Ahmad W, Leal SM. *ADAMTS1, MPDZ, MVD,* and *SEZ6:* candidate genes for autosomal recessive nonsyndromic hearing impairment. Eur J Hum Genet 2021; 30:22-33. PMID: 34135477

5. The body of work on novel variants in known genes for hearing loss, estimation of gene-specific prevalence of variants in populations, and genotype-phenotype correlations has been used to support national policy on genetic screening for hearing loss and newborn hearing screening, and also provides insight on future research directions for hearing loss genetics.
   a. Santos-Cortez RLP, Chiong CM. Cost-analysis of universal newborn hearing screening in the Philippines. Acta Medica Philippina 2014; 47.
   b. Richard EM, Santos-Cortez RLP, Faridi R, Rehman AU, Lee K, Shahzad M, Acharya A, Khan AA, Imtiaz A, Chakchouk I, Takla C, Abbe I, Rafeeq M, Liaqat K, Chaudhry T, Bamshad MJ, Nickerson DA, Schrauwen I, Khan SN, Morell RJ, Zafar S, Ansar M, Ahmed ZM, Ahmad W, Riazuddin S, Friedman TB, Leal SM, Riazuddin S. Global genetic insight contributed by consanguineous Pakistani families segregating hearing loss. Hum Mutat 2019; 40:53-72. PMCID: PMC6296877
   c. Chakchouk I, Zhang D, Zhang Z, Francioli LC, Santos-Cortez RLP, Schrauwen I, Leal SM. Disparities in discovery of pathogenic variants for autosomal recessive non-syndromic hearing impairment by ancestry. Eur J Hum Genet 2019; 27:1456-1465. PMCID: PMC6777454
   d. Yoon PJ,* ***Sumalde AAM,**** Ray DC, Newton S, Cass SP, Chan KH, Santos-Cortez RLP. Novel variants in hearing loss genes and associations with audiometric thresholds in a multi-ethnic cohort of US patients with cochlear implants. Otol Neurotol 2020; 41:978-985. PMID: 32658404 *co-first authors

Complete List of Published Work in MyBibliography:
URL: https://www.ncbi.nlm.nih.gov/myncbi/1PcCZJ9IiHx5e/bibliography/public/

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Carissa Michelle Thomas, MD PhD FACS

eRA COMMONS USER NAME: ct147895

POSITION TITLE: Assistant Professor of Otolaryngology – Head and Neck Surgery

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Luther College, Decorah, IA	BA	05/2004	Chemistry, Biology
Baylor College of Medicine, Houston, TX	MD	05/2013	Medicine
Baylor College of Medicine, Houston, TX	PhD	10/2011	Cell & Molecular Biology
University of Colorado, School of Medicine, Aurora, CO	Resident	06/2018	Otolaryngology – Head & Neck Surgery
University of Toronto/University Health Network/Princess Margaret Cancer Centre, Toronto, ON	Fellow	06/2019	Head & Neck Surgical Oncology and Microvascular Reconstruction

A. Personal Statement

I am an assistant professor and surgeon scientist joining the University of Colorado in the Department of Otolaryngology – Head and Neck Surgery. I have a PhD in cell and molecular biology examining the gut microbiome and immunomodulation by bacteria, as well as experience studying the tumor microenvironment in head and neck cancer (HNC), and most recently, the oral microbiome in oral and oropharyngeal squamous cell carcinoma. I am passionate about improving outcomes in HNC, in particular risk stratification to appropriately tailor treatment and improve survival and long-term quality of life. My research interests are focused on how an altered oral microbiome (dysbiosis) promotes carcinogenesis and metastatic disease. I am investigating the oral microbiome as a biomarker to predict prognosis with the future goal of altering the microbiome to improve treatment response and prevent recurrence and metastases in HNC. I have established a microbiome biobank from all patients with oral cavity squamous cell carcinoma (OSCC). Biospecimen collection includes oral swab and brush specimens, saliva, stool, peripheral blood, and tumor tissue. In addition, we are collecting clinicopathologic data, oral care habits, diet history, and antibiotic use. This biobank is used for collaborative projects on OSCC risk stratification scores that can guide treatment and ultimately improve survival. The current **METS** project fits in seamlessly to our current workflow and collaborations. My experience in the microbiome and bacteria modulation of the host immune system provides the expertise necessary to successfully complete the proposed project on microbiome and metastatic OSCC. We have the pipeline in place to obtain clinicopathologic information and biological samples required to complete this prospective clinical study. Senior mentorship is also in place with Dr. Brad Aouizerat to ensure success of this cancer genomic study and biomarker development. *I will oversee all aspects of the study related to the microbiome including the study design, data interpretation & analysis (mentored by Dr. Brad Aouizerat) and its presentation/publication.*

<u>Ongoing projects to highlight include:</u>

1. O'Neal Comprehensive Cancer Center Catalyst Grant 01/01/2024-12/31/2025
   Otolaryngology – Head & Neck Surgery, University of Alabama at Birmingham $50000.00
   Single Cell Based Immune Profiling and Transcriptomics of Oropharyngeal Cancer
   Role: *Co-principal investigator* (cPI: Bansal)
2. NIH/NIDCR R01 DE031395 08/15/2022-07/31/2027

The REASON Score: An Epigenetic And Clinicopathologic Score to Predict Risk of Poor Survival in Early Stage Oral Squamous Cell Carcinoma Patients
Role: *Co-investigator* (PI: Viet)

3. NIH/NIDCR R01 CA293995
PROSPECT: Premalignant Oral Lesions Pathology and Epigenetic Risk Prediction Tool
Role: *Co-investigator* (PI: Viet)

Recently completed projects to highlight include:

1. Oral Maxillofacial Surgery Foundation Research Grant 01/01/2022-12/31/2023
Otolaryngology – Head & Neck Surgery, University of Alabama at Birmingham $75000.00
OSCC has a Unique Oral Microbiome that Increases Invasiveness & Predicts Risk of Metastases
Role: Principal Investigator
2. Harry Barberian Scholarship Fund 05/01/2019-04/30/2021
Otolaryngology – Head and Neck Surgery, University of Toronto $15000.00
Mapping the Oral Cavity Microbiome in Head and Neck Squamous Cell Carcinoma
Role: Co-Investigator
3. AHNS/AAO-HNSF Young Investigator Award 07/01/2020-06/30/2022
Otolaryngology – Head & Neck Surgery, University of Alabama at Birmingham $40000.00
Understanding Oral Cavity Microbiome and Tumor Microenvironment Cross-talk
Role: *Principal Investigator*
4. UAB Faculty Development Grant 05/15/2021-08/31/2022
Otolaryngology – Head & Neck Surgery, University of Alabama at Birmingham $9215.00
Identification of Oral Cavity and Gut Microbiome Biomarkers of Cancer Pain in OSCC
Role: *Principal Investigator*
5. UAB Global Center for Craniofacial Oral and Dental Disorders Pilot Grant 05/01/2022-4/30/2023
Effect of the Oral Microbiome on OSCC Gene Expression of Invasion $25,000.00
Role: *Principal Investigator*

Citations:

a) **Thomas CM,** Hong T, van Pijkeren JP, Hemarajata P, Trinh DV, Hu W, Britton RA, Kalkum M, Versalovic J. Histamine derived from probiotic *Lactobacillus reuteri* suppresses TNF via modulation of PKA and ERK signaling. *PloS ONE*. 2012: 7(2): e31951. PMID: 22384111
b) **Thomas CM**, Saulnier D, Spinler JK, Hemarajata P, Gao C, Jones SE, Grimm A, Balderas MA, Burstein MD, Morra C, Roeth D, Kalkum M, Versalovic J. FolC2-mediated folate metabolism contributes to suppression of inflammation by probiotic *Lactobacillus reuteri*. *Microbiology Open*. 2016: 5(5): 802-818. PMID: 27353144
c) Viet CT, Yu G, Asam K, **Thomas CM**, Yoon AJ, Wongworawat YC, Haghighiabyaneh M, Kilkuts CA, McGue CM, Couey MA, Callahan NF, Doan C, Walker PC, Nguyen K, Kidd SC, Lee SC, Grandhi A, Cheng AC, Patel AA, Philipone E, Ricks OL, Allen CT, Aouizerat BE. The REASON score: an epigenetic and clinicopathologic score to predict risk of poor survival in patients with early stage oral squamous cell carcinoma. Biomarker Research. 2021: 9(1):42. PMID:34090518
d) Gallant JN, Vivek N, McKeon MG, Sharma RK, Kim YJ, Rosenthal EL, Das SR, **Thomas CM**. Establishing a Role for the Oral Microbiome in Infectious Complications Following Major Oral Cavity Cancer Surgery. Oral Oncol. 2024. 156.

B. Positions, Scientific Appointments, and Honors

POSITIONS and EMPLOYMENT

2023-present	Director of Clinical Research for Department of Otolaryngology, University of Alabama at Birmingham, Birmingham, AL
2022-present	Director of Head and Neck Microvascular Reconstruction, University of Alabama at Birmingham, Birmingham, AL
2022-present	Faculty of Graduate School of Biomedical Sciences, University of Alabama at Birmingham, Birmingham, AL
2020-present	Associate Scientist in Experimental Therapeutics Program, O'Neal Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL

2020-present	Associate Scientist in UAB University Wide Microbiome Center, University of Alabama at Birmingham, Birmingham, AL
2019-present	Assistant Professor, Department of Otolaryngology – Head and Neck Surgery, University of Alabama at Birmingham, Birmingham, AL
2018-19	Head and Neck Surgical Oncology, Microvascular Reconstruction Clinical Fellow, Department of Otolaryngology – Head and Neck Surgery, University of Toronto, Toronto, ON, Canada
2017-18	Administrative Chief Resident, Department of Otolaryngology – Head and Neck Surgery, University of Colorado School of Medicine, Aurora, CO
2013-18	Resident, Department of Otolaryngology – Head and Neck Surgery, University of Colorado School of Medicine, Aurora, CO

PROFESSIONAL ORGANIZATIONS and COMMITTEES

2023-present	ECOG-ACRIN Cancer Research Group Microbiome Working Group, *Member*
2023-24	American Academy of Otolaryngology CORE, Head & Neck Subsection, *Reviewer*
2023	Terry Fox Research Institute (TFRI) Program Project Grants Committee, *Reviewer*
2023-present	American Academy of Otolaryngology Microvascular Committee, *Member*
2023-present	AHNS Population Health & Clinical Research Service Committee, *Member*
2023	NIH Molecular Cancer Diagnosis and Classification (MCDC) Study Section, *ESR*
2022-present	NRG Oncology Head and Neck Cancer General Committee, *Member*
2022	Dept of Defense FY22 CDMRP Peer Reviewed Cancer Research Program, *Scientist Grant Reviewer*
2022-present	Thesis Committee for Abbigael Eli, Graduate Biomedical Sciences, CANB, *Member*
2022-present	Thesis Committee for Logan Stone, Graduate Biomedical Sciences, CANB, *Member*
2021-present	UAB Multidisciplinary Head & Neck Reconstructive Case Conference, *Director*
2021-present	UAB O'Neal Comprehensive Cancer Center Head and Neck Working Group, *Lead*
2021-present	American College of Surgeons, *Fellow*
2021-present	AHNS Reconstructive Head & Neck Surgery Section Research Committee, *Member*
2021-present	AHNS Journal Club Committee, *Member*
2021-present	AHNS Basic/Translational Science Service Committee, *Member*
2020-23	UAB Dept of Otolaryngology Diversity and Inclusion Committee, *Chair*
2018-present	AHNS Reconstructive Head & Neck Surgery Section, *Member*
2018-19	The Canadian Medical Protective Association, *Member*
2018-19	The College of Physicians and Surgeons of Ontario, *Clinical Fellow*
2017-18	The Triological Society, *Resident Member*
2017-present	American Head Neck Society (AHNS), *Member*
2013-present	American Academy of Otolaryngology - Head and Neck Surgery, *Member*
2006-11	International Scientific Association for Probiotics and Prebiotics (ISAPP) Students & Fellows Association, *Member*
2004-13	American Medical Association, *Member*

HONORARY SOCIETIES

2018	Gold Humanism Honor Society
2004	Phi Beta Kappa (National Academic Honor Society)

HONORS and AWARDS

2023	UAB O'Neal Comprehensive Cancer Center Resource Voucher (10K), *Recipient*
2022	AHNS Cancer Prevention Service Community Service Award, "Expressions of the Head & Neck Cancer Journey: Visual Art Experience for Oncology Patients"
2020-24	NIH Clinical Research Loan Repayment Program Grant Recipient, NIDCR
2019	American Head and Neck Society Best Poster, Combined Otolaryngology Spring Meeting, Austin, TX
2018	The Ohio State University Head and Neck Microvascular Fellow Boot Camp Best Mandibular Reconstruction, 2nd place
2018	University of Colorado Department of Otolaryngology – Head & Neck Surgery Resident Teacher of the Year Award

2017	Triological Society Resident Travel Award
2016	University of Colorado Department of Otolaryngology – Head & Neck Surgery Resident Research Award, 1st place
2011	Deborah K. Martin Achievement Award in Biomedical Sciences Cell & Molecular Biology Nominee
2010	Melvin Denis Memorial Travel Award, National MD/PhD Student Conference
2010	International Scientific Association of Prebiotics & Probiotics SFA Travel Award, International ISAPP Meeting, Barcelona, Spain
2005-06	MSTP Award for Excellence in Basic Science Coursework, Baylor College of Medicine
2003-04	Barry M Goldwater Scholarship, Luther College
2000-04	Regent's Scholarship, Luther College

C. Contributions to Science

My diverse scientific contributions range from microbiome-host interactions, collaborative work on risk stratification biomarker development for OSCC, cancer stem cells, and use of fluorescent-labeled antibodies to improve intraoperative surgical margin detection. In addition, I have been broadly interested in clinical aspects of head and neck oncology and microvascular reconstruction, complementing my scientific interests. Here I highlight key papers (20 publications selected from 40; H-index = 13; i10-index = 15; 1,558 citations).

1. I have a longstanding interest in the interactions between the microbiome and the host immune system, starting with the modulation of the gut immune system by beneficial bacteria in chronic inflammatory bowel disease. I discovered specific strains of probiotic *Lactobacillus reuteri* produce histamine, which inhibits TNF production by suppression of ERK/MAPK signaling in macrophages. My first author publication in *PLOS One* on modulation of ERK/MAPK signaling pathways by *L. reuteri*-produced histamine was one of the first mechanistic papers published related to bacterial modulation of the host immune system. Since publication in 2012, it has been cited 495 times. This work led to a patent with collaborators at BioGaia (Stockholm, Sweden) on the production and use of bacterial histamine in therapeutic applications.

a) **Thomas CM,** Hong T, van Pijkeren JP, Hemarajata P, Trinh DV, Hu W, Britton RA, Kalkum M, Versalovic J. Histamine derived from probiotic *Lactobacillus reuteri* suppresses TNF via modulation of PKA and ERK signaling. *PloS ONE*. 2012: 7(2): e31951. PMID: 22384111
b) Jones S, Whitehead K, Saulnier D, **Thomas CM**, Versalovic J, Britton R. Cyclopropane fatty acid synthase mutants of probiotic human-derived *Lactobacillus reuteri* are defective in TNF inhibition. *Gut Microbes*. 2011: 2(2): 69-79. PMID: 21637024
c) Hemarajata P, Gao C, Pflughoeft KJ, **Thomas CM**, Saulnier D, Spinler JK, Versalovic J. Lactobacillus reuteri-specific immunoregulatory gene (RsiR) modulates histamine production and immunomodulation by Lactobacillus reuteri. J Bacteriology. 2013: 195(24): 5567-76. PMID: 24123819
d) **Thomas CM**, Versalovic J. Probiotics-Host Communication: Modulation of signaling pathways in the intestine. *Gut Microbes*. 2010: 1(3): 148-63. PMID: 20672012

2. OSCC has poor survival rates, even for early stage patients. This is largely due to a lack of biomarkers that can accurately risk-stratify patients and appropriately tailor treatment. I have been collaborating on research that combines clinicopathologic data with molecular data to develop novel biomarkers that can predict risk of mortality in patients with OSCC. The ultimate goal is to combine microbiome level data as a biomarker.

a) Viet CT, Yu G, Asam K, **Thomas CM**, Yoon AJ, Wongworawat YC, Haghighiabyaneh M, Kilkuts CA, McGue CM, Couey MA, Callahan NF, Doan C, Walker PC, Nguyen K, Kidd SC, Lee SC, Grandhi A, Cheng AC, Patel AA, Philipone E, Ricks OL, Allen CT, Aouizerat BE. The REASON score: an epigenetic and clinicopathologic score to predict risk of poor survival in patients with early stage oral squamous cell carcinoma. Biomarker Research. 2021: 9(1):42. PMID:34090518
b) Viet CT, Zhang X, Xu K, Yu G, Asam K, **Thomas CM**, Callahan NF, Doan C, Walker PC, Nguyen K, Kidd SC, Lee SC, Grandhi A, Allen CT, Young S, Melville JC, Shum JW, Viet DT, Herford AS, Roden DF, Gonzalez ML, Zhong J, Aouizerat BE. Brush swab as a noninvasive surrogate for tissue biopsies in epigenomic profiling of oral cancer. Biomarker Research. 2021: 9(1):90. PMID: 34930473
c) Chowdhury FN, Reisinger J, Gomez KE, Chimed TS, **Thomas CM**, Le PN, Miller B, Morton JJ, Nieto CM, Somerset HL, Wang XJ, Keysar SB, Jimeno A. Leading edge or tumor core: Intratumor cancer stem cell niches in oral cavity squamous cell carcinoma and their association with stem cell function.

Oral Oncology. 2019: 98: 118-124. PMID: 31586893

3. Current intraoperative strategies lack the sensitivity and specificity to identify the extent of primary lesions and distinguish inflammation from malignancy. Use of panitumumab-IRDye800 and other fluorescent tagged antibodies can improve detection of surgical margins. Having high fidelity to distinguish malignancy from benign tissue is especially important in areas like the larynx where over resection can significantly increase morbidity and permanently alter voice and swallowing. I also have expertise in the use of targeted fluorescence agents to assess regional flap perfusion in a mouse model.

a) Bailey L, Stone LD, Gonzalez ML, **Thomas CM**, Jeyarajan H, Warram JM, Panuganti B. Panitumumab-IRDye800 improves laryngeal tumor mapping during transoral laser microsurgery. The Laryngoscope. 2023. *Online ahead of print.* PMID: 37860983

b) Hicks MD, Ovaitt AK, Morrison DR, Fleming JC, Jeyarajan H, Greene B, Sorace AG, Patel J, Kasten BB, Hartman YE, Rosenthal EL, Warram JM, **Thomas CM.** Determination of flap survival isolated from wound bed vasculature using a murine axial flap model. Ear Nose & Throat J. 2023: Online ahead of print. PMID: 37365848

c) Hicks MD, Ovaitt AK, Fleming JC, Sorace AG, Song PN, Mansur A, Hartman YE, Rosenthal EL, Warram JM, **Thomas CM**. Hyperintensity of integrin-targeted fluorescence agent IntegriSense750^{TM} accurately predicts flap necrosis compared to indocyanine green. Head Neck. 2021: 44(1):134-142. PMID: 34697855

4. My research contributions include several clinical and translational research studies in various areas of head and neck surgery to improve head and neck cancer patient outcomes related to postoperative complications, treatment toxicity, and quality of life.

a) **Thomas CM**, Khan MN, Mohan R, Hendler A, Hosni A, Chepeha DB, Goldstein DP, Cooper RM, de Almeida JR. Lymphatic mapping with SPECT-CT for evaluation of contralateral drainage in lateralized oropharyngeal cancers using an awake injection technique. Head Neck. 2019: 42(3):385-393. PMID: 31778005

b) Hicks MD, Vasudev M, Bishop JL, Garcia N, Chowdhury F, Pham TT, Heslop G, Greene B, Jeyarajan H, Grayson JW, Goddard JA, Tjoa T, Haidar Y, **Thomas CM**. Effect of perioperative antithrombotics on postoperative transfusion and hematoma in head and neck free flaps. OTO Open. 2023. *Online ahead of print.* PMID: 37854346

c) Rao SM, Knott PD, Sweeny L, Domack A, Tang A, Patel R, Pittman AL, Gardner JR, Morena MA, Sunde J, Cave TB, Knight ND, Greene B, Pipkorn P, Joshi AS, Thakkar P, Ji K, Yang S, Chang BA, Wax MK, **Thomas CM**. Microvascular free flap outcomes in maxillectomy defects from invasive fungal sinusitis. The Laryngoscope. 2023. *Online ahead of print.* PMID: 37772913

d) Bishop JL, Vasudev M, Garcia N, Heslop G, Pham TT, Hicks MD, Chowdhury F, Grayson JW, Goddard JA, Tjoa T, Haidar Y, **Thomas CM**. Effect of perioperative antithrombotics on head and neck microvascular free flap survival after anastomotic revision. Otolaryngology-Head and Neck Surgery. 2023:168(6):1353-1361. PMID: 36939436

5. One of my clinical research interests is in frailty, depression and postoperative decision regret in patients with head and neck cancer. This work won best poster from the American Head and Neck Society at the Combined Otolaryngology Spring Meeting (2019, Austin, TX). As a specialty, we are recognizing the unique vulnerabilities of the frail population of patients. It is important to understand this subset of patients as the number of elderly patients with head and neck cancer continues to rise.

a) **Thomas CM,** Sklar MC, Su J, Xu W, de Almeida JR, Alibhai SMH, Goldstein DP. Longitudinal assessment of frailty and quality of life in patients undergoing head and neck surgery. The Laryngoscope. 2021: 131(7):E2232-E2242. PMID: 33427307

b) Grewal R, Sklar MC, de Almeida JR, Xu W, Su J, **Thomas CM**, Alibhai SMH, Goldstein DP. Evaluation of the Braden scale in predicting surgical outcomes in older patients undergoing major head and neck surgery. Laryngoscope Investigative Otolaryngology. 2020: 6(1):103-108. PMID: 33614937

c) **Thomas CM,** Sklar MC, Su J, Xu W, de Almeida JR, Alibhai SMH, Goldstein DP. Longitudinal assessment of frailty and quality of life in patients undergoing head and neck surgery. The Laryngoscope. 2021: 131(7):E2232-E2242. PMID: 33427307

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