Annual Chair’s Message For 2017

Stanford Otolaryngology-Head & Neck Surgery (OHNS) is special. We are blessed with a warm and collegial culture among our community of 286 faculty, trainees, and staff. We strive for, and achieve, excellence in all of our core missions: clinical care, education, and research. In clinical care, we have depth, breadth, and high levels of expertise in all of the specialty areas of contemporary OHNS. We enjoy the finest clinical facilities at Stanford and cutting edge technology in our clinics and operating rooms. Our remarkable group of clinician-scholars in training ensures a bright future for our field. Our peerless basic and translational science faculty are both immensely creative and highly productive.

Stanford OHNS Faculty and Trainees. June 2016

Our Faculty:

The core strength of Stanford OHNS is its outstanding faculty. In 2003, the year we became a department, we had 5 faculty. We begin 2017 with 45 faculty (19 Professors, 6 Associate Professors, 14 Assistant Professors, 6 Instructors). In addition, we have 4 affiliated faculty at Santa Clara Valley Medical Center, and new affiliates in our University Health Care Alliance offices in San Ramon and San Jose.

In 2017 we expect to add 6 additional faculty with searches underway in pediatric OHNS, laryngology, otology - neurotology, facial plastic surgery, head and neck endocrine surgery, and basic science as well as expanding our affiliated network in the South Bay and East Bay regions.
Stanford OHNS is well represented among the medical center and school leadership. Lloyd Minor is the School of Medicine Dean. Eben Rosenthal is the Ann & John Doerr Medical Director of the Stanford Cancer Center and Associate Director of Clinical Care for the Stanford Cancer Institute. Ed Damrose begins his three year term as Stanford Health Care Chief of the Medical Staff this year and Peter Koltai is a recent past Chief of the Medical Staff at Stanford Children’s Hospital.
Departmental Publications:

Stanford OHNS scholars have remained highly productive this year. PUBMED lists 268 peer reviewed publications for Stanford otolaryngology in 2016, which does not include books, chapters, abstracts, or editorials. Working with our departmental web designer Crystal Chen, we have comprehensively modernized our websites (http://med.stanford.edu/ohns.html). Our research community has been especially creative in using latest web design elements (http://med.stanford.edu/ohns/research.html).

This year we produced two publications about our department. A 86 page booklet published in November 2016 describes the ways Stanford OHNS contributes to health care, scientific innovation, education, and our community. In this booklet, we share stories that illustrate the type of care, teaching, and inquiry that makes Stanford OHNS such a special place. We also produced a convenient guide to our adult and pediatric services.

Full text of Stanford OHNS Magazine:
http://med.stanford.edu/content/dam/sm/ohns/documents/about/Stanford_OHNS.pdf

Full text of Stanford OHNS Clinical Services Guide:
http://med.stanford.edu/content/dam/sm/ohns/documents/Health%20Care/OHNS_Referral_Guide.pdf
Education Programs:

Our immensely talented trainee population includes 20 OHNS residents, 2 ACGME accredited fellows (pediatrics, neurotology), and 8 instructors (head & neck surgery (2), sinus surgery (2), facial plastics surgery, laryngology, sleep surgery, and neurotology. We also have a number of graduate students, post-doctoral research fellows, instructors, and visiting scholars. Dozens of Stanford and visiting medical students are on rotation throughout the year.

This year, thanks to the efforts of John Oghalai, Alan Cheng, and Anna Messner we obtained a T32 training grant. This NIH funded program, intended to produce scientist-surgeons, will allow selected residents to undertake 2 years of funded research in addition to their 5 clinical years. To accommodate this new program, and our departmental growth, Stanford OHNS was approved by the Otolaryngology Residency Review Committee (RRC) to increase from 4 to 5 residents per year starting in 2017 for a total of 25 residents in our program by 2021.

Our T-32 research training program now has two tracks. One is a 7-year residency research track, which combines 5 years of clinical training in OHNS with 2 years of research training starting after the PGY2 year. The second is a 2-year post-residency track, which will be used to provide a research experience for those individuals that desire an extended research experience after residency training. Both tracks are post-doctoral fellowships for otolaryngology residents, with the main difference being that the first track has the research block in the middle of residency training and the second track has the research block after residency has been completed. Both tracks provide guidance on how to balance research and clinical responsibilities in order to prepare the trainees to become independent physician-scientists.

Many of our residents and fellows take advantage of the rich educational environment of Stanford. The Stanford Society of Physician Scholars provides training and mentoring core academic skills through evening sessions throughout the year. The SPECTRUM 1 week intensive course in clinical research educates on study design and performance. A number of our trainees and faculty have participated in the renowned Stanford Biodesign program which teaches medical device innovation and entrepreneurship.
The exceptional quality of today’s trainees insures that the future of our specialty will be in the best of hands. Our residents are having great success in obtaining fellowship positions and the graduates of our instructor/fellows programs obtain excellent faculty positions. Among our residency graduating class of 2016, 3 graduates went on to sub-specialty fellowship and one joined a regional private practice with continued Biodesign engagement.

2016 OHNS Residency Graduates:

Jennifer Alyono: Neurotology Fellowship at Stanford
Anais Rameau: Laryngology Fellowship at UC Davis
Ryan Williams: Sleep Surgery Fellowship at Stanford
Elizabeth Zambricki: Palo Alto Medical Foundation & Medical Device Innovation

We have undertaken a number of initiatives designed to enhance the educational value of our website. OHNS grand rounds and CME courses are available online on our departmental website and iTunes U channel. Over 2000 original illustrations are online in our skull base, neurotology, and otology atlases. We are in the midst of expanding this resource to encompass all of OHNS.

Nik Blevins and a team of computer scientists and engineers have created a haptic reinforced sinus and temporal bone surgical simulator. Our Perkins Microsurgery Teaching Laboratory has newly installed LED based microscopes with high definition video displays. Kwang Sung utilized the microsurgery lab for performing a phonomicrosurgical simulation study with the residents. Twice a year Dr. Jennifer Lee, who is trained in surgical simulation, leads all OHNS residents through varied simulations such as “carotid blowout,” “anaphylaxis” and “angioedema.” For student use, we purchased two otoscopy simulators; one for the department and the other was donated to the medical school’s simulation facility.

We have completed our departmental introductory textbook, a multi-authored work created entirely by our faculty and trainees and are in the process of making it available online. It goes under the title SOITO: Stanford Online Interactive Textbook of Otolaryngology. The text is targeted primarily for medical students, beginning residents, and patients interested in a reliable source of sophisticated medical information. The concept is to make available a well-illustrated online text, continuously updated, and made freely available to trainees and patients worldwide. Under the editorial leadership of Dr. Jennifer Lee this 72 chapter project has taken a couple of years to produce and has several hundred original illustrations.

Working with the Stanford Faculty Development Center (SFDC), we launched our surgical teaching course in 2014. Anna Messner, an SFDC-trained facilitator, leads an annual teaching course oriented to teaching skills in the operating room to new OHNS faculty, fellows and the chief residents.

About twenty Stanford students rotate in our department as part of the general surgery core clerkship; and approximately 20 sub-interns come from other institutions. Our visiting sub-
intern rotation has become very popular, highly competitive, draws high outstanding applicants from around the country.

**Stanford OHNS Research Overview:** Stanford is a research intensive school of medicine and we are a research intensive department. Our commitment to basic and translational research is well illustrated by the growth of our annual research budget from under $5,000 (2003) to over an estimated $10 million in 2017. We have some 12,000 sq. ft. of research space with our major laboratory in the Edwards building and additional facilities in Lokey Stem Cell, Grant, and CCSR buildings. All will coalesce into the new Biomedical Innovations Building starting construction this year with anticipated occupancy in late 2019.

In late 2016, departmental faculty have more than competitive extramural grants and are principal investigator on 11 NIH R-01s, U01, 2 DoDs, a CIRM award and 18 industry grants. Our basic science research community consists of 110 faculty, post-docs, researchers, students and other trainees.

At our 7th annual research retreat in October, the entire department participated and each of our faculty presented their research plans for the coming year. Both extramural funding and philanthropy remain strong. Trainees present their research progress as part of our annual graduations ceremonies each June.

The central theme of *Stanford OHNS basic and translational research* is to seek a better understanding of diseases in our field and inventing new therapies. Our research group, which is a mixture of basic scientists and surgeon – scientists, enjoys numerous collaborations throughout Stanford bioscience and technology. A major thrust of our research is to overcome hearing loss through regenerative means. To achieve this goal we have created the *Stanford Initiative to Cure Hearing Loss*, which is a long term, goal oriented, multidisciplinary research effort. (Heller, Ricci, Oghalai, Cheng, Mustapha, Chang, Grillet, Blevins, Fitzgerald, Jackler, and Minor)

**Clinical Programs**

Our *clinical services* continue their traditional double-digit growth annually – a trend which has been sustained annually for over a decade. Our focus is on high quality tertiary care of complex diseases in the head and neck region. We have 8 clinical divisions: facial plastics, head & neck surgery, laryngology, otology/neurotology, pediatric, rhinology, sleep surgery, and comprehensive ENT. Space does not permit a full accounting of our areas of expertise, but I will highlight a few noteworthy examples.

Our clinical programs are housed in a number of locations. Laryngology, rhinology, facial plastic surgery, and comprehensive ENT are all housed in our departmental home building at 801 Welch Road on the Stanford campus. Our head and neck surgery program occupies most of the 3rd floor of the Blake-Wilbur building adjacent to our home building. Across the street are our pediatric clinics at the Mary Johnson Center with additional pediatric clinic space in Los Gatos. Otology/neurotology and pediatric otology are situated at the Stanford Ear Institute at Watson Court and sleep surgery at our Redwood City satellite.
In our Head & Neck Surgery Division Chief Chris Holsinger leads our innovative transoral robotic program in which he is joined by Drs. Damrose, Capasso, and Sirjani. Lisa Orloff heads our very active thyroid-parathyroid program and is internationally renowned for her expertise in ultrasound. She is joined in head and neck endocrine surgery by Drs. Sunwoo and Holsinger. Dr. Davud Sirjani focuses on salivary gland surgery while Dr. John Sunwoo has special expertise in melanoma. Vasu Divi and Eben Rosenthal expertly perform microvascular free flap reconstructions. Michael Kaplan is our highly versatile, extremely busy, senior head and neck cancer surgeon. Speech therapist Ann Kearny provides care for post-laryngectomy voice restoration patients and Heather Starmer supports patients with swallowing disorders.

In our Rhinology Division, Chief Peter Hwang is constantly surrounded by international observation and our residents have begun calling it the “Hwangterage.” Peter has a busy practice of complex endoscopic sinus surgery, often taking on the most challenging cases. Both he, Drs. Jayakar Nayak and Zara Patel collaborate with neurosurgical colleagues on minimally invasive endoscopic skull base surgery including a substantial census of pituitary tumors. Dr. Nayak helped to develop a transnasal approach to the odontoid. The Stanford Sinus Center provides integrated care including cone beam CT imaging and allergic management by allergy specialists on site.

In our Laryngology Division, Chief Ed Damrose has special interests in rehabilitation of laryngeal paralysis and cancer of the larynx. His colleague Dr. Kwang Sung does a wide array of in office laryngeal procedures, including those requiring use of the laser. Kwang also has a strong interest in care of the professional voice, especially in entertainers. Speech therapist Elizabeth DiRenzo provides care for a wide range of voice disorders.

In our Sleep Surgery Division, Chief Robson Capasso tackles a wide variety of procedures to alleviate obstructive sleep apnea and snoring. Dr. Capasso is especially sophisticated in management of sleep disorders as he is dual trained in sleep medicine and sleep surgery. His colleague Dr. Stanley Liu, an MD/DDS oral surgeon specializes in reconstruction of the facial skeleton, such as a maxillomandibular advancement, to open severe constrained upper airways.

In our Pediatric Division, Chief Anna Messner is highly experienced in the management of a wide variety of ear, nose and throat disorders in children. She has a long-standing interest in velopharyngeal insufficiency. Peter Koltai focuses his interest on complex sleep disorders in children while Douglas Sidell tackles aerodigestive tract disorders. Mai Thy Truong is a highly skilled pediatric ENT able to handle a wide spectrum of children’s otolaryngology problems with a special interest in vascular malformations. Dr. Truong and Dr. Kay Chang oversee a dedicated microtia clinic and together they are surgically creating superb ear reconstructions. Drs. Chang, Cheng, and Oghalai focus on pediatric otology (see below)

In our Facial Plastics Division, Chief Sam Most has built a highly successful aesthetic and reconstructive facial plastic surgery practice. Sam, who is known for his refined aesthetic sense and technical excellence, has special interests in rhinoplasty, alleviation of facial paralysis, and rejuvenation of the aging face. Oral surgeon Dr. Stanley Liu has a special interest in facial trauma and computer assisted, minimally invasive repair of facial fractures.
In our Otology-Neurotology Division located in the Stanford Ear Institute, Chief Nikolas Blevins is a renaissance surgeon handling all aspects of ear care and microsurgery. He and I along with our two very capable medical otologists Drs. John Shinn and George Shorago see most adult patients. Matt Fitzgerald, Chief of Audiology, oversees a large group of audiologists who provide diagnostic and rehabilitative services. The Children’s Hearing Center, lead by Dr. John Oghalai, includes Drs. Kay Chang and Alan Cheng. Our very active cochlear implant center includes 4 surgeons (Drs. Blevins, Chang, Cheng, and Oghalai).

In our Comprehensive Otolaryngology Division faculty members Jennifer Lee and Uche Megwalu expertly manage a wide spectrum of otolaryngology medical and surgical diseases. Jennifer has a special interest disorders of the Eustachian tube and has now performed many endoscopies and balloon therapies of this structure.

**New Facilities: Biomedical Innovations Building:**

*Future home of OHNS Research Laboratories in 2019*

**New Sleep Surgery Facility:**

Our new sleep surgery clinic opened in 2016 with 4 specialized exam rooms, a large procedure room, and a simulation center for planning craniofacial procedures. This new facility is located at our Redwood City satellite adjacent to the Sleep Medicine program and Sleep Labs.
The New Stanford and Stanford Children’s Hospitals:

Stanford Medicine is very much looking forward to occupying two splendid, state-of-the-art new hospitals which are in advanced stages of construction with anticipated in the next 18-24 months. This $4 billion project will provide many more ICU beds and operating rooms and have private room for all patients.
Global Health Programs:

We have an ongoing collaboration between with the University of Zimbabwe. Peter Koltai and Lisa Orloff are the most recent faculty members to visit (we have sent a total of 5 faculty members.) Our goal is to send 1-2 faculty members a year. The Chief of their program (Clemence Chidziva) visited Stanford in 2015 and two University of Zimbabwe OHNS junior faculty visited us this past summer and two more are coming in summer 2017. These learning experiences have been funded by the Stanford Center for Innovation in Global Health, the department and the Koltai family.

Sam Most organizes an annual humanitarian mission to Phnom Penh, Cambodia, in conjunction with Face-to-Face, an organization within the American Academy of Facial Plastic and Reconstructive Surgery. Patients treated include adults and children with congenital, post-traumatic and post-ablative defects. On his most recent trip Dr. Most was assisted by one of the Stanford OHNS residents and Elise, his daughter who is a Stanford freshman.

Alumni News

For the second time this year, we moved our alumni event at the American Academy of Otolaryngology-Head & Neck Surgery from Tuesday to Sunday evening. Gratitude to faculty member Mai Thy Truong who hosted in San Diego this fall and has generously offered to host again at next year’s meeting in Chicago.

Visiting professor Albert Mudry, who is probably the only otolaryngologist who also has earned a PhD in history, and I are writing a history of Stanford OHNS. This spans from the Stanford predecessor schools in the 19th century to the present and will be close to 50 pages long. We have compiled a list of discoveries and inventions introduced by department members and also a complete roster of Stanford OHNS residents since the program was founded in 1909. We expect to have a comprehensive history on our website during 2017.

Alumni are always welcome to return to the Farm for a visit! Please email me at jackler@stanford.edu and we can set up a time for a chat and a tour.

— Robert K. Jackler, MD  Sewall Professor & Chair  (December 10, 2016)
Summary of our achievements in 2016.

Last year was another highly successful year for the Research Division. It is very obvious that our department’s research scope has grown far beyond the initial focus on inner ear regeneration. The latitude of projects cover: surgical simulation, improving audiologic training for patients, immune response to cancer, advanced imaging, African elephant communication, novel non-otoxic aminoglycoside antibiotics, stem cells, hair cell regeneration, voice disorders, hair cell mechnano-transduction, synaptic and neural coding of sound information, as well as the impact of tobacco advertising – just to name a few. Clinical work has been focusing quite a bit on adapting principles of precision medicine, where patient-specific information is more and more taken into account. Of course, the core of the basic research group remains the goal of finding a cure for hearing loss and we are happy to report that fundraising for the Stanford Initiative to Cure Hearing Loss (hearinglosscure.stanford.edu) has been at the highest level since we started the initiative a couple of years ago. Funding through grants from federal and other entities continued to grow for the 11th year in a row. The number of grants towards research stands at a record number of 68. Productivity remains high and the quality of work has been recognized by many of our peers as outstandingly strong.

All faculty members who maintain an active endeavors have provided updates on their work and these updates are provided in the following pages. This report highlights basic and translational research in the department. Departmental faculty also contribute a sizable volume of clinically focused research.

Nikolas Blevins

CardinalSim – Development of a Virtual Surgical Rehearsal Platform

The CardinalSim research team, led by Nikolas Blevins and Kenneth Salisbury, continues to develop a platform to enable surgeons to rehearse complex cranial base surgical procedures based on preoperative anatomic imaging data. The primary hypothesis driving this project is that surgical outcomes will improve if surgeons are able to explore relevant anatomic data in an intuitive and surgically-relevant manner, prior to undertaking actual surgery. Clinicians currently have access to a wealth of preoperative imaging data (including both CT and MRI data) which are routinely examined only across-sectional abstractions of the complex 3-dimensional anatomic configurations they represent. The “CardinalSim” platform (http://med.stanford.edu/cardinalsim.html) addresses this, by allowing surgeons to load interact with clinical imaging data using haptic (touch) interfaces and stereoscopic displays (1). By exploring relevant anatomic relationships in a safe environment, the surgeon can be better prepared for otherwise unexpected challenges, thereby potentially minimizing risks.

Over the last year, our team has confirmed that surgical trainees using the workstation are capable of replicating key steps in a variety of temporal bone surgical procedures (2). The confirmation of our ability to accurately produce and display the surgically-relevant details that guide the course of a procedure is a critical step in validating our approach. Also this year, we completed a study demonstrating that the use of the simulation workstation in conjunction with actual anatomic dissections in a surgical laboratory could increase trainee confidence in performing experience-
appropriate challenging segments of otologic surgery (3). This confirms that anatomy-specific rehearsal in our virtual environment can augment preparation for actual dissections.

Plans for the coming year include the facilitation of collaborative rehearsal through a shared database of cases, the incorporation of physics-based sound and deformable tissues into the virtual environment, and the development of effective methods to optimally display the insights from rehearsal within the operation room.


**Electrophysiology and the Classification of Auditory Stimuli**

Our auditory electrophysiology research group has undertaken an investigating of non-invasive methods of assessing the efficacy of hearing restoration. We are using new classification techniques of EEG data to determine if an individual with normal or altered hearing is able to differentiate between auditory stimuli. This approach may provide insights into the optimal means of presenting hearing signals to specific individuals, optimized for both their inner ears as well as their central auditory processing capacity. It is known that patients with hearing loss can respond quite differently to auditory signals. This is particularly the case for cochlear implant recipients in whom normal transduction of signals by the cochlea has been replaced by relatively few electrical contacts. These individuals oftenshow little ability to express the character of their experience – which is especially true for young children and those who have never experienced hearing. It is also clear that over time, such individuals can adapt and change in their response to stimuli, often being able to extract considerably more from the same signals. We hypothesize that a method to extract electrophysiologic data from EEG signals will provide insights into how to best present signals to a cochlear implant user to provide prognostic data and also optimize ultimate outcomes. Our preliminary data establishing these techniques in normal hearing individuals has been quite promising, and will be presented at the next meeting of the Association of Research in Otolaryngology.


**Alan Cheng**

The Cheng laboratory has made important discoveries on several fronts in the past year. In the regeneration program, a new direction of our lab is to characterize the cells surrounding hair cells (the supporting cells). Since supporting cell loss leading to hair cell loss is the major cause of congenital hearing loss, we have been studying whether supporting cells can regenerate and how their loss causes secondary hair cell loss and eventually hearing loss. Moreover, we have been following up on our previous work that the immature mouse cochlea harbors progenitors (also supporting cells) that naturally regenerate hair cells after damage. Ongoing efforts focus on defining mechanisms that initiate or enhance this innate regenerative process.
In parallel, we continue to explore whether hair cell regeneration leads to a functional recovery in mammals. To better understand this process, we have been studying one of inner ear balance organs, the utricle, where a modest level of regeneration occurs. By establishing a time course of hair cell loss and subsequent regeneration and a whole animal vestibular function test, we have found significant differences between the young and mature utricle in terms of the degree and mechanisms of regeneration and also the degree of functional recovery. In the near future, we will be able to precisely describe the anatomy and function of a regenerating mammalian sensory organ, such that we can manipulate the degree of regeneration and assess how that affects functional recovery.

Our research program on cochlear development has been focusing one key signaling pathway, Wnt signaling, and how it regulates hair cell development. The complexity of this pathway lends itself to a step-by-step interrogation of individual components of the pathway. Thus far, we have found that this pathway affects both cell fate decision, maturation as well as organization of the developing cochlea, thus providing important insights into how to manipulate this pathway to promote regeneration.

Lastly, our group has been collaborating with Tony Ricci in developing novel non-ototoxic antibiotics. Using some of the latest technology in physics, we have visualized how our antibiotics interact with bacteria at the molecular level. This is critical information that will help guide us design additional versions of antibiotics that can prevent hearing loss.

Another mission of our group is foster the future generation of researchers to find a cure for hearing loss. We are extremely fortunate to have a talented of young, energetic and motivated scientists who work collaboratively. It has been a stellar year for them to have been awarded 2 grants from the NIH (Zahra Sayyid MSTP student, Tian Wang MD PhD research scientist), and 2 international grants from Australia (Patrick Atkinson PhD postdoctoral fellow) and European Union (Mary O’Sullivan PhD postdoctoral fellow).


Elizabeth DiRenzo

Voice disorders affect millions of people in the United States annually. The Laryngeal Research Laboratory is an interdisciplinary research group that was established by Dr. Elizabeth DiRenzo, PhD, CCC-SLP in 2015. The Laryngeal Research Laboratory uses techniques from the basic sciences and human clinical sciences to improve the prevention and treatment of voice disorders. To truly improve voice disorder management, the cellular and molecular underpinnings of laryngeal disease and the vocal fold response to potentially hazardous external stresses must be understood. Specifically, we investigate how external stresses such as inhaled pollutants, viruses, bacteria, and radiation compromise the structure and function of the vocal fold mucosa and how these changes may influence voice production. We use diverse models and methodologies including animal models and cell cultures. We also collaborate with surgeons within the Division of Laryngology to obtain human tissue samples from patients with a wide-variety of voice disorders. Of note, this year we published on how radiation affects the structure and function of the cells that form the vocal fold mucosa (Erickson-DiRenzo, Annals of Otology, Rhinology, & Laryngology, 2016).

In the coming year, we are embarking on a new line of research aimed specifically at elucidating the etiology and mechanism of action of tobacco product-induced laryngeal disease. Specifically, we are developing a novel mouse model of cigarette smoke and electronic (e)-cigarette vapor-induced inflammation that can be used to study the pathophysiological changes that occur in the larynx of human tobacco users. At the same time, we are also performing a multidimensional study of vocal function in users of conventional cigarettes and e-cigarettes. Such investigations will be the first to systematically examine the effect of e-cigarettes on the laryngeal mucosa and vocal function.
Finally, we also study clinical and quality of life outcomes in patients with voice disorders undergoing a variety of surgical or behavioral interventions. We are currently collaborating with researchers in the Departments of Neurosurgery and Neurology to investigate the effectiveness of deep brain stimulation (DBS) for the treatment of essential vocal tremor. Vocal tremor is a common and often debilitating voice disorder with no known cure and limited effective treatments. In 2016, Dr. DiRenzo was the Principal Investigator on a grant from the American Speech-Language-Hearing Foundation to pursue this line of research and we will be publishing our initial findings in the coming year. Results will provide a necessary foundation for future studies that seek to optimize DBS for the treatment of vocal tremor and have the potential to alter treatment paradigms for these difficult to serve patients. Overall, we look forward to continuing expanding research group, disseminating findings, and utilizing research discoveries to develop novel new interventions for voice disorders.

**Matthew Fitzgerald**

In the Division of Audiology, our research efforts took three forms. First, we continued to investigate novel training procedures to facilitate learning and adaptation in individuals with hearing loss. We have demonstrated that individuals with hearing loss show different patterns of learning than individuals with normal hearing. This suggests that customized training programs may need to be developed for individuals with cochlear implants or hearing aids.

In our second line of research, we have laid the groundwork for a fundamental change in the audiologic test battery; making speech in noise the default clinical test of speech perception rather than word-recognition in quiet. We have collected data on over 1500 individuals which reveal that in most instances, speech in noise testing can replace word-recognition in quiet, and provide clear clinical guidelines for when to perform word-recognition in quiet.

Finally, we continue to investigate the mechanisms by which individuals with bilateral cochlear implants fuse information provided by each device. We have shown that some individuals are sensitive to mismatches in electrode insertion depth, while others are not. We have also demonstrated that self-selection of frequency tables has the potential to overcome any deficits in performance caused by between-ear mismatches in stimulation. Taken together, these lines of research have the potential to directly impact clinical practice, and to facilitate improvements in patient performance in the future.


**Nicolas Grillet**

In 2016, the Grillet lab published three research papers in highly ranked journals, including two that conclude Dr. Grillet’s postdoctoral work. For each of them, new experiments were done at Stanford and involved members of the Grillet lab, Alix Trouillet (Postdoctoral Fellow) and Navid Zebarjadi (Research Assistant).

In the first publication, we characterized a gene responsible for deafness in a randomly mutated mouse strain. This gene, called Neuroplastin, codes for an adhesion molecule with two major splicing variants. These variants differ by the length of their extracellular domain. We showed that the shortest isoform is expressed specifically by the outer hair cells and is necessary for their function at 3 weeks of age. This work identified a new protein necessary for hair cell function in mice, and likely in humans as well.
In the second publication we demonstrated genetically that hair cells have two mechanical ionic channels: When the stereocilia bundle of hair cells is deflected in its normal direction of sensitivity, an electric current is generated. It is the initial current that codes for sound. When the stereocilia bundle is pushed in its reverse direction, no current is produced. Surprisingly, in newborn mice, once this mechanotransduction is abolished either by the rupturing of extracellular links that bridge the top of stereocilia to their taller neighbor, or by the genetic ablation of component of the sound mechanotransduction machinery, the hair cells show now an electric current when stimulated in the opposite direction. During the last five years a debate has emerged in the field about the origin of this current: Are both currents generated from the same ionic channel reconfigured to function in other directionalities or are they coming from distinct mechanosensitive channels? By studying the function the mechanosensitive channel Piezo2 that plays central role other sensory systems such as touch, we demonstrated that the “opposite” or “reverse” current requires Piezo2 while the normal current does not. Therefore, our work ends the debate and opens a new exciting question about the physiological role of this current that can be also triggered by local mechanical damage of the sensory epithelium.

In addition to these two publications, Dr. Grillet helped the research of Dr. Oghalai by providing his expertise in scanning electronic microscopy to image at nanometric resolution the stereocilia bundle of adult mice.

Next year looks very exciting for the Grillet lab as significant progress has already been made on the molecular requirement of a deafness gene. Also, Mattia Carraro joined the lab as a Postdoctoral Fellow upon graduating from the University of Toronto. Mattia is an expert in immunofluorescence staining of the entire inner ear at high resolution, as well as scanning electronic microscopy to image the blood vessels of the inner ear.


Stefan Heller

2016 has been a transitional year for the Heller laboratory (http://hellerlab.stanford.edu). We have completed two major NIH R01 grants that mark the end of a period of research focusing on the functional assessment of a specific class of ion channels, which were once plausible candidates for playing a major role in hearing and balance. Very encouraging was that this planned transition went quite smoothly with the successful competition for a new R01 grant that focuses on assessing the molecular mechanisms by which mouse cochlear hair cells deal with noise-induced stress. This project is important because it can provide insights into the question why some people’s ears are more resistant to noise than others’. It also integrates well with a human genetics project pursued by Nicolas Grillet. We also implemented quite a lot of novel technologies with a major focus on single cells transcriptomics. This topic is a continuation of work that started a few years ago and I anticipate that we will have several major publications coming out next year as we apply this technology to study the triggers that initiate hair cell regeneration in the newborn mouse cochlea and in adult chickens.
We had 3 publications this year. The major one (Ealy et al., see below) describes 4 years of work on developing a way to guide human embryonic stem cells and induced pluripotent stem cells toward an early inner ear phenotype. The second paper is the result of a collaboration with Eri Hashino’s laboratory at the University of Indiana where we contributed tools and intellectual input to optimize the generation of sensory hair cells from mouse pluripotent stem cells. Finally, a previous postdoc of the Heller lab, who is now heading his own laboratory in China has published work on a project that started in the inner ear but concluded in muscle cells; this project begun almost a decade ago when our lab just had moved from Boston to Palo Alto.


Robert Jackler

Stanford Research Into the Impact of Advertising (SRITA) is an interdisciplinary research group which Dr. Jackler established over a decade ago. SRITA studies advertising, marketing, and promotion used by the tobacco industry to recruit and retain its customer. Our priority is research designed to inform regulators and legislators who are considering regulation of tobacco products. The initial priority of SRITA was to create a digital repository of tobacco advertising material to support scholarship, advocacy, legal, and regulatory activity. As of 2016, the collection has grown to become the world’s largest repository with over 40,000 tobacco advertising images many of which are online in a searchable, meta-data rich, annotated database (tobacco.stanford.edu). The collection spans not only cigarette/cigar/pipe/snus/chew advertisements but also e-cigarettes, antismoking campaigns, with a new marijuana section in the to launch soon. As the historical collection is now comprehensive, recent emphasis has been acquiring contemporary tobacco advertising for the US and around the world (eg. “Be Marlboro” campaign).

As of December 2016, the online collection (tobacco.stanford.edu) includes 22,488 tobacco, 11,802 electronic cigarette, and 1152 anti-smoking advertisements. SRITA’s YouTube channel contains 178 tobacco and 157 electronic cigarette videos. Advertising comparison pairs (756) are available such as targeting women then versus now and African American versus mainstream advertisements. As of November 2016, the SRITA online collection has had 424,522 unique users with virtually every country in the world represented. The entire compendium of original tobacco advertisements, spanning 1890 to 2010+ have been donated to the National Museum of American History at the Smithsonian Institution.

My current research has focused upon the marketing of electronic cigarettes with special focus upon informing regulators about the advertising and promotional activities of the rapidly growing vapor industry. In 2016 my group has published on cessation imagery in e-cigarette advertising (AJPH), e-cigarette marketers utilizing of anti-smoking imagery (Tob Control), exotic flavor based advertising (Tob Control) and we have papers submitted on alcohol flavored tobacco products and age gating on tobacco websites. A key collaboration is with Stanford pediatric professor Bonnie Halpern-Felsher who utilizes consumer perception methodology which compliments SRITA’s focus on content analysis. Perception studies extend and validate assumptions made via content analysis of advertisements in the SRITA collection.

In the coming year we are studying the marketing of e-cigarette flavors. The FDA banned flavors from combustible cigarette in 2009 with the exception of menthol. In 2016, the FDA solicited
research into the impact of flavored vapor products on adult smoking cessation and youth initiation. We are studying the youth messaging of flavored e-cigarette advertising. We are also studying the 40 year marketing effort by the menthol brand Newport which led it to become a leading teen starter smoker brand.


Jackler RK, Ramamurthi D. Unicorns cartoons: marketing sweet & creamy e-juice to youth. tob control. doi:10.1136/ tobaccocontrol-2016-053206.


Ramamurthi D, Fadadu RP, Jackler RK. Electronic cigarette marketers manipulate anti-tobacco advertisements to promote vaping. Tob Control 2016; 25:720-722

**Mirna Mustapha**

The Mustapha laboratory published a collaborative study with Dr. Most from our department contributed to understanding the role of the classical complement pathway in recovery after facial nerve injury (Akdagli et al., 2016). We have two papers under revision. One is in PLOS Genetics describing the role of thrombospondins in afferent synapses maintenance and recovery after noise injury. A second paper is in under revision in Hearing Research describing the role of adrenergic receptors in cochlear function.


**Jayakar Nayak**

Airway diseases occur widely due to various pathologies, but their common feature is acute airway tissue damage. Understanding the biology of airway injury (of the airway epithelial barrier) and inflammation (from an altered immune system) in airway sites is of critical importance to preventing and reversing airway tissue damage. My laboratory team has continued to make advances into understanding upper airway biology, in terms of its stem cells activities and the unique nasal immune environment in the laboratory. We have also undertaken clinical research to better understand and treat the enigmatic nasal airway disorder termed empty nose syndrome. We are undertaking some of the world's first airway stem cell transplants using ex vivo culture systems and animal models, based on human nasal basal cells (NBCs) as naturally-occurring, abundant progenitors of the source of cell therapy. We have also undertaken an exciting collaboration with 3 other eminent Stanford
researchers (Drs. Matthew Porteus, Calvin Kuo and Tushar Desai) to use our stem cell culture system as a vehicle for possibly the 1st airway stem cell therapy to treat cystic fibrosis (CF) sinusitis. 100% of CF patients develop some degree of sinusitis, and 85% of these patients have a 3-base-pair mutation in the CFTR chloride transport gene. This conserved mutation produces all of the downstream debilitating sinus and pulmonary symptoms in these patients, and would be a worthwhile target for gene therapy. Indeed, our preliminary experiments suggest that the mutated CFTR gene can be ‘edited’ and corrected in primary NBC cultures from donors using modern molecular techniques. These ‘corrected’ stem cells can then theoretically be re-placed back into the nasal cavity of the same donor in treatment for CF sinusitis. As a group, we have now collectively applied for competitive funding to advance these pilot, pre-clinical experiments, and ultimately hope to develop a viable translational cell therapy for CF patients and others with sinusitis.

We have also discovered that the human upper airway tissues have significant proportions of immune cells in the setting of inflammation - granulocytes, regulatory T cells, and now B cells. These B cells appear to carry unique immunoglobulin families and signatures compared to other immune system compartments in the body, and make the nasal upper airway an microenvironment at the junction between the innate and acquired immune systems. Using high dimensional flow cytometry, we have also discovered unexpected shifts in immune cell populations in the upper airway following steroid use. Also, in collaboration with Northwestern University, have identified high levels of immunoglobulin D (IgD) in the nasal tissues of sinusitis patients, that is not seen in the circulating blood or nasal tissues of control patients. A manuscript regarding this novel finding has just recently been submitted (please see below). Eventually we hope to harness our research findings to develop new research directions in upper airway biology, and novel therapies for treating common but debilitating sinusitis issues.

Finally, in my clinical practice, our groundbreaking translational research efforts in empty nose syndrome (ENS) are becoming nationally recognized for surgical reconstruction techniques and lending improved understanding, definition and treatments for patients with the intriguing nasal disorder termed empty nose syndrome. Following routine, turbinate reduction and poor wound healing we began to see more patients with ENS from both nationally and internationally. Our group sought to be at the forefront of this area of ENS research, and began focusing on establishing the validity of a 6-question intake survey that we designed, and an office-test to assess ENS and candidacy for surgery. We are now prospectively studying our early outcomes with turbinate augmentation surgery to help ENS patients regain a more normal of nasal breathing. Our research and interest in ENS finally led to our group being interviewed and partially featured in a recent February 2016 article on the BuzzFeed.com newsfeed, which is the last citation noted below.


Caitlyn O’Connell-Rodwell

I developed a collaboration with Thomas Hildebrandt at the Institute for Zoo and Wildlife Research (IZW) in Berlin to coordinate and obtain permits to receive elephant temporal bone specimens in order to collaborate with Dr. Sunil Puria and Dr. Charles Steele in 2017 on their NIH grant [NIDCD R01 grant #5R01DC005960-12: WHY DO MAMMALS HAVE A FLEXIBLE THREE-BONE OSSICULAR CHAIN?] I also met with Dr. Ricardo Chavarriaga Lozano, the Defitech Foundation Chair in Brain-machine Interface at Ecole Polytechnique Federale de Lausanne to discuss a possible collaboration and grant proposal on the vibration sense and the potential to drive the development of vibrotactile prosthetics for both hearing and limb regeneration.

In addition to my formal and informal science education outreach lectures and workshop efforts for both adults and STEM students of all ages (February at Ursinus College, PA, sponsored by HHMI), I continued my wild African elephant field studies in Etosha National Park, Namibia, sponsored through the Vice Provost Undergraduate Education (VPUE) program. In addition, I worked with the Howard Hughes Medical Institute (HHMI) to develop an online educational video on my elephant acoustic studies that will post by the end of the year.

And I became Adjunct Professor November, 1.


John Oghalai

The Oghalai laboratory (https://oghalailab.stanford.edu) is continuing to make progress on understanding the mechanisms of normal and impaired hearing. Their goal is to prevent progressive sensorineural hearing loss. Also, they hope to understand how the cochlea processes speech to improve the ability of hearing-impaired patients to understand what people are saying, even in the presence of background noise. They have developed novel technology, termed Volumetric Optical Coherence Tomography and Vibrometry (VOCTV), that uses advanced optical techniques to non-invasively measure the angstrom-level vibrations created by sound within the cochlea in living animals. They use this technology in nearly all of their on-going studies. They have identified new features of the traveling wave that tune hair cell stereociliary bundle deflection. This is important because it underlie the sharp frequency tuning of mammalian hearing. Furthermore, they have compared avian and mammalian inner ear function to learn the key functional differences between hair cells that can and cannot regenerate.

Clinically, the Stanford Children’s Hearing Center is busy managing complex pediatric hearing loss patients and is routinely accruing cochlear implant patients for clinical trials. They are performing brain-imaging in our cochlear implant recipients to maximize the ability of the implant to provide a clear understanding of speech.

Furthermore, a new educational program has been developed for the Department of Otolaryngology – Head and Neck Surgery. The Clinician-Scientist Training Program (CSTP) offers a two-year research post-doctoral fellowship training for one otolaryngology resident per year and for one post-otolaryngology resident graduate every other year. This is funded by an NIH T32 grant.

Finally, a long-awaited surgical atlas that John Oghalai has co-authored with Colin Driscoll, Chair of Otolaryngology at the Mayo Clinic, has finally been published. It is entitled Atlas of Neurotologic and Lateral Skull Base Surgery, and is intended for advanced residents in otolaryngology and neurosurgery,
neurotology fellows, and junior faculty members with interests in the field.


Tony Ricci

Over the past year we have made good progress on the three areas of research on which my lab is focused. These areas include hair cell mechanotransduction, i.e. how does sound get converted into an electrical signal, synaptic transmission, i.e. how does the sensory hair cell communicate with the brain and finally on developing novel antibiotics that do not have the debilitating side effects of ototoxicity and nephrotoxicity.

For mechanotransduction we have identified a membrane based modulation of the mechanosensitive ion channel that controls how fast the channel opens and how long it stays open. We are presently trying to understand the molecular components responsible for this sensitivity. We have also shown that the hair bundle does not move cohesively and that this property is critical to the output of the hair cells. We have several lines of work now investigation how the hair bundle moves in situ as well as in response to different forms of stimulation that may be closer to natural stimulation.

For the past year we have investigated the role of the synaptic ribbon in regulating hair cell transmission. In doing this we have developed and refined technologies for recording from postsynaptic neurons as well as for immunocytochemical characterization of these synapses. In
addition, we are exploring the role of intracellular calcium on regulating synaptic vesicle trafficking.
In the last year we have obtained crystal structures of aminoglycosides with their ribosome binding partners in order to directly assess potential modification sites as well as to find correlations to antimicrobial activity. This work is helping to focus our drug design to better maintain antimicrobial activity while alleviating ototoxic and nephrotoxicity.


Eben Rosenthal
Our lab has recently established the feasibility of contrast enhanced cancer surgery using novel agents that permit real-time visualization of cancer. In addition we have defined the use of antibody directed photoimmunotherapy to eliminate residual disease after gross removal of the tumor.


John Sunwoo
The focus of the Sunwoo laboratory is to understand the immune response to cancer and how tumor and host factors determine the heterogeneity in this response. This past year, the group has published several papers related to this, including those in the Journal of Experimental Medicine, Clinical Cancer Research, Annals of Oncology, Oncotarget, and Biochemistry and Biophysics Reports. The work presented in two of these articles was that of two PhD graduate students in the Immunology Program. These two students, Luhua Zhang and Yunqin Lee, successfully defended
their thesis work, which was performed in the Sunwoo lab under Dr. Sunwoo’s mentorship, and graduated this past summer. The Sunwoo laboratory received additional NIH funding this year through a U54 center grant that was awarded to Sylvia Plevritis, Garry Nolan, Ed Engleman, and John Sunwoo. The overall goal of this new project is to understand how metastases (of head and neck squamous cell carcinoma and of melanoma) to regional lymph nodes affect the systemic immune system and predispose patients to distant metastases. The Stanford group was one of only three centers in the nation that was funded through this mechanism this year.


