

## **Brandon Cox Personal Statement**

I have always had a passion for puzzles. As a child, jigsaw puzzles were my focus; as a teenager, I found a new enthusiasm for logic puzzles; and as an adult, it was this analytical challenge that led me to a career in science. My fascination with understanding the details of biological processes and the mechanism of drug actions provides constant motivation for a life-long career in scientific research and education.

My experience conducting basic science research during my undergraduate career and working at the Chicago Center for Clinical Research inspired me to pursue a doctorate in pharmacology at Georgetown University. Here my research focused on neuronal nicotinic acetylcholine receptors in the visual system. I then completed a postdoctoral fellowship at St. Jude Children's Research Hospital for 5 years where I switched fields to focus on the auditory system and discovered that hair cell regeneration can occur spontaneously in the newborn mouse cochlea (Cox et al., 2014 *Development*). During my postdoctoral training, I was awarded a NIH F32 NRSA fellowship as well as a NIH loan repayment grant to subsidize my student loans. In 2013, I joined SIUSOM as an Assistant Professor in the Department of Pharmacology and was promoted to Associate Professor with tenure in 2018.

### Research

My research at SIUSOM has continued to focus on hair cell regeneration as a treatment strategy for hearing loss. The model I helped develop uses mouse genetics to kill hair cells combined with fate-mapping of neighboring supporting cells. By killing hair cells at later ages, we defined the critical period for hair cell regeneration as limited to the first postnatal week (Cox et al., 2014 *Development*). We also used this model to demonstrate a role for Notch signaling in the mechanism of spontaneous hair cell regeneration (McGovern et al., 2018 *Front Cell Neurosci*) and that multiple supporting cell subtypes are capable of producing new hair cells (McGovern et al., 2019 *Development*). Our most recent work, which was led by an Otolaryngology resident, demonstrated that the regenerated hair cells in the neonatal mouse cochlea are innervated and contain synapses. However these new cells are hybrids, which express known markers of both inner and outer hair cell types (Heuermann et al., 2022 *Front Cell Neurosci*). We have also expanded our research focus to include the vestibular organs, which regulate the sense of balance, and to understanding mechanisms that regulate hair cell survival during aging or in stressed hair cells after noise exposure.

During my entire career at SIUSOM I have maintained research funding from either the NIH or the Department of Defense (DOD). Since my last promotion in 2018, I have successfully obtained two NIH R01 grants as co-PI and a 3 year DOD grant as PI, resulting in total grant funding of over \$8 million. I am also a co-Investigator on 2 additional NIH R01 grants, co-Investigator on a DOD grant, and a consultant on a 5<sup>th</sup> NIH R01 award. In addition, I have recently completed sponsored research projects for two companies, Decibel Therapeutics, Inc and Otonomy, LLC.

Since 2018, my lab has published 14 peer-reviewed articles, where the vast majority included students, postdocs, or residents as authors. Two additional articles are

currently in review. I was also invited to write two book chapters and one review article, all of which were peer-reviewed. Two of our primary research articles are published in the *Journal of Neuroscience* where images from our work were chosen for the journal cover. We have also presented our work at international/national conferences each year with 10 abstracts selected for oral presentations and 34 abstracts presented as posters since 2018. In addition, my trainees have given 15 oral presentations and 2 poster presentations at local symposia during this time. Finally, I have been invited to give talks about my research at 7 universities/institutes over the past 5 years, including a presentation at the NIH/National Institute on Deafness and Communication Disorders. I was also invited to serve as a discussion leader at the 2022 Gordon Research Conference on the Auditory System and will be a keynote speaker at the *Celebrating Corti Hearing Conference* in Wurzburg, Germany (to be held October 29-31 2023).

A good part of my research success has stemmed from long-standing collaborations. Dr. Jenny Stone (University of Washington) and I have been collaborating since 2011 on projects related to vestibular hair cell regeneration and turnover. Together we have maintained NIH R01 funding for 10 years (2014 – 2024) and published 6 peer-reviewed articles. We have used genetically-modified mouse models (CreER/loxP) to fate-map supporting cells and demonstrated that they act as phagocytes to remove hair cells and as progenitor cells to replace hair cells under normal physiological conditions. Fate-mapping results also showed that supporting cells are the source of regenerated hair cells after damage (Bucks et al., 2017 *eLife*). We demonstrated that the transcription factors *Atoh1* and *Sox2* are necessary in supporting cells for vestibular hair cell regeneration to occur (Hicks et al., 2020 *Hear Res*; Ciani Berlinger et al., 2022 *Hear Res*). We also studied the development of type I and type II vestibular hair cells (Warchol et al., 2019 *J Comp Neurol*). Our most recent work demonstrated that adult type II vestibular hair cells convert into type I hair cells (including the development of a specialized type of innervation called a calyx) after deletion of the transcription factor *Sox2* (Stone et al., 2021 *J Neuroscience*).

Joining SIUSOM in 2013 also promoted a collaboration with Dr. Don Caspary, where I have applied my knowledge of neuronal nicotinic acetylcholine receptors (nAChRs) from graduate school to study changes to nAChRs in central auditory structures caused by aging or tinnitus. I have served as co-Investigator on Dr. Caspary's NIH R01 grant since 2015, was co-Investigator on his grant from the Office of Naval Research (2016 – 2019), and am co-Investigator on his current DOD grant (2019 – 2023). Together we have published 3 peer-reviewed articles and have a use patent for the application of nAChR partial agonists to treat tinnitus (US patent #17/428,164). Specifically, we found an age-related loss of nAChR responses in the auditory thalamus, which suggests a subunit change in the nAChR composition. This finding is a potential new target for the treatment of age-related hearing loss (Sottile et al., 2017 *J Physiol*). Next we defined age-related changes in the synaptic connections between inner hair cells and the auditory nerve in a rat model of aging (Cai et al., 2018 *Neurobiol Aging*). Our most recent work found disruption of nAChR signaling in the auditory cortex of rats with tinnitus and demonstrated that 2 drugs, Sazetidine and Varenicline (nAChR partial agonists with desensitizing effects), can ameliorate behavioral evidence of tinnitus

(Ghimire et al., 2023, *Front Cell Neurosci*). Dr. Caspary's NIH R01 grant was just renewed in 2023 (again I am co-Investigator) and we are focusing on the age-related changes in nAChRs in another auditory structure, the inferior colliculus.

In regards to the national/international reputation of my work, I have a h index of 16 and my study demonstrating that hair cell regeneration can occur naturally in the newborn mouse cochlea (Cox et al., 2014 *Development*) has been cited over 200 times. I have been invited to serve on 3 NIH study sections since 2018, two of which were the AUD panel which is the primary study section for the National Institute on Deafness and Communication Disorders. I also reviewed grants for the DOD, a French foundation (Foundation Pour l'Audition), and a UK foundation (Medical Research Council) in the past 5 years. In 2020, I was selected by the past chair of the Association for Research in Otolaryngology (ARO) to serve on the nominating committee which is tasked to identify candidates from our membership to run for election for leadership roles within the organization. In 2022, this nominating committee asked me to run for the Program Committee Chair position, a role responsible for organizing the annual ARO conference. Despite have a more senior scientist as an opponent, I was elected by the ARO community and am currently serving in this role. In addition, my reputation for detailed cochlear histology led to a collaboration with Dr. Daqing Li at the University of Pennsylvania resulting in 2 peer-reviewed publications (Naples et al., 2020 *Otol Neurotol*; Generotti et la., 2022 *Sci Rep*) and a collaboration with Dr. Ram Ramachandran at Vanderbilt University that has resulted in a new NIH R01 grant where I am the co-PI. My expertise in mouse genetics and reputation in the hair cell regeneration field created the opportunity for sponsored research projects funded by Decibel Therapeutics, Inc and Otonomy, LLC. Finally, while COVID has limited international travel in recent years, I will be a keynote speaker at a conference in Germany in October 2023.

### Teaching

In addition to research, I am highly motivated to teach in a manner that demystifies complex topics and builds new knowledge from logical reasoning and associations with old knowledge or example cases. Specifically, I tailor my pharmacology lectures to explain the mechanism of action for each adverse effect caused by a drug which replaces the rote memorization for a list of side effects. I also use multiple figures to explain complicated concepts by first anchoring the foundation of the concept to basic physiology, then building upon that old knowledge to teach new information. Analogies, metaphors, and connections to current events or pop culture can also be useful in helping students retain information.

Since my last promotion, I have served as a tutor group facilitator for the year 2 Neuromuscular and Behavior Unit annually (except for 2021 when I was on maternity leave). I have also taught 4-5 resource sessions to sophomore medical students each year, and given a lecture to Neurology residents each year from 2020-2022. For graduate student teaching, I have taught multiple lectures in the core Pharmacology courses each year that these courses were taught, and have also given lectures in MBMB-504 Research Methods course over the past 2 years. In 2019, I became the

Director of the Pharmacology and Neuroscience graduate program which included the responsibilities of new student recruitment and acting as the course director for all of the core Pharmacology courses (PHRM-500, PHRM-501, PHRM-530, PHRM-550A, PHRM-550B, and PHRM-577).

I have used the Flipped Classroom method to teach the Substance Abuse resource session in the year 2 Neuromuscular and Behavior Unit since 2014. In collaboration with Dr. Carl Faingold, we created 8 short video lectures that were given to students approximately one week prior to the in-class discussion. These videos were accompanied by a mandatory quiz of multiple choice questions to be completed prior to the discussion session. Based on the students' answers to the quiz, we pulled slides from the video lectures for further explanation and discussed the correct answer for each of the quiz questions. We also utilized videos of patients to illustrate the effects of several commonly abused substances and used Participoll for anonymous audience responses to additional multiple choice questions that accompanied each patient video. Importantly, no new material was presented during the in-class discussion. The goal was to focus on topic areas that were confusing to students and to promote questions and open discussion using patient cases as a platform.

As a tutor group facilitator, I have used a modified version of the game Scattergories since 2018 to open an electronic patient case in the group. Here, I separated the students into groups of 2 and gave them 2 minutes to write down as many differential diagnoses that they can think of and which match the simple patient complaint. Unique differentials that were not listed by the other group(s) get a point and conditions that are not related to the patient complaint are excluded. I have used this method for the Simms case where the patient arrives to the ER unconscious after attending a party and for the Zahn case where the primary complaint is a headache. This game has been very well received by the students and pushed them to come up with a large number of differentials. By the time of the year 2 Neuromuscular and Behavior Unit, students have mastered the problem-based learning method and many have lost interest in tutor group activities. I have found this gaming method for opening a case creates some fun and excitement that results in increased engagement in the discussions that followed.

Prior to becoming the Director of the Pharmacology and Neuroscience graduate program, I worked with the Graduate Program Committee in 2018 to redesign the journal club course (PHRM-500/501) for Pharmacology graduate students. Our new format was based on feedback from the students and promotes critical reading and analysis of each paper. It also provides opportunities for students to lead discussions and improve their writing skills. As evident from the course evaluations, our redesign has been well received by the students.

In Fall 2019, I became the Director of the Pharmacology and Neuroscience graduate program and spent significant time in the first year transitioning our courses to remote learning during the COVID-19 pandemic. I also led the effort to execute our Co-Op PhD program with the Department of Pharmaceutical Sciences at SIU Edwardsville by developing the curriculum, policies, and procedures with the assistance of the Graduate

Program Committee. We currently have 3 students in the Co-Op PhD program with one in the Pharmacology & Neuroscience track (taking core courses at SIUSOM) and 2 in the Medicinal Chemistry track (taking core courses at SIUE). All 3 students are completing dissertation research on the SIUE campus. I have also worked with other SIUSOM leaders to develop the RME for the Umbrella Graduate program which will unify the recruitment efforts for all SOM graduate programs and allow more flexibility in student choice of research concentration and dissertation mentor.

In addition to didactic teaching, I have served as the research mentor for 2 postdocs, 3 Otolaryngology residents, and 7 medical students over the past 5 years. My first graduate student, Melissa McGovern, has now completed her postdoctoral training and obtained a tenure-track Assistant Professor position at the University of Pittsburgh. I have a new graduate student who has just joined my lab in January 2023.

### Service

Over the past 5 years, I have served on many SIUSOM committees. Of note, I have been the vice-chair for the Institutional Animal Care and Use Committee (IACUC) since 2019 and the chair of the Research Policy Committee since February 2023. I have also served on several committees for the Association for Research in Otolaryngology (ARO), including my new role as chair of the Program committee. I am a member of the editorial board for *Hearing Research* and recently served as Guest Editor for a special issue in this journal. I have reviewed manuscripts for ~20 different journals and reviewed grants for the NIH, DOD, and 2 Foundations.

In 2018-2019, I organized the Midwest Auditory Research Conference (MARC) which was held at SIUSOM on July 11-13, 2019. With my co-organizer Dr. Don Caspary, we successfully obtained NIH R13 funding to support the conference. We had over 150 attendees from 9 states, 8 keynote speakers, and ~70 abstracts for talks or poster presentations. The primary objective of MARC was to foster collaboration between trainees and principal investigators, exposing all participants to high quality keynote speakers on peripheral and central auditory science. In this vein the oral presentations were primarily given by students, postdocs, or early stage investigators. We also hosted a grant writing workshop which had high attendance from trainees and included advice from several of our keynote speakers.