



Curriculum Vitae

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Place of birth: Buffalo, NY

Education

<u>Year</u>	<u>Degree</u>	<u>Field of Study</u>	<u>Institution</u>
1986	B.S.	Biology	Wofford College
1992	M.S	Physiology	University of Rochester
1995	Ph.D.	Physiology	University of Rochester

Postdoctoral training

1995–1999	Post-doctoral fellow	Neurobiology	Harvard Medical School Massachusetts General Hospital Howard Hughes Medical Institute
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Academic Appointments

1999 – 2001	Instructor	Neurobiology	Harvard Medical School Massachusetts General Hospital
2001 – 2005	Assistant Professor	Neuroscience	University of Virginia
2005 – 2010	Associate Professor	Neuroscience	University of Virginia
2011 – 2015	Associate Professor	Otolaryngology	Boston Children's Hospital & Harvard Medical School
2014 – present	HST Affiliated Faculty		Harvard Medical School & Massachusetts Institute of Technology
2016 – present	Professor	Otolaryngology & Neurology	Boston Children's Hospital & Harvard Medical School

Major Administrative Leadership Positions

Local

2004	Course Director, NGP Seminar Previews	University of Virginia
2008 – 2010	Course Director, Neurobiology 703	University of Virginia
2012 – present	Co-Course Director, Neuro200 /HST130	Harvard Medical School
2014 – present	Director of Research, Dept. Otolaryngology	Boston Children's Hospital

National and International

2007 – 2011	Course Co-Director, Biology of the Inner Ear	Marine Biological Labs, Woods Hole, MA
2016	Vice-chair Auditory Systems Gordon Conference	Bates College, ME
2018	Chair, Auditory Systems Gordon Conference	Bryant College, RI
2019	Co-chair Keystone Conference on Sensory Systems	Seattle, WA
2019	Co-Chair New York Academy of Sciences Meeting	New York, NY
2021– present	Chair, Usher Syndrome Society Scientific Advisory Committee,	Boston, MA

Committee Service:

Local

2002 – 2005	Neuroscience Department, Faculty Search Committee	UVA
2002 – 2011	Ten graduate student thesis committees	UVA
2003	Neuroscience Graduate Program, Admissions Committee	UVA
2004 – 2006	Neuroscience Graduate Program, Seminar Committee, Chair	UVA
2006 – 2007	Neuroscience Department, Faculty Search Committee, Chair	UVA
2006 – 2008	Internal Grant Review Committee	UVA
2006 – 2009	Dean's Research Advisory Committee	UVA
2008	Neuroscience Graduate Program, Admissions Committee	UVA
2009	Neuroscience Department, Faculty Search Committee	UVA
2008	Pharmacology Department, Faculty Search Committee	UVA
2009 – 2011	Faculty Senate, Co-chair, Science and Engineering P&D Committee	UVA
2010 – 2012	Science and Engineering Research Council	UVA
2012 – 2019	Otolaryngology Department, Faculty Search Committee (chair)	BCH
2015 – 2018	TRP grant review committee	BCH
2016 – 2019	Promotions and Reappointments Committee	HMS
2012 – present	Six HMS graduate student thesis Committees	HMS
2012 – present	Eight HMS graduate student QE Committees	HMS
2012 – present	Animal Research at BCH Steering Committee	BCH
2012 – present	Surgical Research Council	BCH
2019 – present	Chair of seven SHBT Qualifying Exam Committees	HMS
2022 – present	SHBT Fund Raising Committee Chair	HMS

National and International

2009 – 2012	Program Committee – Association for Research in Otolaryngology
2013 – 2015	Organizing Committee – 2014 Society of General Physiologist Meeting
2013 – 2014	Program Committee – American Society for Gene and Cell Therapy
2016 – 2018	Nominations Committee – Association for Research in Otolaryngology
2019 – present	Founder Committee – International Society for Inner Ear Therapeutics
2021	Ad Hoc Member of NIH/NIDCD Council

Professional Societies

1990 – 1992	President - Graduate Student Society, University of Rochester
2004 – 2006	International Brain Research Organization
1991 – present	Society for Neuroscience
1994 – present	Biophysical Society
1995 – present	Association for Research in Otolaryngology
2012 – present	American Society for Gene and Cell Therapy
2018 – present	Founder, International Society of Inner Ear Therapeutics

Grant Review Activities

2003, 2005	NIH study section, IFCN6	Ad-hoc Member
2004, 2010	Wellcome Trust, Neuroscience	Ad-hoc Reviewer
2005 – present	Tinnitus Research Consortium	Permanent Member
2005 – 2014	NIH study section, AUD	
	2005	Ad-hoc Member
	2010 – 2014	Permanent Member
2013 – 2018	American Otological Society Advisory Board	Permanent Member
2013	Action on Hearing Loss	Ad-hoc Reviewer
2013	National Agency for Research (France)	Ad-hoc Reviewer
2013	Neurological Foundation of New Zealand	Ad-hoc Reviewer
2013	Auckland Medical Research Foundation	Ad-hoc Reviewer
2014	US Army Medical Research	Ad-hoc Reviewer
2015	National Science Foundation	Ad-hoc Reviewer
2015	NIH – SEP	Review chair
2017	NIH – SEP	Ad-hoc Reviewer
2021 – present	Usher Syndrome Society, Grant review	Review chair
2022	NIH – SEP	Review chair

Editorial Activities

2017 – 2021	Section Editor – Hearing Research
2020	Guest editor, Hearing Research special issue on Inner Ear Gene Therapy

Ad hoc Reviewer: Nature, Journal of Neuroscience, Journal of Physiology, Journal of Neurophysiology, Neuroscience, Brain Research, Journal of Biological Chemistry, Trends in

Neuroscience, Biophysical Journal, Journal of the European Molecular Biology Organization, Hearing Research, Journal of the Association for Research in Otolaryngology, Gene Therapy, Plos One, PNAS, USA, Neuron, Molecular Therapy, Plos Biology

Honors and Prizes:

2001	American Physiological Society	Travel Award for 24th IUPS in New Zealand
2004	W.M. Keck Foundation	Distinguished Young Scholar Award
2005	University of Virginia	Leadership in Academic Medicine
2006	National Organization for Hearing Research	Burt Evans Young Investigator Award
2008	Physik Instruments	NanoInnovation Award
2014	Pilot Award	Boston Children's Hospital
2017	Translational Research Award	Boston Children's Hospital
2019	HMS Scholars in Medicine Excellence in Student Mentoring Award	HMS
2019	Bellucci Prize for Hearing Research	Creighton University
2019	Scientific Grand Prize	Foundation Pour L'Audition
2021	Pioneer Award	Association for Research in Otolaryngology

Funding Information: Current

2013 – 2024	<i>TMC gene function in sensory hair cells – Active</i> Type: NIH, NIDCD R01DC013521 Role: Principle Investigator For this exploratory project we will investigate the function of <i>Tmc</i> genes in hair cells and test the hypothesis that <i>Tmc1</i> and <i>Tmc2</i> are components of the hair cell transduction channel.
2021 – 2023	<i>Translational Gene Therapy for DFNB16 Hearing Loss Patients – Active</i> Type: Rosamund Stone Zander Translational Neuroscience Center Grant Role: Principle Investigator For this project we will develop STRC gene therapy for use in humans.
2017 – 2027	<i>Barber Fund for Gene Therapy Research – Active</i> Type: Private Foundation Role: Principle Investigator For this project we will develop novel gene therapies for hearing loss.

Past

2001 – 2005	<i>Myosin Disruption and Inner Ear Structure and Function</i> NIH, NIDCD R01-DC03279 Subcontract PI This grant supported a collaborative effort to develop a chemical-genetic strategy to study myosin function in hair cells of transgenic mice.
2003 – 2008	<i>Stem Cells and Repair in the Auditory and Vestibular Systems</i> NIH, NIDCD R01-DC006182 Subcontract PI

This grant supported a collaborative project between three UVA investigators to regenerate sensory hair cells from precursor cells and adult and embryonic stem cells.

2005 – 2008

Viral Transfection of Human Hair Cells

Virginia Lion's Club

Co-PI

These funds supported a collaborative project between the Otolaryngology Department and my lab focused on the development of adenoviral vectors to mediate gene transfer into human hair cells in vitro.

2006 – 2011

Identification of the Principal Players Involved in Transduction and Adaptation in the Inner Ear

Carmen Trust for Biomedical Research

Principle Investigator

This grant supports work focused on a developmental approach to identify the molecular components of the hair transduction complex.

2009 – 2011

Ion Channel Function in Auditory and Vestibular Hair Cells

NIH, NIDCD R01-DC05439 – ARRA Administrative supplement

Principle Investigator

This grant focuses on the physiology of several classes of ion channels expressed in inner ear hair cells. Mutations in each channel family under investigation cause inherited human disease including deafness.

2011 – 2014

Inducible Hair Cell Specific Expression of Potassium Channels –

NIH, NIDCD R21

Principle Investigator

For this exploratory project we will develop a transgenic mouse that will express potassium channels under the control of an inducible, hair cell specific promoter. The model will be used to investigate the source of cochlear amplification in outer hair cells, the role of spontaneous activity in inner hair cells and the nature of synaptogenesis in vestibular hair cells.

2013 – 2015

Waking from Hibernation: Recovery of Brain Function Following Reversible Congenital Hearing Loss

Type: Curing Kids Fund Research Program

Collaborator, Principle Investigator: Daniel B. Polley, Ph.D.

For this collaborative project we will use a mouse model, developed in my lab, to investigate how auditory pathways in the brain recover following extended hearing loss.

2012 – 2018

Gene Therapy in Mouse Models of Human Deafness

Bertarelli Foundation for Translational Neuroscience / Neuroengineering

Role: Principle Investigator

Co-investigator: Patrick Aebischer (President of EPFL) For this project we investigate a gene therapy approach to introduce wild-type gene sequences into mice that carry dominant and recessive mutations in genes

that cause human deafness. We will attempt to restore function at the cellular level and at the whole-animal level.

- 2007 – 2019 *Hair Cell Development in the Mouse Embryo*
NIH, NIDCD R01-DC008853
Role: Collaborator. Principle Investigator: Gwenaelle G.S. Geleoc, Ph.D.
This grant supports a collaborative effort to characterize the functional development of hair cell mechanotransduction in the mouse cochlea.
- 2014 – 2019 *Modeling Inner Ear Differentiation with Pluripotent Stem Cells*
Type: NIH, NIDCD R01DC013294
Role: Sub-contract Principle Investigator
PI: Eri Hashino (University of Indiana). For this project we will characterize stem-cell derived cells directed toward inner ear phenotypes. Stem cells will be derived from both mouse and human tissue.
- 2001 – 2021 *Ion Channel Function in Auditory and Vestibular Hair Cells*
NIH, NIDCD R01-DC05439
Role: Principle Investigator
This grant focuses on the physiology of a novel form of mechanotransduction and molecular mechanisms of adaptation in auditory and vestibular hair cells
- 2019 – 2022 *Translation of TMC1 gene therapy for clinical application – Active*
Type: SRA from Audition Therapeutics
Role: Principle Investigator
For this project we will generate preclinical data to support an IND application to the FDA to initiate a clinical trial focused on TMC1 gene therapy for DFNB7/11 patients.

Teaching of Students in Courses:

Local

1990 – 1991	Introduction to Neuroscience 3-4yr undergraduate students	University of Rochester 4, 1hr discussions, 4, 2hr labs
1994	Sensory Transduction 1 st year graduate students	Baylor College of Med. 3, 1hr discussion groups
1997 – 2000	Neuroscience 200 / HST130 1 st year HST students	Harvard/MIT HST Program 6, 2hr conferences (head conference instructor)
1997	Cell Biology 1-2yr undergraduate students	Harvard University, FAS 8, 3hr labs

1999	Neuroscience 3-4yr undergraduate students	Harvard University, FAS 4, 1hr lectures
2001 – present	Neurobiology 703 1 st year graduate students	UVA 2, 2 hour lectures/semester
2002 – present	Medical Neuroscience 1 st year medical students	UVA 4, lecture, 2 labs, 2 discussion groups/semester
2002 – 2006	Neurophysiology 862 2 nd year graduate students	UVA 2, 2hr lectures/semester
2003	Neuroscience 808 All NGP students	UVA 1, 2hr panel
2003	Neuroscience 707 1 st year graduate students	UVA 1, 2hr discussion
2003, 2009	Directed Readings 851 2 nd year graduate students	UVA 10, 2hr sessions
2004 – 2009	Human Physiology 832 2 nd year graduate students	UVA 3, 2hr lectures
2004	NGP Seminar Previews All NGP students	UVA 16, 1hr sessions
2007	BIMS 813, 2 nd year MSTP students	UVA 1, 2hr lecture
2008	Biology 431 4 th year undergrad students	UVA 1, 2hr lecture
2013	Neurobiology 301	HMS, 1, 2hr lecture
2016 – 2018	SHBT 201	2, 2hr lecture
2012 – present	Neurobiology 200 / HST 130 Co-director / lecturer	HMS 8, 1.5 hr sessions
National		
2003, 2004	Pediatric Audiology 1 st year audiology students	James Madison University 1, 2hr guest lecture
2005, 2006	Neurobiology Course graduate level students	Marine Biological Labs 1, 2 hour guest lecture

2007 – 2013	Biology of the Inner Ear graduate level students	Marine Biological Labs 1, 2 hr lecture, 4, 4 hour labs
2008	Neurobiology 4 th year undergraduate students	University of Richmond 1, 1 hour guest lecture
2012 – present	Cellular Physiology & Biophysics Undergraduate, BIOL 1100	Brown University 1, 2 hour guest lecture
2018	Cellular Physiology & Biophysics	Vanderbilt University 1, 2 hour guest lecture
2020	Markey Pathway M.D. course on Hearing	Washington University

Advising Responsibilities

Rotation students (2001-2021) ~5 hrs/week/student for 4 months

Jessica Risner - Published one manuscript in *J. Neurosci* with cover
Eric Stauffer (UVA – NGP)
Micheal Nelson (UVA – NGP)
Peihan Su (UVA – NGP)
Micheala Levin (UVA – NGP)
Geoff Horwitz (UVA – NGP)
Kathryn Barletta (UVA – MSTP)
Charlie Askew (UVA – NGP)
Ye-Hyun Kim (UVA – NGP)
Sarah Gluck (HST – SHBT)
Hannah Goldberg (HST – SHBT)
John Lee (HST – SHBT)
Carl Nist-Lund (HMS – PiN)
Corey Loeb (HMS – SHBT)
Ginnie Hu (HMS – SHBT)
Matthew Mum (HMS – SHBT)
Grace Chaves (HMS – SHBT)

Resident Rotations ~5 hrs/week/resident for 3 months

Garth Essig, M.D.
Sean Miller, M.D.
Chuck Fletcher, M.D. Published one manuscript
Chris Colclasure, M.D. Published one manuscript, resident research award,
Fitz-Hugh symposium

Mentorship of Junior Faculty

2004 – 2008: Brad Kesser, M.D. Professor, Department of Otolaryngology
Published 2 manuscripts, awarded 2 research grants from foundations/

professional societies, 2008 Fowler Award for Best Basic Science Thesis -
Triological Society

2011 – 2014: Michael Tri Do, Ph.D. Assistant Professor, F.M. Kirby
Neurobiology Center, Department of Neurology, BCH. Quarterly meetings
offering guidance on grants, papers, mentorship of students, etc. Awarded RO1
grant on first submission.

2014 – 2016: Selena Heman-Ackah, M.D., Ph.D., Assistant Professor of
Otolaryngology/Neurotology BIDMC/BCH, Awarded FFB grant to develop gene therapy
for Usher Syndrome, type 1C work to be done in our lab.

2015 – 2020: Todd Anthony, Ph.D. Assistant Professor, F.M. Kirby
Neurobiology Center, Department of Neurology, BCH. Quarterly meetings
offering guidance on grants, papers, mentorship of students, etc.

2020 – present: Eliot Shearer, M.D., Ph.D. Assistant Professor of
Otolaryngology, BCH/HMS, mentor on successful K08 award.

Former Ph.D. students

2002 – 2008 Jessica Risner, Ph.D., Post-doc, Imperial College London
Published four manuscripts, awarded NRSA fellowship and Best Neuroscience
Dissertation and six other research awards.
Current position: Research Funding Manager, Cancer Research UK

2003 – 2008 Eric Stauffer, Ph.D. Research Associate, Diffusion Pharmaceuticals
Published six manuscripts, including one first-author *Neuron* paper with cover,
Awarded 1st place in UVA research presentations & Robert Huskey Award for
Excellence in Science, plus four other awards
Current position: Regulatory Affairs Manager, MedImmune LLC.

2008 – 2012 Michaela Levin, Ph.D.
Published one first author manuscript, Huskey Award for Excellence in Science
Current position: Technology Development Associate, Harvard Medical School

2007 – 2012 Geoffrey C. Horwitz, Ph.D.
Received Huskey Graduate Research Award and two other research awards.
Published four manuscripts, three as first author.
Current position: Decibel Therapeutics

2010 – 2014 Ye-Hyun Kim, Ph.D.
Received AAAS Excellence in Science Award and 2 other research awards,
published one first author paper, co-author on two other papers.
Post-Doctoral Fellow at Johns Hopkins with Elizabeth Glowatski, Current
position: Akouos

2009 – 2015 Charles Askew, Ph.D.

Co-author on six manuscripts, including first author on Science Translational Medicine manuscript. Received one merit based travel award, 1st Place Robert J. Huskey Biomedical Sciences Oral Presentation Award (2015).

Current Position: Post-Doctoral Fellow at UNC with Jude Samulski

2016 – 2020 Hannah Goldberg

Student in HMS SHBT program. Project: Gene therapy in mouse models of Usher Syndrome. Co-author on three manuscripts. Current: Scientist nFERENCE.

2017 – 2021 John Lee

Student in HMS SHBT program. Project: Sensory transduction is required for normal development and maintenance of cochlear inner hair cell synapses. First author on three manuscripts including one in eLife. Current: Post Doc at NIDCD

Current Ph.D. students

2023 – present Grace Chaves

Former Postdoctoral Fellows

2002 – 2004 David Abraham, Ph.D.

Published one *J. Neurosci* paper

Current position: Bioscience analyst, Virginia Bioinformatics Institute

2006 – 2019 Yukako Asai, Ph.D.

Awarded Marie Currie International Fellowship, Published two first author manuscript and 10 others. Current position: Research Associate, Akouos

2006 – 2010 Andrea Lelli, Ph.D.

Awarded NanoInnovation Grant, published seven manuscripts including one in *Nature Communications* and one in *JCI*

Current position: Lecturer, Pasteur Institute

2012 – 2016 Xiaoping Liu, Ph.D.

Published one co-author manuscript in *Hum Mol Genetics* and two first authored papers in *Neuron* and *Nature Com*. Post-doctoral Fellow with Xiaoqin Wang, Johns Hopkins, Current position: Allen Institute

2014 – 2017 Swetha Murali, Ph.D. Published one manuscript in *J. Neurophysiol*

2011 – 2018 Bifeng Pan, Ph.D. Published 19 manuscripts, including five first authored manuscripts, two in *Neuron* and two in *Nature Biotech*.

2018 – 2020 Jason Wu, Ph.D., Published two manuscripts, including one first author manuscript in *Molecular Therapy*.

Current Postdoctoral Fellows:

2016 – present, Olga Shubina-Oleinik. Published one first author review article, one first author manuscript in *Science Translational Medicine* and one in *Science Advances*.

2019 – present, Irina Marcovich, one first authored review article, one first primary research article in *Biomolecules*

2019 – present, Wang Zheng, one first authored review article and one first author manuscript in *Science Advances*, one in review in *Cell*.

2019 – present, Stephanie Mauriac, published one first authored manuscript in *Cells*.

2021 – present, Evan Ratzan

2022 – present, Thibault Peineau

2023 – present, Chloe Petit

Invited Presentations *No presentations below were sponsored by outside entities*

Local

- 2000 The role of myosin I β in adaptation by mammalian vestibular hair cells: A targeted mutation confers drug sensitivity / Seminar
Harvard/MIT, Mass Eye&Ear, Eaton Peabody Lab.
- 2002 Mechanotransduction and adaptation in hair cells: A chemical-genetic strategy demonstrates a role for myosin Ic / Seminar
University of Virginia, Neuroscience Graduate Program Seminar Series
- 2002 Molecular motors in the sensory cells of the mammalian inner ear / Workshop
University of Virginia, Interdisciplinary Workshops on Sensory Systems:
- 2005 The molecules and mechanisms of mechanotransduction in sensory hair cells / Seminar
University of Virginia, Biology Department Seminar Series
- 2005 Hereditary hearing loss / Symposium
University of Virginia, Department of Otolaryngology, Fitz-Hugh Symposium
- 2008 The future of clinical audiology / A tribute to Roger Ruth and 30 years of service
University of Virginia, Department of Otolaryngology
- 2008 Mechanotransduction and adaptation in mouse auditory hair cells / Seminar
University of Virginia, Biomedical Engineering Department Seminar Series
- 2010 The molecules and mechanisms of mammalian mechanosensation / Seminar
University of Virginia, Psychology Department Seminar Series

- 2011 The molecules and mechanisms of sensory signaling in the inner ear and the prospects for gene therapy / Seminar University of Virginia, Pathology Department Seminar Series
- 2011 Gene therapy for mouse models of human deafness. / Bertarelli Symposium, HMS
- 2011 Identification of a novel gene family required for mechanotransduction in sensory hair cells of the mammalian inner ear. HMS/BCH Neurobiology Seminar Series.
- 2011 The molecules and mechanisms of mechanotransduction. Department of Otolaryngology, BCH
- 2012 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells F.M Kirby Neurobiology Center / Faculty Seminars
- 2012 Are TMCs The Mechanotransduction Channels of sensory hair cells? EPL/MEEI Seminar Series
- 2013 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells Molecular Biology of the Inner Ear Seminar Series, HMS/MEEI
- 2014 Gene therapy for mouse models of human deafness. / Bertarelli Symposium, HMS
- 2014 Sensory and Viral Transduction in the Mammalian Inner Ear, Voyager Pharmaceuticals
- 2014 Sensory and Viral Transduction in the Mammalian Inner Ear, Editas Medicine.
- 2015 The contributions of TMC proteins to sensory transduction in auditory and vestibular hair cells, Boston University Hearing Research Center.
- 2015 Molecular identity of the elusive sensory transduction channel in auditory and vestibular hair cells, Boston University School of Medicine.
- 2015 TMC gene therapy restores auditory function in deaf mice. Department of Otolaryngology, BCH.
- 2015 TMC gene therapy restores auditory function in deaf mice. InterUrban Clinical Club, Boston, MA.
- 2016 TMC Gene Therapy Restores Hearing in Mouse Models of Genetic Deafness, Decibel Therapeutics.
- 2016 TMC Gene Therapy in Mouse Models of Genetic Deafness. Bertarelli Symposium, Harvard Medical School.
- 2016 Sensory Hair Cell Function, Dysfunction and the Prospects for Hearing Restoration, Massachusetts Medical Society.

- 2017 TMC Function, Dysfunction and Restoration. – invited seminar, Translational Neuroscience Center, BCH
- 2018 TMC Gene Therapy in Mouse Models of Genetic Deafness, Bertarelli Symposium, Harvard Medical School
- 2018 Sensory Hair Cell Function, Dysfunction and the Prospects for Hearing Restoration, Brandeis University.
- 2018 F.M Kirby Neurobiology Center Faculty Lunch Seminar Series, BCH, Structure, Function and Restoration of Hair Cell Transduction Channels, BCH.
- 2018 BCH Department of Otolaryngology, Otology Conference, BCH: Structure, Function and Restoration of Hair Cell Transduction Channels.
- 2019 Broad Institute of Harvard/MIT: Identity, Structure and Function of Hair Cell Transduction Channels.
- 2019 Mass Eye and Ear Resident Research Day: Function, Dysfunction and Restoration of Auditory Transduction Channels.
- 2019 Schepens Eye Institute / Mass Eye and Ear: Function Dysfunction and Restoration of Auditory Transduction Channels.
- 2019 Division of Newborn Medicine at Boston Children’s Hospital Seminar Series: Function, Dysfunction and Restoration of Auditory Transduction Channels
- 2021 BCH Department of Otolaryngology Retreat: Development of Gene Therapy for a Common Form of Genetic Hearing Loss
- 2021 Harvard Catalyst Five Senses Symposium: Function, Dysfunction and Restoration of Auditory Transduction Channels
- 2021 BCH Gene Therapy Seminar Series: Gene Therapy for Genetic Hearing Loss
- 2021 BCH Leadership Forum: Auditory Neuroscience at BCH, Bench to Bedside & Back
- 2022 BCH Gene Therapy Seminar Series: Gene Therapy for DFNB16 Hearing Loss
- 2023 BCH Neurosurgery Roundtable: Gene Therapy for Genetic Hearing Loss

National

- 2001 Molecular physiology in the sensory hair cells of the mouse utricle / Symposium Association for Research in Otolaryngology

- 2001 Mechanotransduction and adaptation in sensory hair cells: A chemical-genetic strategy demonstrates a role for myosin Ic. Podium presentation: Association for Research in Otolaryngology
- 2002 Vestibular influences on movement / Symposium, Barany Society Meeting
- 2002 Mechanotransduction and adaptation in sensory hair cells: A chemical-genetic strategy demonstrates a role for myosin Ic / Seminar University of California, Davis
- 2002 Mechanotransduction and adaptation in sensory hair cells: A chemical-genetic strategy demonstrates a role for myosin Ic / Seminar NIH, NIDCD Seminar Series
- 2002 Mechanotransduction and adaptation in sensory hair cells: A chemical-genetic strategy demonstrates a role for myosin Ic / Seminar Johns Hopkins University, Department of Otolaryngology
- 2002 Gravitational effects on transduction and adaptation on sensory hair cells of a mammalian vestibular organ / Symposium American Society for Gravitational and Space Biology
- 2003 Transduction and adaptation in sensory hair cells / Symposium James Madison University, Innovations in clinical communication sciences symposium
- 2004 Specific inhibition of voltage-gated potassium conductances in mouse hair cells using a mutant form of KCNQ4 / Symposium International Conference on the Molecular Biology of Hearing and Deafness
- 2004 Functional development of sensory signaling in mouse vestibular hair cells / Seminar West Virginia University, Department of Otolaryngology
- 2004 Functional development of sensory signaling in mouse vestibular hair cells / Seminar The Vollum Institute, Oregon Health Sciences University
- 2004 Sensory signaling in inner ear hair cells: mechanotransduction to neurotransmission. Creighton University
- 2004 Virally-mediated gene transfer: from virology to practice / Symposium Association for Research in Otolaryngology
- 2005 The molecules and mechanisms of sensory signaling in the inner ear / Seminar Harvard Medical School, Boston Children's Hospital
- 2005 The molecules and mechanisms of sensory signaling in the inner ear / Seminar Stanford University, Department of Otolaryngology
- 2005 Transduction and signaling in the sensory hair cells of the inner ear / Seminar Marie Biological Labs, Woods Hole, MA
- 2005 Myosin motors modulate mammalian mechanotransduction / Seminar

- Scripps Research Institute, Inaugural speaker for Molecular Neuroscience Seminar Series
- 2005 Hair cells: transduction, transmission, regeneration. A developmental approach for identification of the hair cell transduction channel / Symposium (Symposium Chair) Society for Neuroscience Annual Meeting
- 2006 Carving the space-time continuum in the developing auditory system / Symposium Winter Conference on Brain Research
- 2006 A developmental approach for identification of hair cell genes and proteins / Workshop McLaughlin Research Institute, Workshop on Auditory Research.
- 2007 Mechanosensory transduction: The molecular mechanisms of adaptation in mechanosensory hair cells / Symposium Gordon Research Conference
- 2007 The molecules and mechanisms of sensory signaling in the inner ear / Seminar Northwestern University, Hugh Knowles Scholar
- 2008 Mechanotransduction and adaptation in auditory hair cells / Seminar NIH/NIDCD
- 2008 The molecules and mechanisms of sensory signaling in the inner ear / Seminar University of Texas, Galveston, Neuroscience Research Day, Keynote speaker
- 2008 The molecules and mechanisms of mechanotransduction in the inner ear / Seminar University of Richmond
- 2008 The molecules and mechanisms of sensory signaling in the inner ear / Seminar University of Rochester, Department of Neurobiology
- 2009 Mechanotransduction in physiology and disease / Symposium Keystone Conference
- 2009 The molecules of mechanosensory transduction in the mammalian inner ear / Seminar University of Pennsylvania, Department of Otolaryngology
- 2009 The molecules and mechanisms of transduction in the mammalian inner ear / Seminar East Carolina University
- 2010 The molecules and mechanisms of mechanosensation in the mouse inner ear / Seminar Harvard Medical School / Children's Hospital Boston
- 2010 Hair cell and neuronal function and dysfunction in the mouse inner ear / Symposium The Jackson Laboratory, Conference: The mouse as an instrument for ear research
- 2011 The molecules and mechanisms of mechanosensation in the mammalian inner ear / Seminar. University of Kentucky
- 2012 Mechanotransduction in mouse vestibular hair cells requires transmembrane channel-like genes 1 or 2. Podium presentation / Association for Research in Otolaryngology

- 2012 Introduction of David P. Corey, Ph.D. for the 2012 Award of Merit, ARO
- 2012 Mechanotransduction in mouse inner ear hair cells requires TMC1 or TMC2. Seminar. Columbia University
- 2013 Mechanotransduction in mouse inner ear hair cells requires TMC1 or TMC2. Seminar. Rutgers University
- 2013 Mechanotransduction in mouse inner ear hair cells requires TMC1 or TMC2. Seminar. Johns Hopkins University
- 2013 Mechanotransduction in mouse inner ear hair cells requires TMC1 or TMC2. Seminar. Brown University
- 2013 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Invited podium presentation: Molecular Biology of Hearing and Deafness, Stanford.
- 2013 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Seminar: Marine Biological Labs, Woods Hole, MA
- 2013 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Seminar: University of Indiana
- 2014 Bertarelli Symposium Neuroengineering: Molecules, Minds and Machines. Invited Symposium Speaker and Session Chair
- 2014 TMC Function in hair cell Mechanotransduction. Speaker and Session Chair. ARO.
- 2014 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Invited Symposium Speaker and Session Chair: Biophysical Society
- 2014 Ion Channels: From Structure to Disease. UC Berkeley Molecular Cell Biology/Cellular and Developmental Biology Symposium
- 2014 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Seminar: University of Florida
- 2014 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Seminar: University of Michigan
- 2014 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Seminar: Wayne State University
- 2014 TMC gene therapy in mouse models of human deafness. Invited Symposium Speaker, International Symposium on Usher Syndrome
- 2014 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Key Note Speaker, Gordon Conference on Auditory Systems

- 2014 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Invited Symposium Speaker, Society of General Physiologists
- 2014 The Mouse as an Instrument for Ear Research VI. The Jackson Laboratory in Bar Harbor, ME
- 2015 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. University of Pennsylvania.
- 2015 The Transmembrane Channel-Like Family: Molecules, Mechanisms and Models of Mechanotransduction. ARO Symposium organizer, speaker and chair.
- 2015 Contributions of TMC proteins to sensory transduction in auditory and vestibular hair cells. Janelia Farms Force-Gated Ion Channels conference.
- 2015 TMC gene therapy in mouse models of human deafness. Conference on Implantable Auditory Prostheses.
- 2015 Contributions of TMC proteins to sensory transduction in auditory and vestibular hair cells. University of Washington.
- 2015 Contributions of TMC proteins to sensory transduction in auditory and vestibular hair cells. Stanford University.
- 2015 Contributions of TMC proteins to sensory transduction in auditory and vestibular hair cells. Yale University.
- 2016 Contributions of TMC proteins to sensory transduction in auditory and vestibular hair cells. Duke University.
- 2016 Hair cell function and dysfunction in mouse models of human deafness. Sense to Synapse Symposium, Rockefeller University.
- 2016 Cysteine Mutagenesis Reveals TMC1 Residues that Contribute to Mechanotransduction. Auditory Systems Gordon Conference.
- 2016 Contributions of TMC proteins to sensory transduction in auditory and vestibular hair cells. Emory University.
- 2017 Keynote speaker for Brown University graduate research day. "Auditory Neuroscience, Hear and Now".
- 2017 Contributions of TMC proteins to sensory transduction in auditory and vestibular hair cells. University of Mississippi
- 2017 Tmc Function, Dysfunction and Restoration. NIDCD/NIH.

- 2017 Gene therapy for genetic hearing loss – 2017 Peroxisome Biogenesis Disorders Conference
- 2017 Cysteine Mutagenesis Reveals TMC1 Residues that Contribute to Mechanotransduction. University of Southern California.
- 2018 Molecular identification of sensory transduction channels in auditory hair cells – Vanderbilt University
- 2018 Cysteine Mutagenesis Reveals TMC1 Residues that Contribute to Mechanotransduction. – Oregon Health Sciences University & Vollum Institute
- 2018 Chemical Senses Conference on Smell and Taste Disorders – invited speaker, TMC1 gene therapy for inner ear disorders. Philadelphia, PA
- 2018 American Speech and Hearing Association – invited speaker, TMC1 gene therapy for inner ear disorders. Boston, MA
- 2018 Function, Dysfunction and Restoration of Hair Cell Transduction Channels, University of Rochester, Rochester, NY.
- 2019 Association for Research in Otolaryngology, Baltimore, MD: Cysteine Substitution Identifies the Pore-forming Region of TMC1 in Hair Cell Sensory Transduction Channels
- 2019 Biophysical Society, Baltimore, MD: Cysteine Substitution Reveals the Pore-Forming Region of TMC1 in Hair Cell Sensory Transduction Channels
- 2019 Keystone Meeting, Mammalian Sensory Systems, Seattle, WA: Identity, Structure and Function of the Hair Cell Transduction Channel
- 2019 Keystone Meeting, Protein Replacement via Nucleic Acid Therapies, Steamboat, CO: Improved Gene Therapy Restores Hearing, Balance, and Secondary Measures in Mice with Genetic Inner Ear Disorders
- 2019 Belluci Symposium, Keynote Address, Omaha, NE: Hear at Last: Identity of the Hair Cell Transduction Channel
- 2019 University of Connecticut, Department of Neurobiology: Function, Dysfunction and Restoration of Auditory Transduction Channels.
- 2019 American Speech and Hearing Association – invited speaker, TMC1 gene therapy for inner ear disorders. Boston, MA
- 2020 Association for Research in Otolaryngology, San Jose, CA - invited symposium speaker: Next Generation Gene Therapy for Genetic Hearing Loss
- 2020 American Neurotology Society – Franklin Rizer Memorial Lecture: Function, Dysfunction and Recovery of Auditory Mechanosensory Transduction Channels

- 2020 AAO-HNSF – Gene Therapy for Genetic Hearing Loss
- 2020 East Coast Polytechnic Institute: Function, Dysfunction and Recovery of Auditory Mechanosensory Transduction Channels
- 2020 Palm Springs Hearing Seminars – Function, Dysfunction and Recovery of Auditory Mechanosensory Transduction Channels
- 2021 Association for Research in Otolaryngology – Presidential Symposium – Introduction to Usher Syndrome and Guest Speaker Rebecca Alexander
- 2021 Association for Research in Otolaryngology – Pioneer Award Presentation – Discovery of the Hair Cell Transduction Channel.
- 2021 Association for Research in Otolaryngology – Putting the Pieces Together: The Hair Cell Transduction Complex – Symposium speaker, organizer and chair.
- 2021 National Institute Deafness and Communications Disorders – Wenthold Memorial Lecture: Function, Dysfunction and Restoration of Sensory Transduction Channels in the Mammalian Inner Ear.
- 2021 Association for Research in Vision and Ophthalmology – invited symposium speaker: Function, Dysfunction and Restoration of Auditory Mechanosensitive Channels
- 2021 University of North Carolina – Function, Dysfunction and Recovery of Auditory Mechanosensory Transduction Channels
- 2021 California Association of Audiology - Function, Dysfunction and Restoration of Sensory Transduction Channels in the Mammalian Inner Ear.
- 2021 University of South Florida - Function, Dysfunction and Restoration of Sensory Transduction Channels in the Mammalian Inner Ear.
- 2021 Yale University Department of Physiology - Inner Ear Gene Therapy Restores Sensory Transduction and Auditory Function
- 2021 Society for Neuroscience – invited symposium speaker: My channel got a million hits: The search for the hair cell transduction channel
- 2021 National Institute of Deafness and Communications Disorders Stem Cell Symposium - Inner Ear Organoids as a Platform for Basic and Translational Research
- 2022 Usher Coalition – Family Connect Conference, Austin, TX – Update on USH Research Projects
- 2022 Next Generation Gene Therapy for Genetic Hearing Loss – Auditory Systems Gordon Conference

- 2023 Columbia University, Department of Biological Sciences – Function, Dysfunction and Restoration of Sensory Transduction Channels in the Mammalian Inner Ear
- 2023 Rockefeller University – Function, Dysfunction and Restoration of Sensory Transduction Channels in the Mammalian Inner Ear
- 2023 Medical University of South Carolina – Function, Dysfunction and Restoration of Sensory Transduction Channels in the Mammalian Inner Ear
- 2023 University of South Carolina – Function, Dysfunction and Restoration of Sensory Transduction Channels in the Mammalian Inner Ear

International

- 2001 Viral-mediated gene transfer to study the physiology of the mouse inner ear / Symposium International Congress of Physiological Sciences, Auckland, New Zealand
- 2002 Mechanotransduction and adaptation in hair cells: Chemical-genetic strategy demonstrates a role for Myo Ic / Seminar Flanders Interuniversity Institute of Biotechnology, Belgium
- 2005 The molecules and mechanisms of transduction and adaptation in the inner ear / Seminar Pastuer Institute, Paris, France
- 2006 Functional development of sensory hair cells in the mammalian inner ear / Symposium Physiological Society, London, England
- 2008 Ion channel function and the prospects for gene therapy in the inner ear / Seminar University College London, London, England
- 2008 Ion channel function and the prospects for gene therapy in the inner ear / Seminar University of Bristol, Bristol, England
- 2010 The molecules and mechanisms of mechanosensation in the mammalian inner ear / Seminar. National Institute of Health and Medical Research, Montpellier, France
- 2011 The molecules and mechanisms of mechanosensation in the mammalian inner ear / Seminar. École Polytechnique Fédérale de Lausanne, Switzerland
- 2012 Mechanotransduction in mouse inner ear hair cells requires TMC1 or TMC2. Symposium Force Transduction & Emerging Ion Channels Meeting. Berlin, Germany
- 2012 Mechanotransduction in mouse inner ear hair cells requires TMC1 or TMC2. Seminar. Cambridge University, Cambridge, England
- 2012 Mechanotransduction in mouse inner ear hair cells requires TMC1 or TMC2. Seminar. École Polytechnique Fédérale de Lausanne, Switzerland

- 2014 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Seminar. Institut Curie and the CNRS, Paris, France.
- 2015 Ion channel function and the prospects for gene therapy in the inner ear. Bertarelli EPFL Symposium, Geneva, Switzerland.
- 2015 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. Symposium. European Calcium Channel Conference, Austria.
- 2016 The function of TMC proteins in mechanotransduction in mouse inner ear hair cells. German Physiological Society – Symposium, Leubeck, Germany.
- 2016 Cysteine Mutagenesis Reveals TMC1 Residues that Contribute to Mechanotransduction. Molecular Biology of Hearing and Deafness – Invited Speaker, Cambridge, UK.
- 2016 114th International Titisee Conference on “The molecules and mechanisms of magneto, thermo, and mechanosensation – Symposium, Titisee, Germany.
- 2017 Keynote speaker for McGill University undergraduate research day. “Auditory Sensory Transduction, Structure and Function”. – Montreal, Canada
- 2017 Function, dysfunction and restoration of sensory transduction channels in auditory hair cells – University of Bordeaux, France
- 2017 Next Generation Gene Therapies for DFNB7/11 and DFNA36 – First International Meeting for Inner Ear Therapies Marrakech, Morocco
- 2017 Cochlear Think Tank –TMC Gene Therapy for Genetic Deafness – London, UK
- 2018 Cysteine mutagenesis reveals TMC1 residues that line the pore of sensory transduction channels. – invited speaker, Molecular Biology of Hearing and Deafness Meeting – Göttingen, Germany
- 2018 Next Generation Gene Therapy Restores Hearing, Balance and Quality of Life in Mouse Models of Genetic Inner Ear Disorder – invited speaker, International Symposium on Usher Syndrome Mainz, Germany
- 2018 Force-Gated Ion Channels Meeting, TMC1 Structure and Function Berlin, – invited speaker, Germany
- 2019 International Symposium on Auditory and Audiological Research – invited speaker, Nyborg, Denmark: Function and Restoration of Auditory Transduction Channels.
- 2019 Foundation Pour L’Audition: Function Dysfunction and Restoration of Auditory Transduction Channels. – keynote address, Paris, France
- 2020 University of Buenos Aries – TMC1 Structure and Function, Buenos Aries, Argentina.

- 2021 University of Toronto Department of Otolaryngology – Krista Riko Lecture: Function Dysfunction and Restoration of Auditory Transduction Channels.
- 2021 University of San Luis Potosi, Mexico – Function, Dysfunction and Restoration of Auditory Transduction Channels
- 2022 Function, Dysfunction and Restoration of Auditory Transduction Channels – Symposium Speaker, Argentine Neuroscience Society, Buenos Aires, Argentina.
- 2022 Next Generation Gene Therapy for Genetic Hearing Loss – Invited Speaker, University of Buenos Aires, Buenos Aires, Argentina.
- 2022 Aslla Symposium on Mechanotransduction and Pain – Symposium Speaker, Gangneung, South Korea.
- 2022 International Symposium on Mechanobiology Function Dysfunction and Restoration of Auditory Transduction Channels. – Keynote address, Sydney, Australia.
- 2023 University of Toronto, Toronto, Canada, Krista Riko Lecture – Function Dysfunction and Restoration of Auditory Transduction Channels
- 2023 ISIET, Marrakesh, Morocco – Optimized AAV Vectors for TMC1 Gene Therapy in a Humanized Mouse Model of DFNB7/11
- 2023 Inner Ear Biology, Maria Bitner-Glindzicz Plenary Lecture – Optimized AAV Vectors for TMC1 Gene Therapy in a Humanized Mouse Model of DFNB7/11

Service to the Community

No activities below were sponsored by outside entities

2003	Otology Conferences (O&HNS) UVA	2, 1hr lectures
2004	Guest Lecturer, Montessori School of Anderson	1, 1hr special lecture
2004	NPR (All Things Considered) radio interview	20 second sound bite
2006	Virginia Lion's Club	1, 1hr special lecture
2007	ReachMD Radio Interview	10 minutes
2007	Design News podcast	7 minutes
2007	Genetic Engineering News (podcast)	5 minutes
2008 – 2009	UVA Mini Med School Program	2 hour lab tour and demo
2010	NPR essay: Soccer and the human brain	3 minute radio commentary
2011	Boston Globe: Featured in story titled "Ear researchers think like engineers"	
2011	BCH: Vector Blog "Gene-therapy trial will attempt to restore hearing in mice"	
2011	NPR (Weekend Edition) radio interview	20 second sound bite
2012	Commencement Speaker, Montessori School of Anderson, 20 min. speech	
2013	BCH: Vector Blog "Scientists find cellular channels vital for hearing"	
2014	Newton Public Schools: Understanding our differences, deafness	1, 1hr lecture
2014	BCH: Vector Blog "Hearing restoration has a sound future"	
2014	WBUR: Cognoscenti "Thinking with your feet: Soccer rewires your brain"	

- 2014 Harvard Crimson: Engineering Research Partnerships Launch in January
- 2014 Harvard Otolaryngology Cover Story: Inside the Holt/Geleoc Lab.
- 2015 Bloomberg News: “Drug Makers Try Gene Therapy”
- 2015 News coverage for Askew et al. 2015, *Sci Transl Med*. “TMC gene therapy restores auditory function in deaf mice”. BBC, NPR, Boston Herald, The Scientist, Fierce Biotech, Times of London and 122 other news outlets.
- 2015 NPR –Science Friday, Gene Therapy Aims to Switch on Hearing
- 2017 News coverage for Pan et al. 2017, *Nature Biotech*. “Gene therapy restores auditory and vestibular function in a mouse model of Usher syndrome type 1c” BBC, NPR, Boston Herald, The Scientist, Fierce Biotech, Times of London and 88 other news outlets.
- 2017 Hearing and Deafness lecture – Montessori School of Anderson, South Carolina
- 2018 News coverage for Pan et al. 2018, *Neuron*. “TMC1 Forms the Pore of Mechanosensory Transduction Channels in Vertebrate Inner Ear Hair Cells” Boston Globe, NPR, The Scientist, Scientific American, Forbes, Science Magazine, Harvard Gazette
- 2019 The Scientist – Pan et al. 2018, named one of the top biggest science news stories of 2018.
- 2019 Neuron – Pan et al. 2018 named one of the top ten publications of 2017-2018.
- 2019 News coverage for Gyrogy et al. 2019, *Nature Medicine*, Allele-specific gene editing prevents deafness in a model of dominant progressive hearing loss. Harvard Gazette, HMS News, BCH Vector Blog.
- 2020 News coverage for Yeh et al. 2020, *Sci Transl Med*. “In vivo base editing restores sensory transduction and transiently improves auditory function in a mouse model of recessive deafness”. Medical Health News, Fierce Biotech, Science Daily, MedicalXpress
- 2021 News coverage for Shubina-Oleinik et al., 2021 *Science Advances* “Dual-vector gene therapy restores cochlear amplification and auditory sensitivity in a mouse model of DFNB16” Fox News, Science Magazine, TrialSite News and 14 others.
- 2023 Newton South High School – 1 hour lecture for 47 Neurobiology students

Peer-Reviewed Publications

- 1) **J.R. Holt** and R.A. Eatock. Inwardly rectifying currents of saccular hair cells from the leopard frog. *J. Neurophysiol*, 73:4 pp1484-1502, 1995.
- 2) W. Denk, **J.R. Holt**, G.M.G. Shepperd, D.P. Corey. Calcium imaging of single stereocilia in hair cells: Localization of transduction channels at both ends of tip links. **Cover**. *Neuron*, 15 pp1311-1321, 1995.
- 3) **J.R. Holt**, D.P. Corey, R.A. Eatock. Mechanoelectrical transduction and adaptation in hair cells of the mouse utricle, a low-frequency vestibular organ. *J. Neurosci*, 17:22, pp8739-8748, 1997.
- 4) J.S. Oghalai, **J.R. Holt**, T. Nakagawa, T.M. Jung, N. J. Coker, H.A. Jenkins, R.A. Eatock, W.E. Brownell. Ionic currents and electromotility in human hair cells. *J. Neurophysiol* 79, 2235-2239, 1998.

- 5) **J.R. Holt**, A. Rüscher, M. Vollrath, R.A. Eatock. The frequency dependence of receptor potentials in hair cells of the mouse utricle. *Primary Sensory Neuron*, 2, 233-241, 1998.
- 6) **J.R. Holt**, M. A. Vollrath and R.A. Eatock. Stimulus processing by type II hair cells of the rodent utricle. *Annals of the New York Academy of Science*, 871:15-26, 1999.
- 7) **J.R. Holt**, D.C. Johns, S. Wang, Z.Y. Chen, E. Marban and D.P. Corey. Functional expression of exogenous proteins in mammalian sensory hair cells infected with adenoviral vectors. *J. Neurophysiol*, 81, 1881-1888, 1999.
- 8) J.S. Oghalai, **J.R. Holt**, T. Nakagawa, T.M. Jung, N. J. Coker, H.A. Jenkins, R.A. Eatock, W.E. Brownell. Harvesting human hair cells. *Annals of Otorhinolaryngology*. 109, 9-16, 2000.
- 9) **J.R. Holt**, S.K.H. Gillespie, D.W. Provance, K. Shah, K.M. Shokat, D.P. Corey, J.A. Mercer, P.G. Gillespie. A chemical-genetic strategy implicates myosin-1C in adaptation by hair cells. **Cover**. *Cell* 108, 371-381, 2002.
- 10) R.A. Dumont, Y. Zhao, **J.R. Holt**, M. Bahler, P.G. Gillespie. Myosin-1 isozymes in neonatal rodent auditory and vestibular epithelia. **Cover**. *JARO* 3(4):375-89, 2002.
- 11) **J.R. Holt**. Viral-mediated gene transfer to study the molecular physiology of the mammalian inner ear. *Audiology and Neuro-Otology*. 7: 157-160, 2002.
- 12) G.S.G. Géléoc and **J.R. Holt**. Developmental acquisition of sensory transduction in hair cells of the mouse inner ear. *Nature Neuroscience* 6(10), 1019-20, 2003.
- 13) D.P. Corey*, J. Garcia-Anoveros*, **J.R. Holt***, K.Y. Kwan*, S.Y. Lin*, M.A. Vollrath*, A. Amalfitano, E. Cheung., B.H. Derfler, A. Duggan, G.S.G. Géléoc, P. Gray, M.P. Hoffman, H.L. Rehm, D. Tamasauskas, and D.S. Zhang. TRPA1 is a candidate for the mechanosensitive transduction channel of vertebrate hair cells. *Nature*. 432, 723-730, 2004. ***equal contribution**
- 14) G.S.G. Géléoc, J.R. Risner and **J.R. Holt**. Developmental acquisition of voltage-dependent conductances and sensory signaling in hair cells of the embryonic mouse inner ear. **Cover**. *J. Neurosci*. 24: 11148-11159, 2004.
- 15) E.A. Stauffer, J. Scarborough, M. Hirono, E.D. Miller, K. Shah, J.A. Mercer, **J. R. Holt***, and P. G. Gillespie. Fast Adaptation in Vestibular Hair Cells Requires Myosin-1c Activity. **Cover**. *Neuron* 47:541-553, 2005. ***co-corresponding author**.
- 16) M. Senften, M. Schwander, P. Kazmierczak, C. Lillo, J.B. Shin, T. Hasson, P.G. Gillespie, D. Williams, G.S.G. Géléoc, **J.R. Holt** and U. Müller. Functional interaction between protocadherin 15 and myosin VIIa in hair cell stereocilia. *J Neurosci* 26:2060-2071, 2006.
- 17) J. McGee, R.J. Goodyear, D.R. McMillan, E.A. Stauffer, **J.R. Holt**, K.G. Locke, D.G. Birch, P.K. Legan, P.C. White, E.J. Walsh, G.P. Richardson. The very large G-protein-coupled receptor VLGR1: a component of the ankle link complex required for the normal development of auditory hair bundles. *J Neurosci*. 26:6543-6553, 2006.

- 18) P.G. Gillespie, J.D. Scarborough, E.A. Stauffer and **J.R. Holt**. Fast adaptation in vestibular hair cells depends on myosin 1c. *Auditory Mechanisms: Processes and Models*, A.L. Nuttall, World Scientific, Hackensack, NY, pp. 169-175, 2006.
- 19) J.R. Risner and **J.R. Holt**. A heterogeneous population of potassium conductances contributes to the diverse firing properties of postnatal mouse vestibular ganglion neurons. *J. Neurophysiol* 96(5):2364-76, 2006.
- 20) K. Oshima, C.E. Corrales, C.M. Grimm, P. Sennm, R.M. Monedero, G.S.G. Géléoc, A. Edge, **J.R. Holt**, S. Heller. Differential distribution of stem cells between the inner ear organs of hearing and balance. *J Assoc Res Otolaryngol*. 8(1):18-31, 2007.
- 21) B.W. Kesser, G.T. Hashisaki, K. Fletcher, H. Eppard and **J.R. Holt**. An in vitro model system to study gene therapy in the human inner ear. *Gene Therapy*. 14(15):1121-31, 2007.
- 22) **J.R. Holt**, E.A. Stauffer, D. Abraham, G.S. Géléoc. Dominant-negative inhibition of M-like potassium conductances in hair cells of the mouse inner ear. **Cover** *J Neurosci* 27:8940-51, 2007.
- 23) E.A. Stauffer and **J.R. Holt**. Sensory transduction and adaptation in inner and outer hair cells of the mouse auditory system. *J Neurophysiol*. 98: 3360-3369, 2007.
- 24) M. Schwander, W. Xiong, J. Tokita, A. Lelli, H. Elledge, P. Kazmierczak, A. Sczaniecka, A. Kolatkar, T. Whiltshire, P. Kuhn, **J.R. Holt**, B. Kachar, L. Tarantino, U. Müller, A Mouse Model for Non-Syndromic Deafness (DFNB12) Links Hearing Loss to Defects in Tip Links of Mechanosensory Hair Cells. *PNAS* 106(13):5252-7, 2009.
- 25) A. Lelli, Y. Asai, A. Forge, **J.R. Holt**, G.S.G. Géléoc. A tonotopic gradient in the development of sensory transduction in outer hair cells of the mouse cochlea. *J. Neurophysiol*. 101(6):2961-73, 2009.
- 26) H. Li, H. Liu, C.E. Corrales, J.R. Risner, J. Forrester, **J.R. Holt**, S.Heller A.S.B. Edge, Differentiation of Neurons from Neural Precursors Generated in Floating Spheres from Embryonic Stem Cells. *BMC Neurosci* 10:12, 2009
- 27) Y. Asai, **J.R. Holt**, G.S. Géléoc. A Quantitative Analysis of the Spatiotemporal Pattern of Transient Receptor Potential Gene Expression in the Developing Mouse Cochlea. *J Assoc Res Otolaryngol*. 11(1):27-3, 2010.
- 28) G.C. Horwitz, A. Lelli, G.S.G. Géléoc and **J.R. Holt** HCN Channels Are Not Required for Mechanotransduction in Sensory Hair Cells of the Mouse Inner Ear. (electronic publication) *Plos One* 5:1 e8627, 2010.
- 29) A. Lelli, P. Kazmierczak, Y.Kawashima, U. Müller and **J.R. Holt**. Development and Regeneration of Sensory Transduction in Auditory Hair Cells Requires Functional Interaction Between Cadherin-23 and Protocadherin-15. *J. Neurosci*. 30:11259-69, 2010.

- 30) N. Charizopoulou, A.Lelli, M. Schraders, K. Ray, R.J.C. Admiraal, H.R. Neely, J.R. Latoche, J.K. Northup, H. Kremer, **J.R. Holt**, and K. Noben-Trauth. Mutations in the PDZ domain containing protein Gipc3 cause progressive sensorineural degeneration (*ahl5* and *jams1*) in mice and recessive hearing impairment in humans. *Nature Com.* DOI: 10.1038/ncomms1200, 2011.
- 31) K.A. Steigelman, A. Lelli, X.D. Wu, J. Gao, S. Lin, K. Piontek, C. Wodarczyk, A. Boletta, H. Kim, F. Qian, G. Germino, G.S.G. Géléoc, **J.R. Holt**, J. Zuo. Polycystic kidney disease-1 gene is required for stereocilia structure and maintenance but not for mechanotransduction in mouse inner ear hair cells. *J. Neurosci* 31:12241-50, 2011.
- 32) G.C. Horwitz, J.R. Risner-Janiczek, S.M. Jones and **J.R. Holt**. HCN channels expressed in the inner ear are necessary for normal balance function. *J. Neurosci.* 31:16814-25, 2011.
- 33) Y. Kawashima, G.S. Géléoc, K. Kurima, V. Labay, A. Lelli, Y. Asai, T. Makishima, D.K. Wu, C.C. Della Santina, **J.R. Holt***, A.J. Griffith*. Mechanotransduction in mouse inner ear hair cells requires transmembrane channel-like genes. *J Clin Invest.* 121:4796-809, 2011. *Co-senior authors
- 34) M.E. Levin, **J.R. Holt**. The function and molecular identity of inward rectifier channels in vestibular hair cells of the mouse inner ear. *J Neurophysiol.* 108(1):175-86, 2012.
- 35) R. Geng, S. Melki, D.H.C. Chen, G. Tian, D. Furness, T. Oshima-Takago, J. Neef, T. Moser, C. Askew, G. Horwitz, **J.R. Holt**, Y. Imanishi and K. Alagramam. The mechanosensory structure of the hair cell requires Clarin-1, a protein encoded by Usher Syndrome III causative gene. *J. Neurosci.* 32(28):9485-98, 2012.
- 36) B. Pan, G.S. Géléoc, Y. Asai, G.C. Horwitz, K. Kurima, K. Ishikawa, Y. Kawashima, A.J. Griffith, **J.R. Holt**. TMC1 and TMC2 are components of the mechanotransduction channel in hair cells of the mammalian inner ear. *Neuron* 79(3):504-15, 2013. **Cover**
- 37) Y.H. Kim, **J.R. Holt**. Functional contributions of HCN channels in the primary auditory neurons of the mouse inner ear. *J. Gen Physiol.* 142(3):207-23, 2013.
- 38) W.M. Yu, J.M. Appler, Y-H. Kim, A.M. Nishitani, **J.R. Holt**, L.V. Goodrich. A Gata3–Mafb transcriptional network directs post-synaptic differentiation in synapses specialized for hearing. in press *eLife.* 2:e01341, 2013.
- 39) J. Zou, T. Zheng, C. Ren, C. Askew, X-P. Liu, B.Pan, **J.R. Holt**, Y. Wang, J. Yang. Deletion of PDZD7 Disrupts the Usher Syndrome Type 2 Protein Complex in Cochlear Hair Cells and Causes Hearing Loss in Mice. *Hum Mol Genet.* 23(9):2374-90, 2014.
- 40) G. C. Horwitz, J.R. Risner-Janiczek, **J.R. Holt**. Mechanotransduction and hyperpolarization-activated currents contribute to spontaneous activity in mouse vestibular ganglion neurons. *J. Gen Physiol* 143(4):481-97, 2014.

- 41) C. Askew, C. Rochat, B. Pan, Y. Asai, H. Ahmed, E. Child, B.L. Schneider, P. Aebischer, **J.R. Holt**. Tmc gene therapy restores auditory function in deaf mice. *Sci Transl Med.* 7(295), 2015.
- 42) K. Kurima, S. Ebrahim, B. Pan, M. Sedlacek, P. Sengupta, B.A. Millis, R. Cui, H. Nakanishi, T. Fujikawa, Y. Kawashima, B.Y. Choi, K. Monahan, **J.R. Holt**, A.J. Griffith, B. Kachar. TMC1 and TMC2 localize at the site of mechanotransduction in mammalian inner ear hair cell stereocilia. *Cell Reports* 12:1606-1617. 2015.
- 43) A. Imtiaz, A. Maqsood, A.U. Rehman, R.J. Morell, J.R. Holt, T.B. Friedman, S. Naz. Recessive mutations of TMC1 associated with moderate to severe hearing loss. *Neurogenetics* 17(2):115-23. 2016.
- 44) S.B. Shibata, P.T. Ranum, H. Moteki, B. Pan, A.T. Goodwin, S.S. Goodman, P.J. Abbas, **J.R. Holt**, R.J. Smith. RNA Interference Prevents Autosomal-Dominant Hearing Loss. *Am J Hum Genet* 98(6):1101-13. 2016.
- 45) X.P. Liu, K.R. Koehler, A.M. Mikosz, E. Hashino, **J.R. Holt**. Functional development of mechanosensitive hair cells in stem cell-derived organoids parallels native vestibular hair cells. *Nat Commun* 7:11508. doi: 10.1038/ncomms11508. 2016.
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- 47) Pan B, Askew C, Galvin A, Heman-Ackah S, Asai Y, Indzhykulian AA, Jodelka FM, Hastings ML, Lentz JJ, Vandenberghe LH, **Holt JR**, Géléoc GS. Gene therapy restores auditory and vestibular function in a mouse model of Usher syndrome type 1c. *Nat Biotechnol.* Mar;35(3):264-272, 2017.
- 48) Landegger LD, Pan B, Askew C, Wassmer SJ, Gluck SD, Galvin A, Taylor R, Forge A, Stankovic KM, **Holt JR***, Vandenberghe LH*. A synthetic AAV vector enables safe and efficient gene transfer to the mammalian inner ear. *Nat Biotechnol.* (3):280-284, 2017
*Co-senior author.
- 49) Gao X, Tao Y, Lamas V, Huang M, Yeh WH, Pan B, Hu YJ, Hu JH, Thompson DB, Shu Y, Li Y, Wang H, Yang S, Xu Q, Polley DB, Liberman MC, Kong WJ, **Holt JR**, Chen ZY, Liu DR. Treatment of autosomal dominant hearing loss by in vivo delivery of genome editing agents. *Nature.* 2018, 553(7687):217-221.
- 50) Taylor RR, Filia A, Paredes U, Asai Y, **Holt JR**, Lovett M, Forge A. Regenerating hair cells in vestibular sensory epithelia from humans. *Elife.* 2018 pii: e34817. doi: 10.7554/eLife.34817.
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- 52) Asai Y, Pan B, Nist-Lund C, Galvin A, Lukashkin AN, Lukashkina VA, Chen T, Zhou W, Zhu H, Russell IJ, **Holt JR**, Géléoc GSG. Transgenic Tmc2 expression preserves inner ear hair cells and vestibular function in mice lacking Tmc1. *Sci Rep.* 2018 Aug 14;8(1):12124.

- 53) Pan B, Akyuz N, Liu XP, Asai Y, Nist-Lund C, Kurima K, Derfler BH, György B, Limapichat W, Walujkar S, Wimalasena LN, Sotomayor M, Corey DP, **Holt JR**. TMC1 Forms the Pore of Mechanosensory Transduction Channels in Vertebrate Inner Ear Hair Cells. *Neuron*. 2018 99(4):736-753.
- 54) Nist-Lund CA, Pan B, Patterson A, Asai Y, Chen T, Zhou W, Zhu H, Romero S, Resnik J, Polley DB, Géléoc GS, **Holt JR**. Improved TMC1 gene therapy restores hearing and balance in mice with genetic inner ear disorders. *Nat Commun*. 2019 10(1):236.
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- 56) Thuronyi BW, Koblan LW, Levy JM, Yeh WH, Zheng C, Newby GA, Wilson C, Bhaumik M, Shubina-Oleinik O, **Holt JR**, Liu DR. Continuous evolution of base editors with expanded target compatibility and improved activity. *Nat Biotechnol*. 2019 Jul 22.
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Thesis

J.R. Holt (supervised by R.A. Eatock) The properties and functions of inwardly rectifying currents in leopard frog saccular hair cells. *University of Rochester*, 1995.

Patents / Inventions / Other Non-print Copyrighted Materials

2017	62455197	Materials and Methods for Delivering Nucleic Acids to Cochlear and Vestibular Cells.
2018	62638697	Compositions and Methods for Delivering Nucleic Acids to Cochlear and Vestibular Hair Cells.
2019	PCT/US17/20794	Efficient and specific gene delivery to inner ear sensory cells using AAV9-PHP.B to treat hearing and balance disorders.
2020	62/971,555	Dual AAV delivery of STRC for DFNB16 hearing loss
2020	PCT/US20/40608	Dual vector delivery with disrupt and replace strategy using saCas9-KKH to target dominant and recessive mutations.
2020	PCT/US20/40608	Use of CRISPR to Selectively Disrupt Dominant Mutations

Narrative Report – Research Contributions

My lab focuses on the function and dysfunction of mechanosensory hair cells in the inner ear. Our goal is to identify genes and proteins that contribute to normal hair cell function and to understand why mutations in those genes cause hearing and balance problems. We expect this information will form the foundation of future treatments designed to restore hearing and balance in deaf and dizzy patients. We use the mouse inner ear as a model and manipulate gene and protein activity using viral transfection, generation of transgenic, knock-out and knock-in mice and chemical-genetic approaches. Our technical strength is electrophysiological assays for changes in inner ear function. We are particularly interested in ion channels, myosin motors and

genes involved in hair bundle structure and function.

We pioneered the use of viral vectors to transfect and study hair cell function (Holt et al., 1999; Holt, 2002; Holt et al., 2007; Askew et al., 2015; Pan et al., 2017; Nist-Lund et al., 2019; Lee et al., 2020; Shubina-Oleinik et al., 2021; Marcovich et al., 2022). We have used the technique to introduce mutant potassium channels and identify the role of KCNQ genes in hearing and the dominant deafness, DFNA2 (Holt et al., 2007). We used the same vectors and modified culture techniques to show proof-of-concept transfer of exogenous genes into human hair cells *in vitro* (Kesser et al., 2007). We developed novel stimulation and recording techniques to study mechanotransduction in mouse cochlear hair cells (Stauffer and Holt, 2007) and used these techniques to demonstrate the function of two deafness genes, cadherin-23 and protocadherin-15, as tip-link molecules, required for hair cell transduction. We were the first to use a chemical-genetic strategy in the inner ear to demonstrate a role for myosin Ic in adaptation in vestibular hair cells (Holt et al., 2002; Stauffer et al., 2005). Perhaps most importantly, we identified the transmembrane proteins TMC1 and TMC2 as components of the elusive hair cell transduction channel (Kawashima et al., 2011; Pan et al., 2013), and provided the first definitive evidence that TMC1 forms the pore of sensory transduction channels in hair cells (Pan et al., 2018). Using viral delivery of wild-type TMC sequences, we showed the first ever restoration of mechanosensory transduction in genetically-impaired hair cells. We have used the technique *in vivo* and demonstrated restoration of auditory function in deaf mice, setting the stage for further development of gene therapy for recessive deafnesses, DFNB7/11 (Askew et al., 2015; Nist-Lund et al., 2019; Wu et al., 2021; Marcovich et al., 2022) and dominant deafness, DFNA36 (Gao et al., 2018; Gyorgy et al., 2019; Wu et al., 2021).

As such, our lab is one of few worldwide developing novel techniques for gene and protein manipulation followed by electrophysiological assays to study auditory function from the molecular and cellular level to the systems and behavioral levels. We aim to translate our basic science discoveries into gene therapy approaches for treating hearing and balance dysfunction.

Teaching Contributions

For three years I served as the course director for an introductory Neurobiology course, part of the core curriculum for first year students in the Neuroscience Graduate Program at UVA. I designed and coordinated the lecture material and schedule, led a diverse team of faculty, and introduced a literature discussion program that paralleled the lecture material. During my time as course director, the overall course evaluations rose from 2.7 to 3.8 (4-pt scale).

For 10 years BCH/HMS, I have been the director of the Cellular Neurophysiology section of the HST 130 / Neurobiology 200 comprehensive course on *Neuroscience*. In this capacity, I deliver 8 lectures, coordinate guest lectures and guide small group discussion sections for 30 HST MD students and 10 Ph.D. level graduate students per year.

One teaching contribution I am particularly proud of is the establishment of the *Biology of the Inner Ear* course at the Marine Biological Laboratories (MBL) in Woods Hole, MA. In 2007, co-course-director Jeff Corwin and I wrote and received an NIH/NIDCD grant to establish the course. The grant was renewed for six years beginning in 2009. The course has been running for over 15 years now and has shattered a number of MBL records, including most applicants for any MBL course and largest NIH grant to fund an MBL course. By bringing lead scientists from around the world to the MBL for an intensive 3-week course, we offer students an unprecedented opportunity for hands-on learning about the inner ear, thereby providing them an elevated platform to launch careers in hearing and deafness research. Numerous graduates from the course have gone on to successful careers in academics and industry.