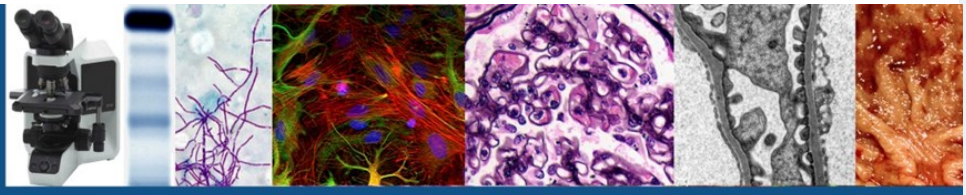
THE PATH WAY

June 2015 **Volume 6, Issue 2**

MUSC
MEDICAL UNIVERSITY of SOUTH CAROLINA



DEPARTMENT of PATHOLOGY & LABORATORY MEDICINE

Steven L. Carroll, M.D., Ph.D.

Inside this issue:

SEAPC

SOUTHEASTERN ASSOCIATION OF PATHOLOGY CHAIRS AND ADMINISTRATORS REGIONAL CONFERENCE

OCTOBER 7-9, 2015
CHARLESTON, SC

WEBSITE LINK:
https://www.musc.edu/pathology/SEAPC/

This newsletter is made possible from the generous contributions of MUSC's Pathology and Laboratory Medicine Faculty and Staff. The success of this publication is dependent upon this support. Thank you for your interest, time and information. For inquiries, suggestions or submission information please contact Lori Roten (roten@musc.edu).

CONGRATULATIONS!

Dr. Steven Carroll, Professor and Chair of Pathology and Laboratory Medicine has been elected to a four-year term as Councilor of The Histochemical Society (2015-2019)

CONGRATULATIONS!

Dr. Dennis Watson on being selected as a recipient of the 2015 Peggy Schachte Research Mentor Award. This award was established to recognize individuals who have excelled in mentoring faculty in obtaining research support from private and public organizations or government agencies, and targets faculty mentor or other colleague who encourages and supports the advancement of others as successful extramurally funded investigators.

CONGRATULATIONS to Dr. Yusheng Zhu!

Dr. Yusheng Zhu received the American Association for Clinical Chemistry Point-of-Care Testing research grant

CONGRATULATIONS to Dr. Julie Woolworth!

Dr. Julie Woolworth was voted as one of the top 10 instructors by the Graduate Students in the College of Graduate Students

Congratulations to Dr. Evelyn Bruner!

Dr. Evelyn Bruner, faculty in our Department of Pathology and Laboratory Medicine, was recently recognized by the American Society for Clinical Pathology as one of their "40 Under Forty" honorees for 2015.
Please join us in congratulating Dr. Bruner on this accomplishment.

CONGRATULATIONS!

Dr. Spyropoulos for the following research articles:

Oil spill study raises 'red flag' about commonly-used compound

http://academicdepartments.musc.edu/pr/newscenter/2015/DOSS-study-endrocrine-disruptors.html#.VZVhjijs624

&

Effects of Crude Oil/Dispersant Mixture and Dispersant Components on PPARγ Activity *in Vitro* and *in Vivo*: Identification of Dioctyl Sodium Sulfosuccinate (DOSS; CAS #577-11-7) as a Probable Obesogen

http://ehp.niehs.nih.gov/1409672/#tab1

Sara Faulks

CONGRATULATIONS!!

AS THE RECIPIENT OF THE 2014-2015

THOMAS W. HOLBROOK AWARD

This award is presented to a student who, in their second year, demonstrated excellence in their academic performance in Pathology and Laboratory Medicine, Microbiology and Immunology.

CONGRATULATIONS TO DANIEL WEINBERG!!

AS THE RECIPIENT OF THE 2014-2015

SANDY NELSON MEMORIAL AWARD:

EXCELLENCE IN COMMUNITION

This award is in honor of Ms. Sandy Nelson, the COM2 Administrative Coordinator who affected over 25 classes of medical students and doctors with her character, poise, and passion, until her untimely death in July 2014. She was the ultimate student advocate, tirelessly working behind the scenes on behalf of the students. Her ability to effectively communicate with and between students and faculty earned her eight student Golden Apple Special Recognition Awards. The award is presented to a COM3 or COM4 student who has demonstrated excellence in communication, acting as a mediator or arbitrator in the pursuit of improving medical education.

CONGRATULATIONS to Tiffany Baker and Kendall Brewer!

Tiffany Baker (1st year Resident) and **Kendall Brewer** (1st year Resident) have been recognized by the American Society for Clinical Pathology (ASCP) for their excellence.

Tiffany Baker was selected as the 2015 Gold Recipient of the ASCP Academic Excellence and Achievement in Pathology Award
and
Kendall Brewer was selected as a recipient of the ASCP Academic Excellence and Achievement in Pathology Award.

CONGRATULATIONS to Jonathan Gullett!

Jonathan Gullett, M.D. won the Southeast Section of the American Association for Clinical Chemistry Gerald R. Cooper

CONGRATUATIONS to our Residents!

Our residents were in the top four residencies to respond to the AHRQ Safety Culture survey.

- General Dentistry
- Peds Dentistry
- Pathology
- OB/GYN

CONGRATULATIONS to Beth Hansell!

Beth Hansell, Department Administrator, has been elected to a six year term as Chair-Elect, Chair, and past Chair
for the Pathology Department of Administrators Section (PDAS)
of the Association of Pathology Chairs (APC)

CONGRATULATIONS to all of our 2014-2015 4th year residents!!!

Shannon Butler-Williams, MD, Sherry Okun, MD, Tiffany O'Neill, DO,
Kirtesh Patel, MD and Tom Soike, MD passed their boards.

CONGRATULATIONS to Angelina Phillips!

Angelina Phillips, M.D, our 2015-2016 Forensic Pathology Fellow has passed the AP and CP portions of her Pathology board examination!

Lowcountry Heart Walk

Saturday, October 3, 2015 at 9 am

Amy Haynes is the Team Captain
for Pathology and Laboratory Medicine

MORE INFORMATION TO COME AS CONFIRMED VIA EMAIL

GRADUATE STUDIES UPDATE

STUDENTS DEFENDED:

- ◊ **Dayvia Laws (Dr. LaRue) successfully defended MS on March 10, 2015**
- ◊ **Jamie Mills (Dr. Ethier) successfully defended her PhD thesis on March 16, 2015**
- ◊ **Katie Wilson (Dr. LaRue) successfully defended MS on March 17, 2015**
- ◊ **Ryan Kelly (Dr. LaRue) successfully defended PhD on March 31, 2015**
- ◊ **Qi Guo (Dr. Findlay) successfully defended MS on April 8, 2015**
- ◊ **Katie Walter (Dr. Turner) successfully defended MS on May 8, 2015**

- ♦ **IDP after admission to candidacy and annually thereafter (PhD Students)**

IDP weblink is active:
http://academicdepartments.musc.edu/grad/students/curr_students/IDP%20Policy_091614.pdf

UPCOMING DATE

- ♦ Pathology Research/Exposure Day
  Thursday, August 27th (afternoon 2-5 pm) in the Drug Discovery Lobby

COUNCIL NEWS

- ♦ **GCS Curriculum Committee is reviewing all existing courses approved before 2010**
- ♦ **Nominations for faculty representative for CGS Honor Council are still open. This is on an as needed basis**

ARRIVALS / DEPARTURES

ARRIVALS:

- ♦ **Dr. Hoon Jae Jeong, Post Doc Scholar arrived on 5/18/15 in Dr. Singh's lab**
- ♦ **Norma Evans, Administrative Coordinator 1 arrived on 7/1/15 in Anatomic Pathology**
- ♦ **Stuart Worley, Research Specialist I arrived on 6/1/15 in Dr. Carroll's lab**
- ♦ **Amy Haynes, Grants Administrator I arrived on 7/1/15 in the Business Office**
- ♦ **Uday Baliga, Research Specialist I arrived on 7/13/15 in Dr. Mehrotra's lab**

DEPARTURES:

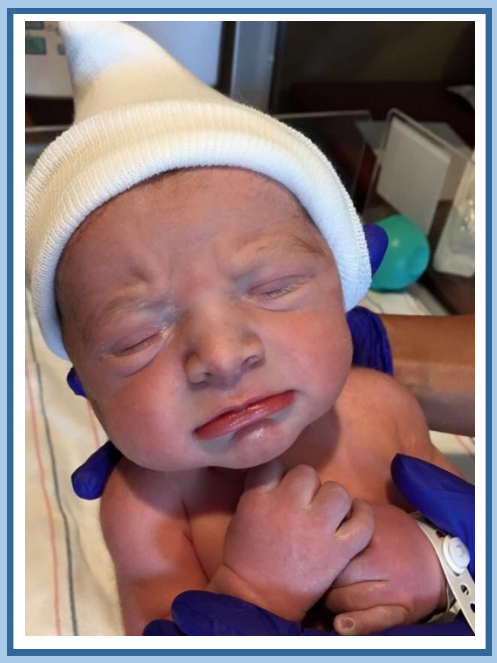
- ♦ **Kevin Hildreth left as Grants Administrator I on 5/22/15**
- ♦ **Dr. Balasubramanaim transferred to Othalmology on 5/31/15 from Dr. Singh's lab**

CONGRATULATIONS!

TO: Courtney McFaddin, M.D. and her husband

IT'S A BOY!

Westin Lee McFaddin arrived on June 16, 2015
7 lbs. 6 oz.



TO: Natalie Matics, M.D. and her husband

IT'S A BOY!

Calvin Alexander Matics arrived on
July 19, 2015
6 lbs. 7 oz.

2014-2015 END OF THE YEAR AWARDS

RESEARCH DIVISION UPDATE

Statistics for the Division of Research from April through June.
Ten grant proposals were submitted requesting $1,675,205
in total first year costs.
Also, during this period seven grants were awarded totaling $993,040.

Bradley Schulte, Ph.D., Vice Chair of Research

SUBMITTED 4/1/15 – 6/30/15:

Steven L. Carroll, M.D., Ph.D.
Title: Combinatoreal therapy with receptor Tyrosine Kinase Inhibitors for Malignant Peripheral Nerve Sheath Tumors $85,000 - Proposed Start Date 7/1/2015

Steven L. Carroll, M.D., Ph.D.
Title: Prevention and Treatment of Neurofibromatosis Type 1 -Associated Malignant Peripheral Nerve Tumors $36,007 - Proposed Start Date 4/1/2015

LaShardi Conaway-Ph.D. Candidate
Title: The Aging Ear: Macrophage Dysfunction in Auditory Nerve Degeneration $5,000—Proposed Start Date 5/18/15

Victoria Findlay, Ph.D.
Title: MicroRNA as Biomarkers of Response to Platinum-Based Chemotherapy $371,473-Proposed Start Date 4/1/16

Hainan Lang, Ph.D.
Title: Auditory Nerve Degeneration and Repair $373,750-Proposed Start Date 7/1/15

Amanda LaRue, Ph.D.
Title: Disaccharide cryopreservation strategies for hematopoietic stem cells $50,000-Proposed Start Date 8/1/16

Meenal Mehrotra, M.D., Ph.D.
Title: Role of HSCs in Establishing the Osteosarcoma Microenvironment $198,000-Proposed Start Date 1/1/16

Jamie Mills-MD, PhD Candidate
Title: Investigating the Oncogenic Role of WHSC1L1 in Breast and Lung Cancer Cells Bearing the 8p11-p12 Amplicon $45,283-Proposed Start Date 9/1/15

Avtar Singh, M.D.
Title: Nitri Oxide Mechanisms and Therapy in Alzheimer's disease $458,176 – Proposed Start Date 4/1/16

Demetri Spyropoulos, Ph.D.
Title: Viable Lung Tissue Cryopreservation Technology $52,516 – Proposed Start Date 9/1/15

AWARDED 1/1/15-3/31/15:

Steven L. Carroll, M.D., Ph.D.
Title: Combinatoreal therapy with receptor Tyrosine Kinase Inhibitors for Malignant Peripheral Nerve Sheath Tumors $85,000 - Awarded Date 7/1/2015

Steven L. Carroll, M.D., Ph.D.
Title: Prevention and Treatment of Neurofibromatosis Type 1-Associated Malignant Peripheral Nerve Tumors $36,007 - Awarded Date 4/1/2015

LaShardi Conaway-Ph.D. Candidate
Title: The Aging Ear: Macrophage Dysfunction in Auditory Nerve Degeneration $5,000 - Awarded Date 5/18/15

Hainan Lang, Ph.D.
Title: Auditory Nerve Degeneration and Repair $373,750-Awarded Date 7/1/15

John Lazarchick, M.D.
Title: VSP P391-US/A Rivaroxaban Calibrator & Control $30,182-Awarded Date 4/23/15

Avtar Singh, M.D.
Title: Mechanisms of Krabbe Disease Pathobiology and Therapy $322,656 – Awarded Date 4/1/15

David Turner, Ph.D.
Title: PQ3: AGEs and Race Specific Tumor Immune Response in Prostate Cancer $140,445 - Awarded Date 5/6/15

FACULTY FOCUS

Bart M. G. Smits, Ph.D.

Adventures in Life (and) Science

The essence of science is making discoveries by observation and experimentation. Majoring in biology at Utrecht University, I discovered that I always scored high grades in any subject dealing with DNA. Therefore, I chose to specialize in molecular genetics. Throughout my training I have done genetics experiments using a variety of model organisms, ranging from invertebrates such as yeast and worms to vertebrates such as zebrafish and mice. These were exciting times, as sequencing technologies became advanced enough to result in complete genome sequences for many model organisms. This facilitated the design of strategies to manipulate the sequence of genes of our interest to study their function. While for many model organisms such gene targeting technologies were becoming routinely available, genetics approaches were largely lacking for one of the most widely used model organisms, namely the laboratory rat. The availability of gene targeting in embryonic stem (ES) cells resulted in the popularity of the mouse as a mammalian genetic model organism, but ES cells were not available for rats. As a graduate student I decided to join the Hubrecht Institute for Developmental Biology and Stem Cell Research focusing on pioneering novel genetics strategies for the rat, including gene knockout technology. Due to the lack of ES cells, we developed an alternative knockout strategy making use of the DNA-alkylating agent *N*-ethyl-*N*-nitrosourea (ENU). Male rats were treated with ENU to randomly mutagenize their germ line. When mated with untreated females, this procedure resulted in mutant rat progeny harboring induced heterozygous point mutations with a frequency of 1 in $2x10^6$ base pairs. Using robotics and the newest high-throughput (Sanger) sequencing technologies at that time period, I screened thousands of mutant rats for induced mutations in genes of our interest, hoping that some mutations would be nonsense. In this way, we produced the first knockout rats worldwide for genes of interest to neurobiology researchers.

The laboratory rat has been widely used for neurobiology, physiology and drug testing. However, not many researchers know that the rat is the preferred rodent model for human breast cancer. Rat mammary carcinomas closely resemble characteristics of the most common form of human breast cancer, namely the hormone-dependent luminal-A subtype. After obtaining my Ph.D. degree, I decided to pursue a postdoc at the University of Wisconsin-Madison focusing on rat-human comparative genetics approaches to discover loci involved in the susceptibility to breast cancer. Using positional cloning approaches to map genetic elements involved in mammary cancer susceptibility, we discovered that most of the rat loci were located in non-protein coding areas of the genome. With the publication of genome-wide association studies for human breast cancer susceptibility it became evident that the vast majority of human breast cancer-associated genetic elements are also located in non-protein coding genomic regions. It is still largely unknown how these loci affect risk to develop breast cancer, but is highly likely that the regulation of gene expression is involved.

During my job hunt for faculty positions back in 2012, Dr. Ethier spearheaded my recruitment to MUSC and our Department. After starting my lab in January 2013, I have been able to combine both my graduate and postdoctoral training into our research strategies, since we use novel rat and mouse models for non-protein coding human breast cancer loci for mechanistic studies on breast cancer prevention and intervention. Already we can see clear advantages of targeting non-protein coding genetic elements, as our mutants do not show lethality in homozygous state and are mostly free of deleterious pleiotropic effects that frequently occur in mammalian gene knockout models. Importantly, these mutations do have anti-breast cancer abilities, which shows great promise for the development of therapeutic strategies without side effects.

My (rather short) scientific career so far has been a great adventure. I consider it an adventure to dive into the great unknown of non-protein coding areas of the genome. For example, in close collaboration with the Gene Function Core facility, we have established rat knockout technology here at MUSC last year. We are using the recently discovered CRISPR-Cas9 genetic engineering strategy to make non-protein coding mutations in the rat genome at sites important for human breast cancer susceptibility. It will be a great adventure to characterize these rats and discover novel mechanisms to help eradicate human breast cancer.

As many of you will be aware, a career as a scientist also creates adventures on the personal level. I was born and raised in a small Dutch city called Roosendaal (Rosevalley), about 3 miles from the Belgian border. To pursue my undergrad and graduate studies, I lived in Utrecht for over 9 years. That was already pretty wild considering that my entire extended family lived (and still lives) in Roosendaal, about 90 minutes south of Utrecht. But science took me across the Atlantic to the United States. Me, my wife and our dog arrived in Madison, WI in 2006. We lived there for 7 years and I can highly recommend it. We found Madisonians to be very friendly and hospitable. In addition, I was able to ride my bike (almost) year round and speed-skate on the lakes every winter! No one will hear me complain about the WI climate after living in The Netherlands having to endure mild and rainy winters, as well as mild and rainy summers. Madison will always be special to us, because our son Xem (now almost 9) and our daughter Sterre (now almost 6) were born there.

Then, science spun the wheel-of-fortune again and we hit the jackpot with Charleston. I feel really fortunate that my wife is willing to move with me time after time. Currently, my family is happily living on James Island and enjoying the beach life, fishing, playing soccer and not having to worry about a snowsuit. Charleston and MUSC have been extremely welcoming to us and we hope to enjoy staying here for a long time to come.

Bart M. G. Smits, PhD

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Pathology IT News - MUSC's New Laptop Encryption Policy

By: Tony Eisenhart

MUSC's data needs protection wherever it goes. Computing equipment and other endpoint devices used for sensitive MUSC business – including computers, smartphones and tablets – must be configured to provide that protection. In 2012, the Office of the CIO began a multi-pronged approach to securing MUSC data which accessed or stored data on portable devices. The first phase was securing smartphones and tablets using Mobile Device Management (MDM). The second phase was the implementation of Two Factor Authentication (2FA). Phases one and two have been successfully completed and we now begin the third phase: Encrypting data on laptop computers.

The South Carolina Department of Information Security has mandated that **all entity owned laptops** be encrypted. MUSC disk encryption project will comply with this new standard by protecting MUSC data on laptop computers using NIST-approved encryption of the hard disk. Encrypting the data stored on laptop computers is the single most important step we can take to protect MUSC's data in the event the device is lost or stolen.

The MUSC Disk Encryption service is for both Windows and Macintosh laptop computers that run a supported operating system and version. This service secures data using standard NIST-Approved encryption of the computer hard disk. Once installed, all files are automatically encrypted. The data is protected while the computer is in standby or hibernation mode as long as the hard disk is password protected.

HOW & WHAT IT PROTECTS OR PREVENTS

Encryption is a method for garbling data so it cannot be accessed without a key or password. It protects data from unauthorized access. In the event it is lost or stolen. If someone tries to break into your system or remove your hard drive to retrieve files, they will not be able to access the computer and/or the data.

WHAT IT DOES NOT PROTECT OR PREVENT

The MUSC Disk Encryption service is limited to protecting the files while they are on your laptop computer. It does not provide encryption of files that are sent via email; Kept on a separate flash drive/thumb drive/USB drive/floppy disk; or protect data being moved over the network via shared folders. When you move an encrypted file off of your computer, it is no longer encrypted.

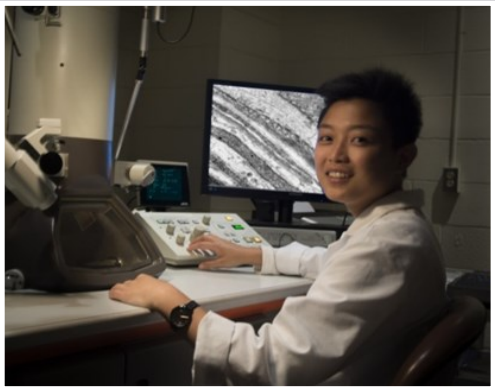
WHAT IS RESTRICTED INFORMATION

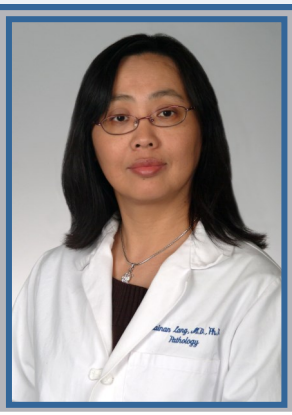
"Restricted Information" (as defined by UC Policy IS-3, Electronic Information Security) describes any confidential or Personal Information that is protected by law or policy and that requires the highest level of access control and security protection, whether in storage or in transit. This includes Personal information, PHI and ePHI but could also include other types of information such as intellectual property, proprietary information, research protocols, research results, student information, animal research information, passwords, and other confidential information that could damage the reputation of the institution.

Our patients, employees, students, research subjects and others trust us to protect their sensitive data. Federal and state laws require protection for some kinds of restricted information and may require notification if there is unauthorized access to restricted information. Failure to protect sensitive data can cause reputational, financial and legal harm to the university. There are also substantial financial penalties that the University, the Medical Center and/or the Physicians group could accrue for failing to protect Restricted Information.

Health Insurance Portability and Accountability Act (HIPAA), 45 CFR 160-164
South Carolina DIS Information Security Policy – Mobile Security
FERPA (Family Educational Rights Privacy Act)

Over the next few months you can expect to be contacted by a member of the Pathology & Laboratory Information Services Team who will assist you in complying with this new policy. If you wish to be proactive and encrypt your MSUC owned laptop on your own, or would like to read more about this new policy, please follow the below link.
https://sp.musc.edu/ocio-is/infrastructure/est/Pages/laptopencryption.aspx
(Log in with your MUSC NET ID credentials)





The Nodes of Ranvier

- A Different Focus on Auditory Nerve Development and Degeneration

By: Clarisse H. Panganiban / Mentor: Hainan Lang, M.D., Ph.D.

Nodes of Ranvier are unmyelinated gaps between myelin sheaths and contain clusters of ion channels that are necessary for fast saltatory conduction throughout the nerve fibers. In the peripheral auditory nerve, they are located along the myelinated type I afferent fibers, which make up more than 95% of the nerve and innervate the inner hair cells responsible for most of the sensory transduction of sound stimuli [1]. The node of Ranvier contains clustering proteins necessary for constraining the ion channels within the nodes and are bordered on either side by paranode junctions, where the myelin layers terminate and form axo-glial connections with the axolemma [**Figure 1**]. The flanking paranodes act as diffusion barriers to keep the node proteins clustered within the node region and separate from the rest of the axonal domains in order to maintain proper conduction [2]. Needless to say, the nodes play an integral role in high velocity action potential propagation from the very distal end of the peripheral auditory nerve and ultimately to the auditory cortex for processing.

To date, there are only a handful of papers focusing on the nodes of Ranvier and flanking nodal segments in the auditory system, much less in the peripheral auditory nerve. Not much is known about how nodal development contributes to auditory nerve development, hearing onset, and further maturation, or how nodal degeneration may contribute to age-related declines in hearing function. One of the few studies questioned the effects of acoustic over-exposure on auditory nerve nodal structural integrity and its relationship with the subsequent loss of function. It was found that acoustic over-exposure in mice lead to the elongation of the nodes that corresponded to significant reduction in auditory brainstem response [3]. A consequent study found that node of Ranvier elongation and abnormal ion channel localization within the node may be fundamental in precipitating the decreases in conductivity and overall auditory brainstem response [4]. Furthermore, previous nodal studies in the sciatic nerve point to the loss of important nodal cellular adhesion molecules, which are responsible for nodal ion channel clustering and paranodal integrity, as causative of slowed nerve conduction velocity and decreased excitability [2, 5]. It is therefore a goal of the project to determine the contribution of nodal functional and structural development to postnatal hearing onset, and the causal relationship between nodal degeneration and age-related auditory nerve function declines.

In mice, the onset of hearing occurs at approximately postnatal days (P) 12-14, around the time the ear canals open and spontaneous activity is replaced by stimulus-dependent response of the cochlea [6]. Enhanced auditory brainstem response is then seen from P14 to P15, post hearing onset [7]. Multidisciplinary studies have been done in collaboration with Dr. Jeremy L. Barth at the MUSC Proteogenomics Facility and Ms. Nancy Smythe at the Electron Microscopy Laboratory, along with the help of members of the Lang Lab, especially Dr. Yazhi Xing and LaShardai Brown. We used our mouse auditory nerve microarray to analyze the expression profiles of node-related genes within the developmental time period, P0-21, and further validated our findings via immunohistochemistry of cochlear sections. We found that nodal structural development follows a staged progression - from the initial formation of the nodes of Ranvier at around P0-P3, followed by the formation of flanking paranodal junctions from P7, and the emerging prevalence of the major nodal sodium channel, $Na_v1.6$, responsible for action potential propagation of mature nerves by P14 [**Figure 2**]. The completion of the node-paranode structure and abundance of nodal $Na_v1.6$ by P14 is important in contributing to the onset of hearing and further enhancement of auditory function.

Mouse models of aging show declines in auditory brainstem response at 1.5 years and neuron and sensory hair cell loss by 2 years. Previous nodal studies in the optic nerves of aged rats and monkeys presented the mislocalization of paranodal cellular adhesion molecules, which are necessary for the axo-glial connections, in the aged nodes versus the young controls [8]. Their research was suggestive of cognitive decline in these aged animals. Our immunohistochemical and ultrastructural analyses of the 2 year-old mouse auditory nerves show disruption of the node-paranode structure [**Figure 3**], with a trend towards node of Ranvier elongation, in aged animals compared to the young-adult controls. Our studies are indicative of a link between nodal deterioration and age-related hearing loss.

Keeping in mind the importance of nodal and paranodal cellular adhesion molecules for maintenance of proper electrical function, future studies will question the effects of genetic mutation models of these molecules on auditory nerve development and hearing onset. Functional analysis of the nodes of Ranvier during the different stages of postnatal development and later, in aged versus young-adult auditory nerve to validate the importance of nodal structural maturation and maintenance for normal auditory processing will also be a main focus. Our research project was partially supported by NIH R01 DC7506, NIH P50 DC0422, and NIH R25 GM072643.

References:

1. Purves D. Neuroscience. Sinauer Associates Incorporated; 2001.
2. Boyle ME, Berglund EO, Murai KK, Weber L, Peles E, Ranscht B. Contactin orchestrates assembly of the septate-like junctions at the paranode in myelinated peripheral nerve. Neuron. 2001;30(2):385-97.
3. Tagoe T, Barker M, Jones A, Allcock N, Hamann M. Auditory nerve perinodal dysmyelination in noise-induced hearing loss. J Neurosci. 2014;34(7):2684-8.
4. Brown AM, Hamann M. Computational modeling of the effects of auditory nerve dysmyelination. Front Neuroanat. 2014;8:73.
5. Amor V, Feinberg K, Eshed-eisenbach Y, et al. Long-term maintenance of Na+ channels at nodes of Ranvier depends on glial contact mediated by gliomedin and NrCAM. J Neurosci. 2014;34(15):5089-98.
6. Safieddine S, El-amraoui A, Petit C. The auditory hair cell ribbon synapse: from assembly to function. Annu Rev Neurosci. 2012;35:509-28.
7. Song L, Mcgee J, Walsh EJ. Frequency- and level-dependent changes in auditory brainstem responses (ABRS) in developing mice. J Acoust Soc Am. 2006;119(4):2242-57.
8. Hinman JD, Peters A, Cabral H, et al. Age-related molecular reorganization at the node of Ranvier. J Comp Neurol. 2006;495(4):351-62.

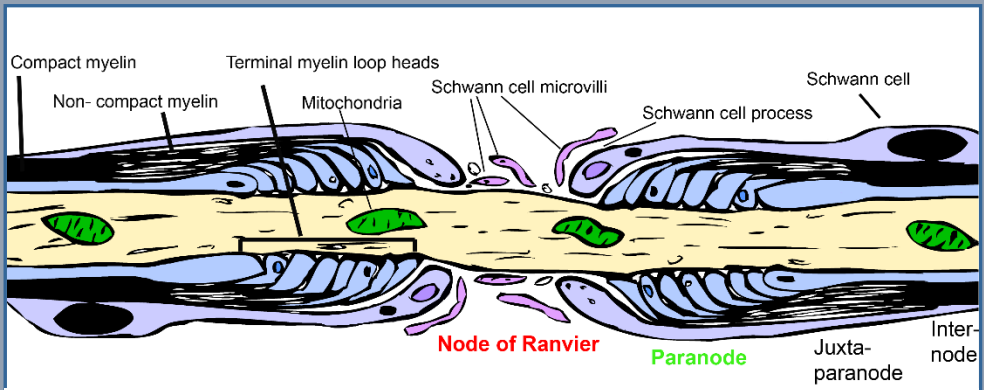


Figure 1. Schematic of nodal structural components in type I afferent auditory nerve fiber

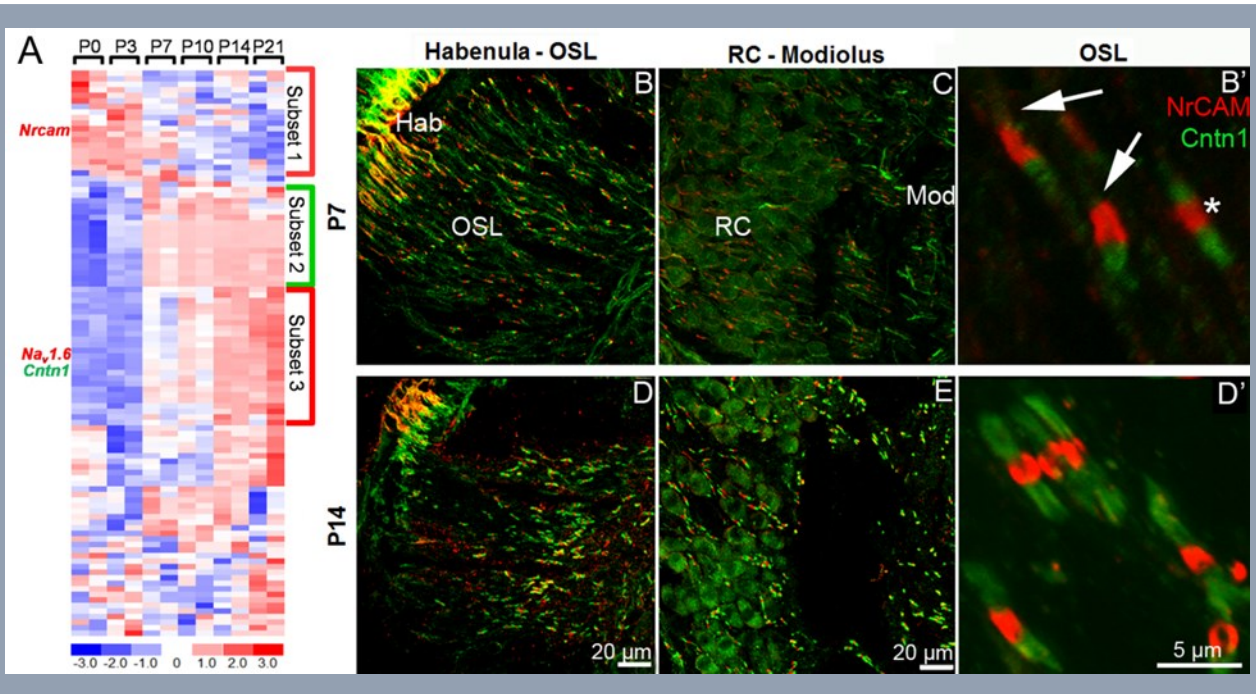


Figure 2. Nodal molecular and structural development in mouse postnatal auditory nerve

A. Heat map of node-related genes shows a staged progression of node development, beginning with early node formation at P0-P3, paranode formation starting at P7, and up-regulation of mature $Na_v1.6$ by P14. **B-E.** Immunoreactivity of nodal cellular adhesion molecule **NrCAM** and paranodal cellular adhesion molecule **Cntn1** at habenula (hab), osseous spiral lamina (OSL), Rosenthal's canal (RC), and modiolus (mod) at P7 and P14. **B'.** Incomplete OSL nodal structures at P7. Arrows show nodes that are not fully flanked by two paranodes. Asterisk shows complete node-paranode structure. **D'.** Complete OSL node-paranode structures at P14.

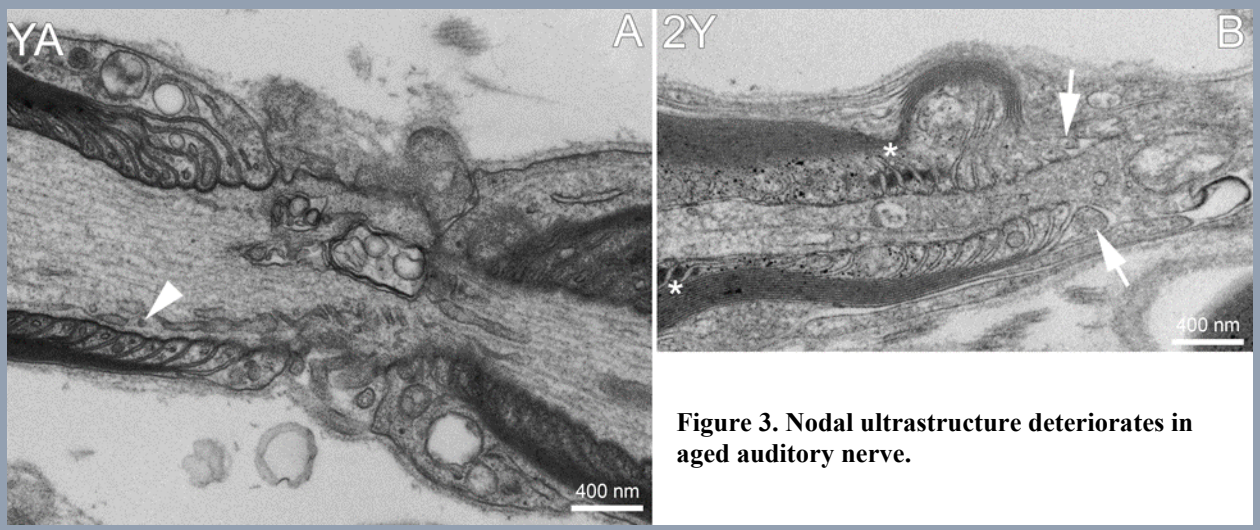


Figure 3. Nodal ultrastructure deteriorates in aged auditory nerve.

A. Electron micrograph of an auditory nerve nodal ultrastructure of a young-adult (YA) mouse. The unmyelinated node of Ranvier is fully flanked by adjacent paranodes. Arrowhead shows well-organized myelin loops terminating at the paranodal axolemma region. **B.** 2 year-old (2Y) mouse nodal ultrastructure. Arrows point to myelin loops failing to terminate at the paranodal axolemma. Asterisks emphasize changes in myelin loop architecture.

UPCOMING MEETINGS

- **ASCP / AFP - (American Pathology Foundation) Meeting, October 28-30, 2015**
- **SNO - Society for NeuroOncology Meeting, November 19 - 22, 2015**

NEXT ALL HANDS MEETING

WEDNESDAY, SEPTEMBER 16,2015

DEPARTMENT HOLIDAY CELEBRATION

AT THE SC AQUARIUM

ON DECEMBER 11, 2015

MUSC Department *of* Pathology & Laboratory Medicine Mission Statement:

To serve patients, health care providers, research scientists, scholars, and society by providing excellence and innovation in diagnostic services and educational resources in a respectful, professional and culturally diverse atmosphere.

Vision:
To become a preeminent leader in academic anatomic and clinical pathology while translating basic science discovery to improved clinical care.

www.musc.edu/pathology