ASSOCIATION FOR RESEARCH IN OTOLARYNGOLOGY

FOUNDED IN 1973

ABSTRACT BOOK

40th Annual MidWinter Meeting

February 11 - 15, 2017

Baltimore Marriott Waterfront
Baltimore, MD

ARO OFFICERS FOR 2016-2017

PRESIDENT:

Matthew W. Kelley. PhD (16-17)
NIDCD/NIH-Porter Neuroscience Research Center
Building 35, Room ID-993, 35 Convent Drive
Bethesda, MD 20892 USA

PRESIDENT ELECT:

John P. Carey, MD (16-17)
Johns Hopkins School of Medicine
Department of Otolaryngology-HNS
601 North Caroline Street, Room 6255
Baltimore, MD 21287-0910 USA

PAST PRESIDENT:

Lawrence R. Lustig, MD (16-17)
Columbia University Medical Center
Department of Otolaryngology-HNS
Harkness Pavillion, Suite 818
180 Fort Washington Avenue
New York, NY 10032 USA

SECRETARY/ TREASURER:

Elizabeth S. Olson, PhD (14-17)
Columbia University
Otolaryngology & HNS
630 West 168th Street
New York, NY 10032 USA

EDITOR:

Barbara G. Shinn-Cunningham, PhD (15-18)
Boston University
Center for Computational Neuroscience & Neural Technology
677 Beacon Street
Boston, MA 02215 USA

HISTORIAN:

David J. Lim, MD
UCLA Geffen School of Medicine
Department of Head & Neck Surgery
1000 Veterans Ave, Rm 31-27
Los Angeles, CA 90024

COUNCIL MEMBERS AT LARGE:

Shi Nae Park, MD, PhD (16-19)
Professor, Dept of Otolaryngology – HNS
Seoul St. Mary's Hospital
The Catholic University of Korea
College of Medicine
505 Banpo-dong, Seocho-su
Seoul, Lorea 137-040

Sharon G. Kujawa, PhD (14-17)
Massachusetts Eye and Ear Infirmary
Department of Otology and Laryngology
243 Charles Street
Boston, MA 02114 USA

Jennifer S. Stone, PhD (15-18)
Research Associate Professor
Department of Otolaryngology
VM Bloedel Hearing Research Center
CHDD CD 176 Box 357923
University of Washington
Seattle, WA 98195 USA

ARO Executive Director:

Haley J. Brust
Talley Management Group
19 Mantua Road
Mt. Royal, NJ 08061 USA
Ph: 1 (856) 423-7222 Ext. 103
Fax 1 (856) 423-0041
Email: hbrust@talley.com
headquarters@aro.org

ABSTRACTS OF THE 40TH ANNUAL MIDWINTER MEETING OF THE

Welcome to the 40th Annual ARO Midwinter Meeting, being held for the sixth time at the Marriott Waterfront in Baltimore, Maryland. This year's meeting includes a record 1096 submitted abstracts, 13 symposia and 23 podium sessions. In addition, there will be daily mentoring sessions (*Saturday, Sunday, Monday, 4:00pm -5:00pm and Tuesday, 12:15-1:30 pm*) and workshops aimed at providing new investigators with valuable tools for career success. Credit for the organization of all these activities into a well-coordinated and exciting meeting goes to Ruth Litovsky and the other members of the Program Committee. Their exemplary efforts in this regard cannot be underestimated.

The **Presidential Symposium** (*Saturday 8:00am – 12:15pm*), "Big data from tiny samples; using comprehensive molecular profiling to understand development" will examine new technologies that are rapidly changing the scope of our ability to characterize the state of individual cells. Specific presentations will discuss the use of RNA sequencing, from both single cells and populations of cells, to generate comprehensive mRNA profiles of different development processes and the use of ATAC-Seq and other novel technologies to characterize epigenetic landscapes. Additional talks will discuss advances in the use of Mass Spectrometry to profile protein expression in single cells and examine the use of all these techniques to build a comprehensive understanding of cell and organ development.

Two separate Symposia will honor the lives and contributions of John Niparko (*Tuesday, 10:15 am – 12:15 pm*) and Norman Weinberger (*Monday, 8:00 am-10:00 am*), who both passed away in 2016.

For trainees, spARO will hold a **Town Hall Meeting** on *Saturday, 5:00-6:00 pm* and a **spARO Social** at Heavy Seas Alehouse, 1300 Bank Street, Baltimore also on *Saturday at 8:30 pm*.

At the **ARO Business Meeting** (*Sunday 6:00pm-7:00pm*), we will present an update on the state of the Association, transfer leadership from the 2016 Council to the 2017 Council, including the new President, Dr. John Carey, and hand out prizes – which you can enter to win when you visit the exhibits.

The External Relations Committee has arranged two very exciting events. First, on *Friday* evening (*7:30 pm-9:30 pm*), in conjunction with Project Bridge, there will be a **Baltimore Science Café** featuring talks from Drs. Karen Avraham, Dan Polley and Phillip Alvelda. This event will be held at Homeslyce at 3336 North Charles Street in Baltimore. Then, on *Sunday* evening at *7:30 pm*, following the Business Meeting, Mr. Vint Cerf, Vice President and Chief Internet Evangelist at Google will present the **ARO Public Lecture** entitled "The Power of Technology to Heal and Enhance". This presentation will take place in the Harborside Ballroom at the Baltimore Marriott and was arranged in honor of John Niparko.

At the **Awards** ceremony (*Monday 6:00 - 7:30 pm*) and reception (*7:30-8:30 pm*), we will honor individuals that have contributed to auditory research in different ways. These include the **Geraldine Dietz Fox Young Investigator Award**, a special recognition for the important contributions of Drs. Art Popper and Richard Fay as Editors of the long-running and highly successful Springer Handbook of Auditory Research series, and the **ARO Award of Merit** which will be conferred on **Dr. Alan Palmer** for his pioneering research in auditory processing.

Finally, the ever-popular **Hair Ball** (*Tuesday 8:00 pm –12:00am*) returns with live music by the *Rollex Band*. This event began in 2006 as a maverick "Patch-Clampers Ball" instigated by Bill Roberts, Mark Rutherford and Paul Fuchs, but has grown to be one of the most fun traditions of the Midwinter Meeting.

The success of each Midwinter Meeting depends on the hard work and innovative contributions of the many ARO members who serve on different committees, in particular the Program and External Relations Committees, and on the energetic and professional assistance provided by the staff at Talley Management. Without their combined efforts, the Midwinter Meeting could not continue to be the outstanding event that is has become. But because we can always do better, please help us continue to improve by responding to a survey you will be sent after the meeting. We absolutely listen to the likes and dis-likes of the attendees. Also, if you aren't a member of ARO, please consider joining, and if you are already a member, consider becoming a member of one of our committees. This is your best opportunity to play a role in the direction of the Midwinter Meeting and the ARO. Learn more at "About Us" at www.aro.org for options or contact headquarters@aro.org to volunteer.

Best wishes for a productive and enjoyable meeting,

Matthew Kelley
ARO President, 2016-2017

CONFERENCE OBJECTIVES

At the conclusion of the MidWinter Meeting, participants should be better able to:

- Explain current concepts of the function of normal and diseased states of the ear and other head and neck structures
- Recognize current controversies in research questions in auditory neuroscience and otolaryngology
- Describe key research questions and promising areas of research in otolaryngology and auditory neuroscience

REGISTRATION

The 2017 MidWinter Meeting Registration Desk is located in the Grand Ballroom Foyer and will be open and staffed during the following hours:

Friday, February 10	4:00 PM-7:00 PM
Saturday, February 11	7:00 AM-6:00 PM
Sunday, February 12	7:00 AM-6:00 PM
Monday, February 13	7:00 AM-6:00 PM
Tuesday, February 14	7:00 AM-6:00 PM
Wednesday, February 15	7:00 AM-10:00 AM

SPEAKER READY ROOM

The 40th Annual MidWinter Meeting Speaker Ready Room is located in the Falkland Room and will be open and staffed during the following hours:

Friday, February 10	4:00 PM-7:00 PM
Saturday, February 11	7:00 AM-6:00 PM
Sunday, February 12	7:00 AM-6:00 PM
Monday, February 13	7:00 AM-6:00 PM
Tuesday, February 14	7:00 AM-6:00 PM
Wednesday, February 15	7:30 AM-10:00 AM

ADMISSION

Conference name badges are required for admission to all activities related to the 40th Annual MidWinter Meeting, including the Exhibit Hall and social events.

MOBILE APP AND ONLINE WEBSITE

The 40th Annual MidWinter app is available at your app store. Look for ARO2017. For your laptop go to http://bit.ly/ARO2017 for access to all of the presentations and conference schedule.

MOBILE DEVICES

As a courtesy to the speakers and your fellow attendees, please switch your mobile device(s) to silent while attending the sessions.

RECORDING POLICY

ARO does not permit audio or photographic recording of any research data presented at the meeting.

BREAKS

Complimentary coffee and tea will be available during all morning and afternoon breaks.

ASSISTED LISTENING DEVICES

A limited amount of assisted listening devices are available at the ARO MidWinter Meeting Registration Desk, courtesy of Phonak.

A SPECIAL NOTE FOR THE DISABLED

ARO wishes to take steps that are required to ensure that no individual with a disability is excluded, denied services, segregated or otherwise treated differently than other individuals because of the absence of auxiliary aids and services. If you need any auxiliary aids or services identified in the Americas with Disabilities Act or any assistance please see the ARO staff at the Registration Desk.

43608-P to MSM and Grant PSI2013-49348-EXPLORA to CE and MSM), Spanish JCYL (Grant JCYL-SA343-U14 to MSM), the European Social Fund/ Spanish JCYL (Ph.D. Fellowship to JND under the Operational Programme ESF Castilla y León 2007-2013), and Spanish MINECO (Ph.D. Fellowship BES-2014-069113 to GGP).

Vestibular: VEMPs, SHIMPs, and Other Novel Approaches

PS 441

Comparative Characterization of Vertigo Associated Symptoms in a Preclinical Model Using Videonystagmography and Wireless Inertial Measurement of Head Kinematics

Cindy Gueguen[1]; **Jonas Dyhrfjeld-Johnsen**[1]; Matthieu Pasquet[2]; Pierre Liaud[1]; Guillaume Dugué[3]; Mathieu Petremann[1]; Stéphanie Bressieux[1]; Désiré Challuau[1]; Christophe Tran Van Ba[1]

[1]Sensorion; [2]Technical Consultant; [3]Ecole Normale Supérieure, CNRS UMR 8197, IBENS S4.9

The successful selection of preclinical drug candidates for clinical development is strongly dependent on validated, quantitative translational endpoints. In the treatment of vestibular pathologies, the primary clinical endpoint of vertigo is subjective and not accessible in animal models, emphasizing the need for surrogate markers. One well-established vertigo associated symptom is spontaneous nystagmus, which can be evaluated quantitatively in both animal models and clinical populations, whereas eg. posturographic preclinical evaluations typically rely on scoring scales (Dyhrfjeld-Johnsen et al., 2013; Beck et al., 2014). We report initial results comparing vertigo associated symptoms in a rat model of acute unilateral vestibular loss determined using infrared videonystagmography and wireless inertial measurement of head kinematics to determine posturographic deviations in head pitch and roll angles.

A head-post was surgically implanted on 9 adult female Long-Evans rats (200-225 g) under ketamine-xylazine anesthesia for head-fixation during VNG recordings and mounting of the 9-axis digital inertial sensor with onboard battery and Bluetooth transmitter. Following a baseline posturography recording (10 min), an excitotoxic vestibular lesion was induced using transtympanic injection of 40-45 mM kainate under isoflurane anesthesia. Videonystagmography and posturography recordings were subsequently performed at 1/3/5/24/48 hours after lesion induction. All rats developed spontaneous nystagmus with t=1h frequencies ranging from 0-2.8 Hz bimodally distributed below or above 0.5 Hz. Mean pitch and roll angle deviations relative to baseline could be determined as early as t=1h post-lesion (0.1-15.4 deg and 0.6-10.8 deg respectively), but contrary to nystagmus frequency which generally peaked at t=1h, peak mean postural deviations were seen at t=3h (roll) and t=24h (pitch) post-lesion. There was no clear correlation between the degree of lesion reflected by nystagmus frequency and head angle deviations at early time-points, but rats initially displaying high (>0.5 Hz) spontaneous nystagmus frequency had higher degree of remaining postural deviations at t=48h. Furthermore, while mean spontaneous nystagmus frequency was already reduced to 13% of peak mean frequency at t=48h, both mean pitch and roll angle deviations remained above 80% of peak values at this time-point.

The described differential recovery time-course of spontaneous nystagmus and postural deficits is consistent with the clinical situation for eg. vestibular neuritis patients (Halamagyi et al., 2010) and suggest that wireless inertial measurement of head kinematics in animal models can provide complementary and relevant information for translational R&D efforts. Further experiments (including later time-points post-lesion) and analysis are required to complete the understanding and exploitation of the posturographic data in this model.

PS 442

Head Movements During Locomotion in Vestibular Schwannoma Patients: Decreased Variability After Unilateral Vestibular Lesion

Omid Zobeiri[1]; Carol Zhang[1]; Susan King[2]; Richard Lewis[3]; Kathleen E. Cullen[1]

[1]McGill University; [2]MEEI, Harvard University; [3]Harvard University

The vestibular system plays a key role in a wide range of functions from basic reflexes to high-level behaviors. By detecting head motion and then generating the appropriate reflexes, the vestibular system is vital for maintaining balance and stabilizing gaze. In turn, it is well known that immediately following unilateral vestibular loss, patients experience impaired balance, postural, and gaze control. However, to date, much less is known about the effects of vestibular loss on voluntary behavior. Here, to assess how vestibular loss alters voluntary behaviour, we analyzed locomotive behavior in a group of patients with a diagnosis of vestibular schwannoma (VS) who had undergone a primary surgical resection of their tumor via suboccipital craniotomy and retrosigmoid approach with

sectioning of the vestibular nerve. Head movements were recorded before the surgery, as well as two and six weeks after surgery using a micro-electromechanical systems (MEMS) module (Carriot et al., 2014), which contains three linear accelerometers (recording linear accelerations along the fore-aft, inter-aural, and vertical axes) and three gyroscopes (recording angular velocity about pitch, roll, and yaw). Patients were asked to complete the Functional Gait Assessment, and we focused our analysis on short, 15-to-30-second long gait tasks including: normal walking, walking with eyes closed, and walking backwards on a level surface. We then compared pre- and post-operative data to determine if and how patients' movements were altered. We quantified gait asymmetry, gait cycle speed, and gait variability. We found no significant changes in movement asymmetry. However, surprisingly, we found that even though locomotor speed decreased two weeks after surgery, it actually increased six-weeks post-surgery as compared to pre-operative testing. Furthermore, although previous studies using age-matched controls have found increased variability in gait, we found that this was not the case when using the patients' pre-operative measures as their own control. Instead, movement variability was lower two weeks as well as six weeks after the surgery than before the surgery. Specifically, the standard deviation of both linear acceleration and angular velocity in all dimensions consistently decreased after surgery. While variability is often seen as the result of noise in the nervous system, it has been shown that variability could contribute to motor learning. Taken together, our results suggest that variability is an important indicator of how patients adapt to altered motion and their recovery process.

PS 443

Cooperative Nucleocytoplasmic Shuttling of Merlin and p53 by nutlin-3 Treatment in Vestibular Schwannomas

Hao Wu[1]; Hongsai Chen[2]; Zhaoyan Wang[2]

[1]Department of Otolaryngology Head & Neck Surgery, The Ninth People's Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; [2]1. Department of Otolaryngology Head & Neck Surgery, The Ninth People's Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Background

Vestibular schwannomas (VS) are benign tumors and attributed to the deficiency of NF2 gene product merlin. Current treatment options are limited to surgery and radiation, which may pose unacceptable risks; therefore, novel medical treatments are urgently needed. In current study, we analyse the inhibitory effects of Nutlin-3 (a p53 activator) on the proliferation activities of VS cells, thus providing foundations for the clinical application of the drug in VS treatment.

Methods

The NF2 gene mutation rates of VS were evaluated by Direct Sequencing Analysis. The correlation between NF2 mutation and expression of merlin, p53 and cyclinD1 in tumor tissues was investigated by Western Blotting. RNA interference experiments were performed to knockdown merlin expression in Human Schwann Cell (HSC) to mimic VS tumorigenesis, and the change of cell cycle distributions was determined by Cell Cycle Analysis. The implication of cell growth in response to Nutlin-3 treatment in RT4 schwanoma cell lines and primary cultured VS cells was evaluated by CCK-8 assays. The resulting alterations in expression and subcellular localization of related proteins was investigated by Western Blotting and Fluorescence.

Results

Here we showed that NF2 gene mutation is a common event in the VS development. NF2 mutations resulted in merlin deficiency, which was concomitant with p53 downregulation, leading to elevated cyclinD1 levels. Likewise, silencing of merlin gene expression in HSC resulted in down-regulated p53 and up-regulated cyclinD1, suggesting that deregulated p53 pathway was a crucial process involved in VS tumorigenesis. Interestingly, p53 was required to maintain merlin levels in HSC cells. These data above pointed out the possibility to recover merlin level in VS through p53 activation. Nutlin-3 was found to induce dose-dependent cell growth inhibition in RT4 schwanoma cell lines and primary VS cells, and at protein level, render a recovery of p53 and merlin. Furthermore, nutlin-3 rendered a shuttles of merlin-p53 signalling from cytoplasm to the nucleus.

Conclusion

Our findings establish a position feed-back loop between merlin and p53 triggered by merlin deficiency may play a very important role in the pathogenesis of vestibular schwannomas, and provide a clue that nutlin-3 might be a potential therapeutic option to VS treatment.

PS 444

The Vestibular Implant: Hearing Preservation During Intralabyrinthine Electrode Insertion

Raymond Van de Berg[1]; Robert Stokroos[2]; Joost Van Tongeren[3]; Nils Guinand[4]; Jean-Philippe Guyot[4]; Herman Kingma[1]; Angelica Perez Fornos[4]

[1]Division of Balance Disorders, Department of Otorhinolaryngology and Head and Neck Surgery, Faculty of Health Medicine and Life Sciences, School for Mental