KEYNOTE ADDRESS

Thomas C. Südhof, M.D.
Avram Goldstein Chair,
Professor of Molecular and Cellular Physiology, and Investigator of the Howard Hughes Medical Institute,
Stanford University School of Medicine, 2013 Nobel Laureate in Physiology or Medicine
Dear Colleagues,

The American Neurological Association (ANA) is delighted to welcome you to the 139th Annual Meeting being held October 12-14, 2014, in Baltimore, MD. We are particularly pleased to report that we will sponsor a keynote address on synaptic physiology by Thomas C. Südhof, M.D., Avram Goldstein Professor at the Stanford University School of Medicine, Investigator at the Howard Hughes Medical Institute, and recipient of the 2013 Nobel Prize in Physiology or Medicine.

The annual meeting will feature a wide range of educational sessions, including courses in career development, scientific symposia covering a broad spectrum of subspecialty areas, clinical updates and the stunning announcement of results from clinical trials in C9ORF72 ALS/FTD and in migraine. Attendees will also find a slate of up-to-the-minute presentations from disease-specific interest groups.

The ANA continues to evolve to meet the needs of our ever changing academic neurology community. We have a growing set of new members among neurologists from the U.S., an expanding roster of Ph.D. neuroscientists within neurology departments as well as colleagues from overseas. Our mission remains unchanged: our goal is to develop an even stronger cadre of neuroscientists to participate in investigations of neurological illnesses and their therapies.

In addition to the outstanding programming, we are pleased to mention that our 2014 Annual Meeting will afford each of us the opportunity to welcome and celebrate our colleagues from the Mexican Academy of Neurology. We are thrilled to continue the tradition of recognizing colleagues and collaborators from overseas as was done in the last two years with the Societe Francaise de Neurologie in 2013 and the Association of British Neurologists in 2012. This coincides with new efforts within the ANA to consider potential programs to extend collaborations in neurological teaching and research with academic neurologists overseas.

We are confident that this year’s ANA Annual Meeting will be exceptional. Take a moment to peruse the enclosed onsite program and be sure to participate in the many offerings this year.

With best regards,

Robert H. Brown, Jr., D.Phil., M.D.
ANA President
University of Massachusetts

Samuel Pleasure, M.D., Ph.D.
Chair, Scientific Program, Advisory Committee
University of California, San Francisco
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<td>Symposium: Novel Concepts in Pain Generation and Treatment Grand Ballroom 5-6</td>
<td>Symposium: Diseases of the Synapse Grand Ballroom 5-6</td>
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<td>Presidential Symposium: The Expanding Roles of Repeat Mutations in ALS and Related Diseases Grand Ballroom 5-6</td>
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<td>Executive Session of Membership Grand Ballroom 5-6</td>
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<td>Motor Recovery After Stroke - Grand Ballroom 1-2</td>
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<td>Prion Diseases - Grand Ballroom 3-4</td>
<td>Minimally Invasive Surgery ICH and IVH - Grand Ballroom 3-4</td>
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<td>Micro-RNA in Neurological Diseases: Insights into Biology and New Treatments - Grand Ballroom 7-8</td>
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<td>Cognitive Outcomes in Sepsis/Critical Illness - Grand Ballroom 9-10</td>
<td>New Therapeutics for Epilepsy: Drugs and Devices - Grand Ballroom 9-10</td>
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<td>Meet the Neurology Department Chairs - Dover A-C</td>
<td>Meet the NINDS - Dover A-C</td>
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<td>AUPN’s Networking Lunch for Small Academic Departments of Neurology - Kent A-C</td>
<td>Interactive Lunch Workshops</td>
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<td>New Member Meet and Greet - Essex A-C</td>
<td>Autoimmune Encephalitis and FIRES: Causes and Treatment Strategies in the Refractory Patient - Grand Ballroom 1-2</td>
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<td>ABPN MOC Program: Lifelong Learning for Neurologists - Essex A-C</td>
<td>Multimodal Neuromonitoring in Critical Care - Grand Ballroom 3-4</td>
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<td>Women of the ANA Luncheon - Waterview A-D</td>
<td>Small Vessel Phenotype: Lumping, Splitting, Reimaging - Grand Ballroom 7-8</td>
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<td>NeuroNEXT - Grand Ballroom 9-10</td>
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<td>Meet the Editors - Dover A-C</td>
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<td>Symposium: Derek Denny Brown Young Neurological Scholar Symposium Grand Ballroom 5-6</td>
<td>Symposium: BRAIN and Connectome: Initiatives Shaping the Future of Clinical Neuroscience Grand Ballroom 5-6</td>
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<td>Case Studies - Grand Ballroom 1-2</td>
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<td>Cerebrovascular Disease - Grand Ballroom 3-4</td>
<td>Dementia and Aging - Grand Ballroom 3-4</td>
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<td>Education - Grand Ballroom 7-8</td>
<td>Epilepsy - Grand Ballroom 7-8</td>
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<td>Headache and Pain - Grand Ballroom 9-10</td>
<td>Neurocritical Care - Grand Ballroom 9-10</td>
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<td>Sleep Disorders and Circadian Rhythm - Dover A-C</td>
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<td>Poster Reception #1 Harborside Ballroom</td>
<td>Behavioral Neurology - Grand Ballroom 1-2</td>
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<td>Health Services Research - Grand Ballroom 3-4</td>
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<td>President’s Reception OFFSITE - The Maryland Science Center 601 Light St., Baltimore, Maryland 21230</td>
<td>Interventional Neurolgy - Grand Ballroom 7-8</td>
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<td>Multiple Sclerosis - Grand Ballroom 9-10</td>
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<td>Regulatory Science - Essex A-C</td>
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FLOOR PLANS

THIRD LEVEL

FOURTH LEVEL

LOBBY FLOOR
**GENERAL INFORMATION**

**HOTEL INFORMATION**
Baltimore Marriott Waterfront
700 Aliceanna St.
Baltimore, MD 21202
(410) 385-3000

**REGISTRATION HOURS**
*Harbor Registration AB, Fourth Level*

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**POSTER HOURS**
*Harborside Ballroom, Fourth Level*

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**SPEAKER READY ROOM**
*Galena, Fourth Level*

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**PRESS ROOM**
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**WIRELESS CONNECTION**
A wireless connection is available to attendees. To connect, turn on Wi-Fi in the device. Look for the network SSID: *Marriott_CONF*. A splash page will pop up for Guest-Tek. Enter the Passcode: *ANA2014* (Please Note: This is not case sensitive and there are no spaces) Enter First and Last Name. Hit the button “I Accept”. Proceed to internet as normal.

**MOBILE APP**
The ANA is pleased to continue the mobile application for the 2014 Annual Meeting.

**How to download:** For phones with iTunes or Google Play: Visit the App Store or Google Play on your phone and search for *American Neurological Association*. For all other web-enabled devices, including those listed above and Blackberry, enter *m.core-apps.com/ana_annual2014* to be automatically directed to the proper download version for your phone.

Should you have any questions, please contact *support@core-apps.com*.

**ACCREDITATION & DESIGNATION STATEMENT(S)**
The American Neurological Association is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The American Neurological Association designates this live activity for a maximum of *26.25 AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Please Note: A session that has an asterisk (*) next to the session title, is a session not available for AMA PRA Category 1 Credits™.

**EVALUATIONS ONLINE**
Within a week following the event, you will receive an email containing a link to the evaluation. Please complete the online evaluation within a week of receipt in order to obtain any CME. You will be provided with a certificate following completion of the evaluation. If you have any questions, please contact ANA Meeting Manager, Paul Urso, at *purso@aneuro.org* or *1.856.642.4423*

**iPOSTERS**
ANA is excited to announce that it will again offer iPosters, an online access to poster presentations found at the Annual Meeting. Poster presenters will have the option of uploading their posters to the iPoster website so attendees can view their posters in advance. Attendees can search by topic or category and view research and interact directly with the presenters online that have authorized the creation of an iPoster. iPosters are available online throughout the year. To view the Annual Meeting iPosters, please visit *ana.posterview.com*. 
SATURDAY, OCTOBER 11

3:00 – 7:00 PM
Registration
Harbor Registration AB, Fourth Level

SUNDAY, OCTOBER 12

6:00 AM – 5:45 PM
Registration
Harbor Registration AB, Fourth Level

7:00 – 9:00 AM
Breakfast
Harbor Registration Foyer, Fourth Level

7:30 – 9:00 AM
Grand Ballroom 1-2, Third Level

EARLY CAREER LEVEL FACULTY DEVELOPMENT COURSE
Session I: Choosing Your Career Path: The Sky is the Limit

Chair: David Greer, M.D., M.A., F.C.C.M., F.A.N.A., F.N.C.S., Yale University
Speakers: Martin Samuels, M.D., D.Sc.(hon), F.A.A.N., M.A.C.P., F.R.C.P., Brigham and Women’s Hospital
Charlotte Sumner, M.D., Johns Hopkins University
David Greer, M.D., MA, F.C.C.M., F.A.N.A., F.N.C.S., Yale University
Arie Struyk, Merck/UT Southwestern
Susanne Muehlschlegel, M.D, M.P.H., University of Massachusetts Medical School

Session I presents examples of successful careers in academic Neurology and industry. The five speakers will share with the audience how they chose their path, how they identified mentors that proved influential on their career path, and how they have been able to manage patient care and academic work as well as extracurricular activities. They will describe key steps in their career, their struggles and rewarding experiences.

7:30 – 9:00 AM
Grand Ballroom 3-4, Third Level

MID/SENIOR LEVEL FACULTY DEVELOPMENT COURSE
Session I: Developing a Novel, Transparent, and Equitable Departmental Compensation Plan

Chairs: William Schwartz, M.D., University of Massachusetts
Daniel Lowenstein, M.D., University of California, San Francisco
Speakers: David Paydarfar, M.D., University of Massachusetts

Faculty in academic neurology departments are responsible for a wide range of activities that include caring for hospitalized and ambulatory patients, performing neuropsychological and neurophysiological tests, conducting extramurally-funded research programs, and educating students, residents, and fellows. Such job heterogeneity is a challenge for compensation plans, since it is clear that departments cannot function with plans that would drive faculty to choose their activities based only on revenue considerations, leaving other duties unfulfilled.

7:30 – 9:00 AM
Grand Ballroom 7-8, Third Level

AUPN/CHAIR LEVEL FACULTY DEVELOPMENT COURSE
Session I: Recruitment and Retention of Women in Academic Neurology

Chair: David J. Fink, M.D., University of Michigan
Speakers: Robin L. Brey, M.D., University of Texas Health Science Center at San Antonio
Karen L. Furie, M.D., M.P.H., Brown University

Despite the fact that women now represent half of the students in most medical school classes, women remain under-represented in most Neurology departments; a problem that is particularly acute on the tenure track and in senior leadership positions. Two women chairs of Neurology, Dr. Robin Brey (University of Texas Health Science Center at San Antonio) and Dr. Karen Furie (Brown University) will discuss this issue, using their own experience as faculty and now as chair, to identify key challenges and potential solutions.

9:00 – 9:15 AM
Coffee Break
Harborside and Grand Ballroom Foyers, Third and Fourth Levels
9:15 – 11:15 AM  
**SYMPOSIUM:** 
**NOVEL CONCEPTS IN PAIN GENERATION AND TREATMENT**

**Chairs:** Steve Scherer, M.D., Ph.D., University of Pennsylvania  
Charlotte Sumner, M.D., Johns Hopkins University

Neuropathic pain is one of the most difficult treatment challenges in clinical neurology. In this symposium, recent advances in our understanding of the molecular and anatomical organization of nociceptors and their circuits will be reviewed. In addition, novel concepts of pain generation in painful peripheral neuropathies and headache will be discussed as well as the rationale for novel therapeutics currently in clinical trials.

**Learning Objectives:** Having completed this symposium, participants will be better prepared to do the following in practice:

1. Identify the functional organization of mammalian nociceptors and distinct nociceptive circuits governing different skin areas.
2. Explain the genetic cause and neurological progression of hereditary sensory and autonomic neuropathy type 1 (HSAN1) and to be aware of clinical trials of treatment for HSAN1 patients.
3. Discuss the role of sodium channels in normal and diseased peripheral nerves and as therapeutic targets for novel therapeutics.
4. Describe the mechanisms of migraine pathogenesis and be aware of novel treatments, which are currently in clinical trials.

9:20 – 9:45 AM  
**Dissect Neural Mechanisms Underlying Differential Pain Acuity of Body Regions**  
Wenqin Luo, M.D., Ph.D., University of Pennsylvania

9:50 – 10:15 AM  
**L-serine Supplementation in HSAN1: Overcoming Altered Substrate Selectivity**  
Florian Eichler, M.D., Harvard Medical School

10:20 – 10:45 AM  
**Soriano Lectureship Award Winner**

**Chasing Men on Fire: Na Channels and Peripheral Nerve Disease**  
Stephen G. Waxman, M.D., Ph.D., Yale University School of Medicine, VA Connecticut

10:50 – 11:15 AM  
**Calcitonin Gene-Related Peptide (CGRP) and Migraine: Gepants and MABs**  
Peter J. Goadsby, M.D., Ph.D., University of California, San Francisco

11:00 AM – 7:00 PM  
**ALL DAY POSTER PRESENTATIONS**  
Poster presenters will be in attendance from 5:30 – 7:00 pm

11:30 AM – 1:00 PM  
**Lunch**  
Harborside and Grand Ballroom Foyers, Third and Fourth Levels

11:45 AM – 1:00 PM  
**INTERACTIVE LUNCH WORKSHOPS**

**Motor Recovery After Stroke**  
Grand Ballroom 1-2, Third Level

**Moderator:** Bradford B. Worrall, M.D., M.Sc., University of Virginia Health System  
**Faculty:** John W. Krakauer, M.D., Johns Hopkins University  
Alexander W. Dromerick, M.D., Georgetown University Medical Center  
Steven C. Cramer, M.D., University of California, Irvine

The last decade has seen a radical change in our understanding of the processes of motor recovery after brain injury such as stroke and how this improved understanding is being applied to rehabilitation and recovery. This interactive session will focus on the role of plasticity and learning (Krakauer), advancement in targeted rehabilitation strategies (Dromerick) and the use of augmentary strategies - robots (Cramer) in recovery of motor function after stroke.

**Prion Diseases**  
Grand Ballroom 3-4, Third Level

**Moderator/Faculty:** Stanley B. Prusiner, M.D., University of California, San Francisco

Recent advances in the study of prions argue that they cause Alzheimer’s and Parkinson’s diseases as well as the tauopathies including PSP and CTE. The data for and against these arguments will be discussed. In addition, new diagnostic and therapeutic approaches will be topics of discussion.
Micro-RNA in Neurological Disease: Insights into Biology and New Treatments

Grand Ballroom 7-8, Third Level

**Moderator:** Sudha Seshadri, M.D., *Boston University*
**Faculty:** Roger Abounader, M.D., Ph.D., *University of Virginia*

MicroRNAs are small (22 nucleotide), endogenous, non-coding RNA that play a key role in post-translational gene expression. Each miRNA typically targets multiple mRNA and their size and versatility has made them attractive therapeutic targets. In 2014 alone there have been over 6000 papers highlighting the therapeutic and diagnostic potential of miRNA in a wide variety of neurological diseases, ranging from brain tumors and neurodegeneration (Alzheimer, Parkinson’s, Huntington’s) to epilepsy and muscular dystrophies.

The two invited speakers are cutting-edge researchers in the field. **Roger Abounader** will provide an overview of miRNA biogenesis and expression regulation in the brain and describe his work identifying “master regulatory microRNAs” which are single microRNAs that target multiple oncogenic pathways in brain tumors. He will share novel approaches to the therapeutic delivery of these microRNAs or their inhibitors to brain tumors. **Hermona Soreq** will highlight the diagnostic and therapeutic potential of miRNA a wide range of neurodegenerative diseases. The moderator, Sudha Seshadri, will briefly address the insights miRNA have provided into the biology of stroke, traumatic brain injury, various epilepsies and muscular dystrophies.

There will be a full half hour devoted to an interactive, audience lead discussion wherein the panel will respond to questions, ideas and insights offered by attendees. The session is open to all.

Interested attendees can bring up their questions during the session or send advance emails with topic suggestions, or specific questions to the moderator at suseshad@bu.edu.

Cognitive Outcome in Sepsis/Critical Illness

Grand Ballroom 9-10, Third Level

**Moderator:** Paul Nyquist, M.D., F.C.C.M., F.A.H.A., *Johns Hopkins University*
**Faculty:** Fred Rincon, M.D., M.Sc., F.A.C.P., *Jefferson University Hospital*
Neeraj Badjatia, M.D., M.S., *University of Maryland*
Thomas Bleck, M.D., *Rush University Medical Center*

This Interactive Lunch Workshop will be a review of the cognitive end points associated with outcomes in the Neuro intensive care unit.

Meet the Neurology Department Chairs*

Dover A-C, Third Level

**Moderator:** Rebecca Gottesman, M.D., Ph.D., *Johns Hopkins University*
**Faculty:** Justin C. McArthur, M.B.B.S., M.P.H., F.A.A.N., *Johns Hopkins University*
Barney I. Stern, M.D., *University of Maryland*
Martin Samuels, M.D., DSc(hon), F.A.A.N., M.A.C.P., F.R.C.P., *Brigham and Women’s Hospital*
Karen C. Johnston, M.D., M.Sc., *University of Virginia*
Stephen L. Hauser, M.D., *University of California, San Francisco*

Prominent chairs of neurology will discuss how they handle their position, including what’s involved with being a chair, what is the process for attaining their position, and how to interact with chairs.

*This session is not available for AMA PRA Category 1 Credit™.

AUPN’S Networking Lunch for Small Academic Departments of Neurology*

Essex A-C, Fourth Level

**Faculty:** Gretchen E. Tietjen, M.D., *University of Toledo*

While all Neurology departments share some common attributes, there are challenges unique to smaller academic departments, including handling teaching and clinical service responsibilities, while protecting time for research and faculty development. This lunch, sponsored by the AUPN and hosted by Gretchen Tietjen, M.D., Chair of Neurology at the University of Toledo since 1998, provides an opportunity for chairs of smaller departments to meet, discuss issues and share strategies.

*This session is not available for AMA PRA Category 1 Credit™.

NEW MEMBER MEET & GREET*

Essex A-C, Fourth Level

**Moderator:** Robert H. Brown Jr., D.Phil, M.D., *University of Massachusetts*

This session is open to all new members of the ANA who want to learn more about the ANA and what it can offer. This interactive discussion will also allow new members to provide feedback to the ANA.

*This session is not available for AMA PRA Category 1 Credit™.
1:15 – 3:15 PM
Grand Ballroom 5-6, Third Level

SYMPOSIUM:
DEREK DENNY-BROWN YOUNG NEUROLOGICAL SCHOLAR SYMPOSIUM

Chair: Thomas P. Sutula, M.D., Ph.D., University of Wisconsin, Madison

The Derek Denny-Brown Young Neurological Award in Basic Science is a single session within the conference that provides an opportunity for young researchers to share groundbreaking research in the field of Neurology. Presenters are personally invited by ANA leadership (Tom Sutula, MD, PhD) to present to their peers during the conference – it is a great honor. Two of the presenters are recipients of the award. This year’s award winners will present on: Molecular mechanisms and emerging biomarkers of sudden unexpected death in epilepsy (SUDEP); and Intracortical Neurotechnologies for the Restoration of Communication and Mobility. The finalists will present briefly on: TorsinA Hypofunction Causes Abnormal Twisting Movements and Sensorimotor Circuit Neurodegeneration; The ALS/FTD C9ORF72 hexanucleotide expansion disrupts nucleocytoplasmic transport; Adherence to Guidelines: Are Ischemic Stroke Patients Receiving Guideline-Concordant Cardiac Stress Testing?; TALEN-Mediated Gene Editing Leads to Complete Loss of Intranuclear Foci in DM1 Neural Stem Cells Derived from Human DM1 iPS Cells.

Learning Objectives: Having completed this symposium, participants will be able to:

1. Identify the clinical definition and epidemiology of SUDEP
2. Describe the principal hypothesis about SUDEP mechanisms
3. List the emerging clinical and molecular risk factors for SUDEP
4. Explain key requirements for discussing SUDEP with patients and families
5. Describe a basic function of Brain-Computer interfaces.
6. List at least one source for ongoing trials of intracortically-based brain-computer interfaces for people with paralysis.
7. Identify a potential role of neuronal ensemble analysis in the diagnosis and management of epilepsy

1:25 – 1:40 PM
Presentation of Derek Denny-Brown: Young Neurological Award in Basic Science

Molecular Mechanisms and Emerging Biomarkers of Sudden Unexpected Death in Epilepsy (SUDEP)
Alica M. Goldman, M.D., Ph.D., Baylor College of Medicine

1:55 – 2:10 PM
Presentation of Derek Denny-Brown Young Neurological Scholar Award in Clinical Science

Intracortical Neurotechnologies for the Restoration of Communication and Mobility
Leigh R. Hochberg, M.D., Ph.D., F.A.A.N., F.A.N.A., Massachusetts General Hospital, Harvard Medical School, Brown University, Providence VA Medical Center

DEREK-DENNY BROWN FINALISTS:

2:15 – 2:25 PM
TorsinA Hypofunction Causes Abnormal Twisting Movements and Sensorimotor Circuit Neurodegeneration
Richard Liang, Ph.D., University of Michigan

2:30 – 2:40 PM
The ALS/FTD C9ORF72 Hexanucleotide Expansion Disrupts Nucleocytoplasmic Transport
Thomas E. Lloyd, M.D., Ph.D., Johns Hopkins University

2:45 – 2:55 PM
Adherence to Guidelines: Are Ischemic Stroke Patients Receiving Guideline-Concordant Cardiac Stress Testing?
Jason J. Sico, M.D., VA Connecticut Healthcare System, Yale University School of Medicine

3:00 – 3:10 PM
Genome Modification Leads to Ablation of Nuclear RNA Foci in Human DM1 Neural Stem Cells
Guangbin Xia, M.D., Ph.D., University of Florida

3:15 – 3:30 PM
Coffee Break
Harborside and Grand Ballroom Foyers, Third and Fourth Levels

3:30 – 5:30 PM
SPECIAL INTEREST GROUP SYMPOSIA

Neuromuscular Disease
Dover A-C, Third Level

Chair: Tahseen Mozaffar, M.D., University of California, Irvine
Co-Chair: Catherine Lomen-Hoerth, M.D., Ph.D., University of California, San Francisco

This session is on neuromuscular and we intend to cover the latest in research, and therapeutics in key areas of Neuromuscular Diseases. We are planning “senior” leader talks on ALS and other motor neuron diseases, Muscular Dystrophies and other myopathies and Peripheral Nerve disorders.

LEADERS IN THE FIELD PRESENTATIONS:

3:30 – 3:45 PM
Advances in ALS, Sporadic and Familial
Jeffrey Rothstein, M.D., Ph.D., Johns Hopkins University
3:45 – 4:00 PM
Advances in Inflammatory Myopathies
Marinos Dalakas M.D., Thomas Jefferson University

4:00 – 4:15 PM
Advances in Muscular Dystrophies
Kathryn Wagner, M.D. Ph.D., Kennedy Krieger Institute

4:15 – 4:30 PM
Advances in Peripheral Neuropathies
Eva Feldman, M.D., Ph.D., University of Michigan

DATA BLITZ PRESENTATIONS:

4:50 – 5:00 PM
Phase 2 Study of ISIS-SMNRx in Children with Spinal Muscular Atrophy
Kathryn Swoboda, M.D., University of Utah School of Medicine

5:00 – 5:10 PM
The ALS/FTD C9ORF72 hexanucleotide expansion disrupts nucleocytoplasmic transport
Thomas Lloyd, M.D., Ph.D., Johns Hopkins University

5:10 – 5:20 PM
Rescue Abnormal Myelin Permeability in PMP22 Deficiency by Suppressing Actin Polymerization
Jun Li, M.D., Ph.D., Vanderbilt University

5:20 – 5:30 PM
A Phase 3 Trial of FirdapseTM Tablets in Lambert-Eaton Myasthenic Syndrome
Douglas Winship, B.S., Catalyst Pharmaceutical Partner, Inc.

Headache and Pain
Grand Ballroom 9-10, Third Level

Chair: James Couch, M.D., Ph.D., University of Oklahoma Health Sciences Center
Co-Chair: Andrew H. Ahn, M.D., Ph.D., University of Florida Medical Center

Headache, and migraine in particular, is singularly the most common neurological condition, and the treatment of the primary headache disorders is a major role for neurologists regardless of subspecialty. This SIG will provide an update on the increasingly complex and rapidly evolving medication and procedure options for migraine, and will provide a roadmap to the latest research that provides key insights into the understanding and treatment of headache.

LEADERS IN THE FIELD PRESENTATIONS:

3:30 – 3:45 PM
Long Term Effects of the Post-Concussion Syndrome at 4-12 Years Following Traumatic Brain Injury in the Veterans of the Iraq and Afghanistan War
James Couch, M.D., Ph.D., University of Oklahoma Health Sciences Center

3:50 – 4:25 PM
Chronic Pain: A View Through the Lens of Migraine
K.C. Brennan, M.D., University of Utah, Medical School

DATA BLITZ PRESENTATIONS:

4:40 – 4:50 PM
Post-Explosion Syndrome, The Triad of Hearing Loss, Tinnitus, and Headache Due to Ophthalinic Nerve Concussion Secondary to Primary Blast Injuries
Fereshteh S. Soumekh, M.D., VA Boston Healthcare System

4:50 – 5:00 PM
Use of a Closed-Loop Neurotechnology, HIRREM, Is Associated with Symptom Reduction and Improved Autonomic Regulation in Migraineurs
Charles H Tegeler, M.D., Wake Forest School of Medicine

5:00 – 5:10 PM
Canal-Otolith Interactions in Vestibular Migraine
Susan King, B.A., Boston University

5:10 – 5:20 PM
gammaCore® Use for Prevention and Acute Treatment of Chronic Cluster Headache: Findings From the Randomized Phase of the PREVA Study
Charly Gaul, M.D., Migraine and Headache Clinic, Ölmühlweg 31: Königstein, Germany

5:20 – 5:30 PM
A Randomized Controlled Trial of Pregabalin versus Amitriptyline in Chronic Low Backache
Jayantee Kalita, M.D., D.M., Sanjay Gandhi Post Graduate Institute of Medical Sciences

Autoimmune Neurology
Grand Ballroom 1-2, Third Level

Co-Chairs: Josep Dalmau, M.D., Ph.D., University of Barcelona, University of Pennsylvania
Sean Pittock, M.D., Mayo Clinic, Rochester

Autoimmune Neurology is a rapidly emerging new subspecialty that encompasses the diagnosis and treatment of neurological disorders with an autoimmune (paraneoplastic or non-cancer associated) basis. The last decade has seen a dramatic increase in discovery of neural-specific autoantibodies and their target antigens. This SIG is designed to help neurologists stay current in clinical practice and our three invited faculty will provide an up to date review of what’s “new” in Autoimmune Neurology.

LEADERS IN THE FIELD PRESENTATIONS:

3:30 – 3:50 PM
Autoimmune Movement Disorders: Update
Andrew McKeon, M.D., Mayo Clinic, Rochester
3:55 – 4:15 PM
Pediatric NMO, ADEM, and Antibodies to Aquaporin-4 and MOG
Kevin Rostasy, M.D., Medical University of Innsbruck

4:20 – 4:40 PM
Modeling Symptoms in anti-NMDAR Encephalitis
Frank Leyboldt, M.D., Ph.D., University Hospital Schleswig-Holstein Campus Kiel

DATA BLITZ PRESENTATIONS:

4:45 – 4:55 PM
Specificity of Antibody Binding in Anti-Yo Antibody Mediated Purkinje Cell Cytotoxicity
John E. Greenlee, M.D., Veterans Affairs Medical Center

4:55 – 5:05 PM
Passive Transfer of Glycine Receptor-Antibody IgG induces Motor Dysfunction in Mice
Alexander Carvajal, M.D., University of Oxford

5:05 – 5:15 PM
Characterization of Caspr2 Autoimmune Encephalitis
Jun-Sang Sunwoo, M.D., Seoul National University Hospital

5:15 – 5:25 PM
Clinical and Electrophysiological Analyses in Guillain-Barré Syndrome with Anti-GAL-C Antibody
Makoto Samukawa, M.D., Ph.D., Kinki University Faculty of Medicine

Cerebrovascular Disease
Grand Ballroom 3-4, Third Level

Co-Chairs: Steven Warach, M.D., Ph.D., University of Texas Southwestern
Anthony Kim, M.D., M.A.S., University of California, San Francisco

The Cerebrovascular Special Interest Group session will feature prominent leaders in stroke prevention, acute treatment, and recovery along with new investigators making innovative contributions to the field. The focus of the session will be review and dissemination of key recent clinical evidence in stroke and to identify targets for ongoing clinical discovery in an interactive format to maximize opportunities for collaboration and mentorship.

LEADERS IN THE FIELD PRESENTATIONS:

3:30 – 3:50 PM
Mobile Stroke Units
Jim Grotta, M.D., University of Texas, Health Science Center

3:50 – 4:10 PM
Redefining the Cardioembolic Evaluation After Stroke/TIA
Karen Furie, M.D., M.P.H., Brown Medical School, Rhoad Island Hospital

4:10 – 4:30 PM
Latest in Stroke Rehab and Recovery
Steve C. R. Cramer, M.D., University of California, Irvine

4:30 – 4:50 PM
tPA, Glucose and Risk of ICH
Karen C. Johnston, M.D., M.Sc., University of Virginia

DATA BLITZ PRESENTATIONS:

4:50 – 5:00 PM
Adherence to Guidelines: Are Ischemic Stroke Patients Receiving Guideline-Concordant Cardiac Stress Testing?
Jason Sico, M.D., Yale University

5:00 – 5:10 PM
Vitamin D, Vitamin D Binding Protein (DBP) Gene Polymorphism, and Risk of Incident Stroke: the Atherosclerosis Risk in Communities (ARIC) Study
Andrea Schneider, Ph.D., Johns Hopkins University

5:10 – 5:20 PM
Long Term Blood-Brain-Barrier Permeability Changes in Cerebral Small Vessel Disease
Branko Huisa, M.D., University of New Mexico

5:20 – 5:30 PM
miRNA in acute ischemic stroke and their predicted gene targets in blood
Glen Jickling, M.D., University of California

Movement Disorders
Essex A-C, Fourth Level

Chair: William Dauer, M.D., University of Michigan
Co-Chair: Nicole Calakos, M.D., Ph.D., Duke University

Our limited understanding of the pathogenesis of movement disorders is a barrier to preventing the discovery and development of novel therapeutic strategies. In the 2014 Movement Disorders SIG, leading scientists will present the latest findings on the molecular pathogenesis of Parkinson disease, Huntington disease, Tourette’s syndrome and primary Dystonia. The SIG will also include a collection of short talks by junior investigators featuring recent, exciting discoveries in Movement Disorders. All speakers will emphasize how these novel findings may translate into new therapeutic approaches for movement disorders.

LEADERS IN THE FIELD AND DATA BLITZ PRESENTATIONS:

3:30 – 3:50 PM
The Histamine Deficient HDC Knockout Mouse as a Genetic Model of Tourette Syndrome
(Leader in the Field Presentation)
Christopher Pittenger, M.D., Ph.D., Yale University
3:55 – 4:05 PM  
**A Genome Wide Study on Fine Motor Control**  
(Data Blitz Presentation)  
Claudia Satizabal, Ph.D., Boston University

4:05 – 4:25 PM  
**Protein Lowering Approach for Huntington's Disease: Will they Work?**  
(Leader in the Field Presentation)  
Marie-Franciose Chesselet, M.D., Ph.D., University of California, Los Angeles

4:30 – 4:40 PM  
**Purkinje Neuron Atrophy in Spinocerebellar Ataxia Type 1 Represents a Compensatory Mechanism for Increased Membrane Excitability**  
(Data Blitz Presentation)  
Vikram Shakkottai, M.D., Ph.D., University of Michigan

4:40 – 5:00 PM  
**TorsinA Dysfunction and Dystonia: Insights from a Novel TOR1A Mutation in Sporadic Focal Disease**  
(Leader in the Field Presentation)  
Nicole Calakos, M.D., Ph.D., Duke University

5:05 – 5:15 PM  
**Pioglitazone As a Potential Disease Modifying Therapy in Early Parkinson's Disease**  
(Data Blitz Presentation)  
Tanya Simuni, M.D., Northwestern University

5:15 – 5:35 PM  
**LRRK2 and Protein Overproduction in Parkinson's Disease**  
(Leader in the Field Presentation)  
Ted Dawson, M.D., Ph.D., Johns Hopkins University

**EDUCATION**  
**Mentorship: A Key Component for Professional Success**  
Grand Ballroom 7-8, Third Level

**Chair:** Ralph F. Józefowicz, M.D., University of Rochester  
**Co-Chair:** Steven L. Lewis, M.D., Rush University

Mentorship is key to a successful career, but it is not always available or effectively implemented. Mentorship at all levels of the professional continuum should occur, including medical student, graduate student, resident, fellow and faculty member. The 2014 Education SIG will present an overview of what constitutes effective mentorship, followed by succinct presentations about mentorship at various levels of one’s career, including residency, junior faculty, and senior leadership. Special consideration will also be given to the mentorship of women and minorities, as well as the role of the mentee in this process. A lively discussion is expected to follow these presentations.

3:30 – 3:45 PM  
**The Effective Mentor**  
Ralph F. Józefowicz, M.D., University of Rochester

3:45 – 4:00 PM  
**Mentoring Residents**  
John Engstrom, M.D., University of California, San Francisco

4:00 – 4:15 PM  
**Mentoring Junior Faculty**  
Allison Brashear, M.D., Wake Forest School of Medicine

4:15 – 4:30 PM  
**Mentoring Senior Leaders**  
Timothy A. Pedley, M.D., Neurological Institute

4:30 – 4:45 PM  
**Mentoring Women and Minorities**  
Emma Ciafaloni, M.D., University of Rochester

4:45 – 5:00 PM  
**The Role of the Mentee**  
Jennifer R. Molano, M.D., University of Cincinnati

5:00 – 5:30 PM  
**Panel – Audience Discussion**

5:30 – 7:00 PM  
*Harborside Ballroom, Fourth Level*

**POSTER PRESENTATIONS AND WINE & CHEESE RECEPTION**

**Poster Categories:**  
Behavioral and Cognitive Neurology – Poster #S102 - S122  
Epilepsy and Episodic Disorders – Poster #S201 – S223  
Health Services Research – Poster #S301 – S310  
Movement Disorder – Poster #S401 – S454  
Neurogenetics – Poster #S501 – S514  
Neuroinfectious Disease – Poster #S601 – S611  
Neuromuscular Disease – Poster #S701 – S738  
Neuro-oncology – Poster #S801 – S807  
Pediatric Neurology and Developmental Disorders – Poster #S901 – S910  
Rehabilitation and Regeneration – Poster #S1001 – S1006

Full abstracts for all posters are available in the abstract supplement booklet and the mobile application.
The purpose of this session is to raise awareness of the importance of fostering a vibrant and dynamic environment of inclusion in Neurology departments of the 21st Century, and to understand that this involves active engagement with trainees and faculty of various ethnicities, races, genders, gender identities, sexual orientations, historical traditions, ages, religions, disabilities, veteran status, and socioeconomic backgrounds. We will also explore unconscious bias as a potential barrier to inclusion in fields like neurology. Participants will consider the role of mentorship and other supports in facilitating the career advancement of persons from disadvantaged or historically underserved groups. Finally, participants will be challenged to consider specific strategies that may work to enhance diversity in their home institutions.

7:30 – 9:00 AM
Grand Ballroom 7-8, Third Level

AUPN/Chair Level Development Course
Session II: What Neurology Departments Look Like from the Perspective of the Dean’s Office

Chair: David J. Fink, M.D., University of Michigan
Speaker: Ray L. Watts, M.D., University of Alabama at Birmingham

Neurologists come to the table with a deep-seated belief that neurology is important and brings value to the academic, clinical and research missions of their institutions; a view that is not always shared by the institutional administration. Ray Watts has a unique perspective on the relationship between the Neurology Department and the institutional leadership, having served as Chair of the Department of Neurology, then Senior Vice President and Dean of the School of Medicine, and now as President of the University of Alabama at Birmingham. Every institution is unique, but Dr. Watts will use his experience to discuss how one institution sees neurology, and what general principles we might glean regarding interaction with senior administration.

9:00 – 9:15 AM
Coffee Break
Harborside and Grand Ballroom Foyers, Third and Fourth Levels
9:15 – 11:15 AM  
**Grand Ballroom 5-6, Third Level**

**SYMPOSIUM: DISEASES OF THE SYNAPSE**

**Chairs:** Stanley B. Prusiner, M.D., *University of California, San Francisco*  
Ming Guo, M.D., Ph.D., *University of California, Los Angeles*

The development and maintenance of synapse are crucial for neuronal function, and dysfunction of synapse can lead to neuropsychiatric disorders such as autism, schizophrenia and neurodegeneration. In this symposium, we will have 3 distinguished physicians and/or scientists, including the Nobel Laureate in 2013, Dr. Thomas C. Südhof, to discuss the latest advance in synapse biology as it relates to human diseases. This will benefit academic neurologists and neuroscientists and hopefully guide future therapies.

**Learning Objectives:** Having completed this symposium, participants will be better prepared to do the following in practice:

1. Discuss how neurexin dysfunction can potentially lead to diseases such as schizophrenia
2. State how development of synapse impact function, and malformation of synapse leads to autism.
3. Recall how immune systems including complement systems regulates development, and dysregulation of the process leads to disease such as Alzheimer’s disease.

9:20 – 10:20 AM  
**The Neurexin Enigma – From Synapse Formation to Schizophrenia**

Thomas C. Südhof, M.D., Avram Goldstein Chair, Professor of Molecular and Cellular Physiology, and Investigator of the Howard Medical Institute, *Stanford University School of Medicine*, 2013 Nobel Laureate in Physiology or Medicine

10:25 – 10:50 AM  
**F.E. Bennett Memorial Lectureship Award Winner**

**Gene Discovery and the Emerging Biology of Autism Spectrum Disorders: The Synapse and Beyond**

Matthew State, M.D., Ph.D., *University of California, San Francisco*

10:55 – 11:15 AM  
**Immune Mechanisms Underlying Synaptic Pruning in Development & Disease**

Beth Stevens, Ph.D., *Boston Children’s Hospital, Harvard Medical School*

11:15 – 11:45 AM  
**Executive Session of Membership**

11:30 AM – 1:00 PM  
**Lunch**  
Harborside and Grand Ballroom Foyers, Third and Fourth Levels

11:45 AM – 1:00 PM  
**Interactive Lunch Workshops**

**Next Generation Sequencing for Diagnosis of Neuromuscular Diseases**  
**Grand Ballroom 1-2, Third Level**

**Moderator:** Thomas E. Lloyd, M.D., Ph.D., *Johns Hopkins University*  
**Faculty:** Matthew B. Harms, M.D., *Washington University*  
Stephan Züchner, M.D., Ph.D., *University of Miami School of Medicine*

Next generation sequencing methods are rapidly revolutionizing the way neuromuscular specialists and neurologists in general are diagnosing patients with inherited diseases. This workshop will discuss this new technology, its strengths and limitations, and how to evaluate “variants of uncertain significance.”

**Minimally Invasive Surgery ICH and IVH**  
**Grand Ballroom 3-4, Third Level**

**Moderator:** Daniel F. Hanley, M.D., *Johns Hopkins University*  
**Faculty:** Wendy C. Ziai, M.D., M.P.H., *Johns Hopkins University*

The NINDS sponsored CLEAR III and MISTIE III trials highlight the potential role of Minimally invasive Surgical approaches to removal of intracranial hematomas. This lunch reviews the background for these approaches and some of the data supporting the potential for image guidance and minimally invasive techniques to add value to patient care for ICH.

**Tau Imaging Session**  
**Grand Ballroom 7-8, Third Level**

**Moderator:** Madhav Thambisetty, M.D., *Johns Hopkins University*  
**Faculty:** Mark A. Mintun, M.D., *Avid Pharmaceuticals*  
Bradford C. Dickerson, M.D., *Harvard Medical School, Massachusetts General Hospital*

This workshop will feature an interactive discussion on the emerging modality of PET imaging to visualize in vivo tau deposition in the human brain.
New Therapeutics for Epilepsy: Drugs and Devices
Grand Ballroom 9-10, Third Level

**Moderator:** Nathan E. Crane, M.D., Johns Hopkins University  
**Faculty:** Gregory Kent Bergey, M.D., Johns Hopkins University

**Meet the NINDS**
Dover A-C, Third Level

**Moderator:** Stephen J. Korn, Ph.D., Director, Office of training, Career Development and Workforce Diversity, NIH/ NINDS

This is your chance to get your questions answered by representatives from the National Institute of Neurological Disorders and Stroke (NINDS).

*This session is not available for AMA PRA Category 1 Credit™.

11:45 AM – 1:00 PM
Essex A-C, Fourth Level

**ABPN MAINTENANCE OF CERTIFICATION (MOC) PROGRAM: LIFELONG LEARNING FOR NEUROLOGISTS**

**Faculty:** Larry Faulkner, M.D., President and CEO at ABPN

Dr. Faulkner will lead the session off by providing background on the ABMS MOC program, recent changes to the MOC program, and perspective on the future of MOC. Dr. Faulkner will detail the four-part ABPN MOC Program, giving specific requirements related to self-assessment, CME, and performance in practice components.

*This session is not available for AMA PRA Category 1 Credit™.

11:45 AM – 1:00 PM
Waterview A-D, Lobby Level

**14TH ANNUAL WOMEN OF THE ANA LUNCH PROGRAM**

Co-Chairs: Kathleen Digre, M.D., University of Utah  
Karen C. Johnston, M.D., MSc, University of Virginia  
**Speaker:** Story C. Landis, Ph.D., Director of the National Institute of Neurological Disorders and Stroke (NINDS)

The Women of the ANA have been meeting for over 10 years to promote woman in academic neurology.

1:15 – 3:15 PM
Grand Ballroom 5-6, Third Level

**SYMPOSIUM: BRAIN AND CONNECTOME: INITIATIVES SHAPING THE FUTURE OF CLINICAL NEUROSCIENCE**

**Chairs:** Samuel Pleasure, M.D., Ph.D., University of California, San Francisco  
William Seeley, M.D., University of California, San Francisco

This symposium will discuss the goals of the BRAIN and Human Connectome Initiatives with talks explaining these efforts from two of the leading scientists involved in their conception and planning. Then there will be two talks from scientists using complex approaches to examine connectivity and function in human and model organisms.

**Learning Objectives:** Having completed this symposium, participants will be better prepared to do the following in practice:

1. Discuss methods used to monitor activity of large groups of neurons in brain function in disease and health.
2. Identify potential collaborative clinical or research opportunities for interacting with the BRAIN or Connectome initiatives.
3. Describe the relative goals of the BRAIN and Connectome initiatives and how they interact with modern neuroscience.
4. List approaches used to examine large-scale connectivity within the CNS in health and disease.

1:15 – 1:20 PM
Grass Award Winner  
Joshua M. Shulman, M.D., Ph.D., Baylor College of Medicine

1:20 – 1:45 PM
**View From Above: The Human Connectomes**  
Marcus Raichle, M.D., Washington University in St. Louis

1:50 – 2:15 PM
What the BRAIN Initiative is About  
Joshua R. Sanes, Ph.D., Harvard Medical School

2:20 – 2:45 PM
**Microdissecting the Function of Human Brain Circuits...at the Speed of Thought**  
Edward Chang, M.D., University of California, San Francisco

2:50 – 3:15 PM
**Connectomics and the Allen Institute’s MindScope Project**  
R. Clay Reid, M.D., Ph.D., Allen Brain Institute

*This session is not available for AMA PRA Category 1 Credit™.*
3:15 – 3:30 pm  
**Coffee Break**  
Harborside and Grand Ballroom Foyers, Third and Fourth Levels

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3:30 – 5:30 pm  
**SPECIAL INTEREST GROUP SYMPOSIA**

**Dementia and Aging**  
*Updates on Dementia and Cognitive Aging*  
Grand Ballroom 3-4, Third Level

**Chair:** Henry Paulson, M.D., Ph.D., *University of Michigan*  
**Co-Chair:** Mike Greicius, M.D., *Stanford University*

This symposium will provide updates on three highly topical issues in age-related dementia from three leaders in the field. Brad Dickerson will consider recent advances in tau PET imaging. Applications in Alzheimer’s disease and non-Alzheimer dementias will be discussed. Jeff Rothstein will describe new insights into the mechanisms by which the C9ORF72 expansion causes neurodegeneration in FTD and ALS. Our final speaker, Nilufer Ertekin-Taner, will discuss novel genetic insights into Alzheimer’s disease. She will highlight some of the limitations of genome-wide association studies (GWAS) and explore complementary approaches that can strengthen or expand upon GWAS findings. In addition, three submitted abstracts complementing these themes will be chosen for brief presentations. The symposium will conclude with a question and answer session involving all the speakers.

**LEADERS IN THE FIELD PRESENTATIONS:**

3:30 – 3:50 PM  
**Tau PET Imaging in Alzheimer’s and Non-Alzheimer’s Dementias**  
Bradford Dickerson, M.D., *Harvard University*

4:00 – 4:20 PM  
**C9ORF72 Provides Novel Insights into FTD/ALS Pathogenesis**  
Jeffrey Rothstein, M.D., Ph.D., *Johns Hopkins University*

4:30 – 4:50 PM  
**AD Genetics: Going Beyond GWAS**  
Nilufer Ertekin-Taner, M.D., Ph.D., *Mayo Clinic, Jacksonville*

**DATA BLITZ PRESENTATIONS:**

5:00 – 5:10 PM  
**Development of miRNA-Modulating Drug for Alzheimer’s Disease**  
Soon-Tae Lee, M.D., Ph.D., *Seoul National University Hospital*

5:10 – 5:20 PM  
**Mild Cognitive Impairment (MCI) Preceding Dementia with Lewy Bodies: Comparison with Amnestic Mild Cognitive Impairment**  
Parul Jindal, M.D., *University of Oklahoma*

5:20 – 5:30 PM  
**Life Extension Factor Klotho Enhances Cognition**  
Dena Dubal, M.D., Ph.D., *University of California, San Francisco*

**Neurocritical Care**  
Grand Ballroom 9-10, Third Level

**Chair:** Alejandro A. Rabinstein, M.D., F.A.N.A., *Mayo Clinic, Rochester*  
**Co-Chair:** J. Claude Hemphill III, M.D., M.A.S., F.N.C.S., *University of California, San Francisco*

The session will aim at closing the knowledge gap in key Neurocritical Care topics through presentations from experts who will integrate available evidence with their clinical experience. A second part of the session will highlight the best new original research in the Neurocritical Care field.

**LEADERS IN THE FIELD PRESENTATIONS:**

3:30 – 3:50 PM  
**Neurocritical Care for Acute CNS Infections**  
J. Claude Hemphill III, M.D., M.A.S., F.N.C.S., *University of California, San Francisco*

4:00 – 4:20 PM  
**Current State of Cooling for Brain Protection after Cardiac Arrest**  
Romer Geocadin, M.D., *Johns Hopkins University*

4:30 – 4:50 PM  
**Toxic Encephalopathies in the ICU**  
Alejandro A. Rabinstein, M.D., F.A.N.A., *Mayo Clinic, Rochester*

**DATA BLITZ PRESENTATIONS:**

5:00 – 5:10 PM  
**Pretreatment BBB Damage and Post Treatment ICH after Endovascular Therapy**  
Richard Leigh, M.D., *Johns Hopkins University*

5:10 – 5:20 PM  
**Rate of Peri-Hematomal Edema Expansion Predicts Mortality after Intracerebral Hemorrhage**  
Sebastian Urday, M.Phil., *Yale University*

5:20 – 5:30 PM  
**Trapped Ventricle: Prognosis And Benefit From Surgical Decompression**  
Gabriel Pagani-Estevez, M.D., *Mayo Clinic, Rochester*
Epilepsy
Grand Ballroom 7-8, Third Level

Chair: Sydney Cash, M.D., Ph.D., Harvard Medical School, Massachusetts General Hospital
Co-Chair: Robert Knowlton, M.D., University of California, San Francisco

This session will cover emerging research topics in epilepsy research. The invited speakers’ work covers a broad range of different aspects of epilepsy research from basic science to translation investigations. This includes pathophysiology, epidemiology, genetics and physiology as well as the opportunities and hurdles in doing research for the improving care of patients with epilepsy.

LEADERS IN THE FIELD PRESENTATIONS:

3:35 – 3:50 PM
Afterdischarges: Phenomenology, Dynamics, and Mechanisms
Giridhar Kalamangalam, M.D., University of Texas, Houston

3:55 – 4:10 PM
The Natural History of an Epileptic Focus (Part 1: The Early Stages)
Kevin Staley, M.D., Ph.D., Harvard Medical School, Massachusetts General Hospital

4:15 – 4:30 PM
Bringing CLARITY to the Role of Interneurons in Epilepsy
Atul Maheshwari, M.D., Baylor College of Medicine

4:35 – 4:50 PM
Better Exploiting Multimodality Functional Imaging to Localize Epilepsy
Robert Knowlton, M.D., University of California San Francisco

4:55 – 5:10 PM
Individualized Epilepsy Surgical Outcome Prediction Based on Neural Network Architecture
Leonardo Bonilha, M.D., Ph.D., Medical University of South Carolina

5:15 – 5:25 PM
General Discussion of SIG Content for Future Years

Case Studies
Cases in the Interface Between Neurology and Internal Medicine
Grand Ballroom 1-2, Third Level

Chair: Martin Samuels, M.D., D.Sc.(hon), F.A.A.N., M.A.C.P., F.R.C.P., Brigham and Women’s Hospital
Co-Chair: S. Andrew Josephson, M.D., University of California, San Francisco

Neurologists are often faced with problems that fall in the interface between neurology and internal medicine. This is particularly evident when functioning as the consultant on the wards and in the ambulatory center of general hospitals. This special interest group will be led by two experienced clinical neurologists, S. Andrew Josephson and Martin A. Samuels, who have a special interest in medical neurology. The session will be case-based and audience participation will be encouraged.

LEADERS IN THE FIELD PRESENTATIONS:

3:30 – 5:30 PM
Case Presentations (Case Numbers 1-6)
Martin Samuels, M.D., D.Sc.(hon), F.A.A.N., M.A.C.P., F.R.C.P., Brigham and Women’s Hospital
S. Andrew Josephson, M.D., University of California, San Francisco

Neuro-Oncology
Advances in Translational Neuro-Oncology
Essex A-C, Fourth Level

Co-Chairs: Amy Pruitt, M.D., University of Pennsylvania
John Laterra, M.D., Ph.D., Johns Hopkins University

This Special Interest Group will focus on recent discoveries in the genetic, epigenetic, and tumor micro-environmental mechanisms relevant to the diagnosis, subclassification and therapy of adult and pediatric primary brain malignancies. Lead speakers will include Elizabeth Gerstner (Harvard University), Ingo Mellinghoff (Memorial Sloan Kettering) and Scott Pomeroy (Harvard University). This SIG will address practice gaps related to the application of molecular diagnostics and antiangiogenic agents to brain cancer diagnosis and therapy.

LEADERS IN THE FIELD PRESENTATIONS:

3:30 – 3:55 PM
Dysregulated Epigenetic Mechanisms Drive the Growth of Malignant Childhood Brain Tumors
Scott Pomeroy, M.D., Ph.D., Harvard Medical School

4:00 – 4:25 PM
Targeting Mutant Signaling Pathways for Glioma Therapy
Ingo Mellinghoff, M.D., Ph.D., Memorial Sloan Kettering Cancer Center

4:30 – 4:55 PM
Anti-Angiogenesis: Opportunities and Obstacles for Glioma Management
Elizabeth Gerstner, M.D., Harvard Medical School

DATA BLITZ PRESENTATIONS:

5:00 – 5:10 PM
Bacteriolytic Tumor Therapy: Bioengineering of Therapeutic Clostridium novyi-NT
Verena Staedtke, M.D., Ph.D., Johns Hopkins University
5:15 – 5:25 PM
Forcing Differentiation: Functional Genomics Identifies a Novel Regulator of Glioblastoma Tumor Initiating Cell State
Milan Chheda, M.D., Memorial Sloan Kettering Cancer Center

Sleep Disorders and Circadian Rhythm
Dover A-C, Third Level
Chair: Louis Ptacek, M.D., University of California, San Francisco
Co-Chair: Clifford B. Saper, M.D., Ph.D., Harvard Medical School

We understand very little about sleep despite that the average human spends ~1/3 of his/her life in this state. It has become clear that chronic sleep disruption and desynchrony of the clock has broad implications for human health and disease. However, appreciation for the risks of sleep deprivation are where our understanding of the risk of smoking was 40 or 50 years ago. The purpose of this SIG is to promote broader understanding of sleep phenotypes and the implications these have on health of the nervous system.

LEADERS IN THE FIELD PRESENTATIONS:

3:30 – 4:10 PM
A Patient Who Found Me on the Internet
William Schwartz, M.D., University of Massachusetts

4:20 – 4:50 PM
The Potential Role of Amyloid-beta and Tau in Neurodegeneration-Related Sleep Disorders
David M. Holtzman, M.D., Washington University

DATA BLITZ PRESENTATIONS:

5:00 – 5:15 PM
Oral ADX-N05 (JZP-110) for the Treatment of Excessive Daytime Sleepiness in Adults With Narcolepsy
Richard Bogan, M.D., SleepMed of South Carolina

5:15 – 5:20 PM
Objective Sleep Assessments in Patients with Postural Tachycardia Syndrome Using Overnight Polysomnogram
Kanika Bagai, M.D., Vanderbilt University

5:30 – 7:00 PM
Harborside Ballroom, Fourth Level

POSTER PRESENTATIONS AND WINE & CHEESE RECEPTION

Poster Categories:
- Autoimmune Neurology – Poster #:M1101 – M1120
- Cerebrovascular Disease – Poster #:M1201 – M1230
- Dementia and Aging – Poster #:M1301 – M1336
- Education – Poster #:M1401 – M1405
- Headache and Pain/Neuro-otology – Poster #:M1501 – M1508
- Interventional Neurology – Poster #:M1601 – M1612
- Multiple Sclerosis – Poster #:M1701 – M1713, M1714 – M1716
- Neurodegenerative Disorders – Poster #:M1801 – M1837, M1838 – M1845
- Neurology Critical Care – Poster #:M1901 – M1907
- Regulatory Science – Poster #: M2191
- Sleep Disorders and Circadian Rhythm – Poster #: M2201 – M2209
- Trauma/Injury – Poster #: M2301 – M2306

Full abstracts for all posters are available in the abstract supplement booklet and the mobile application.

7:30 – 9:00 PM
The President’s Reception at The Maryland Science Center

Address:
601 Light St. Baltimore, Maryland 21230
Academy of the Sciences

Transportation:
There will be bus transportation starting at 7:00 PM from the Baltimore Marriott Waterfront Hotel to The Maryland Science Center. The last bus will depart from The Maryland Science Center at 10:00 PM.
7:30 – 9:00 AM
Grand Ballroom 7-8, Third Level

**AUPN/CHAIR LEVEL
FACULTY DEVELOPMENT COURSE**
Session III: Structuring Compensation in Academic Neurology

**Chair:** David J. Fink, M.D., *University of Michigan*
**Speakers:** Merit E. Cudkowicz, M.D., *Massachusetts General Hospital*
Robert L. Macdonald, M.D., Ph.D., *Vanderbilt University*

The increased emphasis in recent years on matching faculty workplan to salary source has created new challenges to neurology departments. Funds flow for activities important for the department academic mission may not adequately cover the faculty effort required, while conversely clinical revenue generated in some subspecialties puts pressure on the traditional academic compensation model. There is no simple solution to this problem, but Robert Macdonald, Chair of Neurology at Vanderbilt and Merit Cudkowicz, Chief of Neurology at MGH will discuss their experience and approach to the problem.

7:30 – 9:00 AM
Grand Ballroom 1-2, Third Level

**EARLY CAREER LEVEL
FACULTY DEVELOPMENT COURSE**
Session III: A Survival Kit for the Academic Neurologist

**Chair:** Joachim Baehring, M.D., D.Sc., *Yale University*
**Speakers:** Justin McArthur, M.B.B.S., M.P.H., F.A.A.N., *Johns Hopkins University*
Clifford B. Saper, M.D., Ph.D., *Beth Israel Medical Center (Annals of Neurology)*

Day III helps course participants understand the finances of academic Neurology including P&L statements, RVUs, indirect costs, and more. The editor of *Annals of Neurology* will provide insight in the review process, and offer his advice on how to identify the appropriate journal for a certain type of work and get it published.

9:00 – 9:15 AM
Coffee Break
Harborside and Grand Ballroom Foyers, Third and Fourth Levels

9:15 – 11:15 AM
Grand Ballroom 5-6, Third Level

**SYMPOSIUM:
PRESIDENTIAL SYMPOSIUM: THE EXPANDING ROLES OF REPEAT MUTATIONS IN ALS AND RELATED DISEASES**

**Chair:** Robert H. Brown Jr., D.Phil, M.D., *University of Massachusetts Medical School*
Laura Ranum, B.A., Ph.D., *University of Florida*

A hexanucleotide repeat expansion mutation was recently reported as the most common cause of amyotrophic lateral sclerosis and frontotemporal dementia (ALS/FTD). This discovery has ignited an explosion of research into the molecular mechanisms and potential therapeutic targets of this disease. Recent evidence suggests three distinct pathways may contribute to disease: protein loss of function, RNA gain of function and the accumulation of six unexpected aggregation-prone proteins expressed by a novel mechanism of protein translation: repeat associated non-ATG (RAN) translation.
**Learning Objectives:** Having completed this symposium, participants will be better prepared to do the following in practice:

1. Diagnose diverse categories of ALS and FTD.
2. Understand new concepts in the pathogenesis of neurodegeneration.
3. Acquire some insight into new research methodologies in DNA analysis that are transforming clinical medicine.

**9:15 – 9:20 AM**

**Wolfe Neuropathy Research Prize**

Jun Li, M.D., Ph.D., Vanderbilt University

**9:20 – 9:45 AM**

**The Expanding Landscape of ALS Genetics**

Robert H. Brown Jr., D.Phil, M.D., University of Massachusetts Medical School

**9:50 – 10:15 AM**

**C9ORF72: A Tale of Two Neurodegenerative Diseases**

Bryan Traynor, M.D., National Institutes of Health (NIH)

**10:20 – 10:45 AM**

**Toxic Peptides from C9ORF72 Expansions**

Leonard Petrucelli, M.D., Mayo Clinic, Florida

**10:50 – 11:15 AM**

**Repeat Associated non-ATG (RAN) Translation: New Starts and Directions in Neurological Disease**

Laura Ranum, B.A., Ph.D., University of Florida

**11:30 AM – 1:00 PM**

**Lunch**

Harborside and Grand Ballroom Foyers, Third and Fourth Levels

**11:45 AM – 1:00 PM**

**INTERACTIVE LUNCH WORKSHOPS**

**Autoimmune Encephalopathies and FIRES: Causes and Treatment Strategies in the Refractory Patient**

Grand Ballroom 1-2, Third Level

**Moderator:** Arun Venkatesan, M.D., Ph.D., Johns Hopkins University

**Faculty:** Josep Dalmau, M.D., Ph.D., University of Barcelona, University of Pennsylvania

Ariane Soldatos, M.D.C.M., M.P.H., National Institutes of Health (NIH)

John W. Probasco, M.D., Johns Hopkins University

This session will focus on current concepts and investigational approaches to the establishment of etiology and to the management of patients with autoimmune encephalopathies and febrile refractory seizure conditions.

**Multimodal Neuromonitoring in Critical Care**

**Grand Ballroom 3-4, Third Level**

**Moderator:** Jan Claassen, M.D., Ph.D., F.N.C.S., Columbia University

**Faculty:** Thomas Bleck, M.D., Rush University Medical Center

Multimodality monitoring of brain physiology following acute brain injury is increasingly utilized to improve patient outcomes. EEG findings following acute brain injury are at times controversial and multimodality monitoring may offer insights into underlying mechanisms and identify harmful patterns. This workshop will discuss current knowledge of applying multimodality monitoring for these purposes using a case based approach. We will further highlight areas of future research and limitations of the techniques.

**Small Vessel Phenotype: Lumping, Splitting, Reimaging**

**Grand Ballroom 7-8, Third Level**

**Moderator:** Michael J. Schneck, M.D., F.A.H.A., F.A.A.N., F.A.C.P., Loyola University

**Faculty:** Rebecca Gottesman, M.D., Ph.D., Johns Hopkins University

Peter Kochunov, Ph.D., University of Maryland

James F. Meschia, M.D., Mayo Clinic, Jacksonville

Natalie S. Rost, M.D., Massachusetts General Hospital

In this session, the four speakers will discuss the genetic, epidemiologic, and radiographic bases of small vessel phenotypes. Dr. Natalia Rost will discuss the concept of small vessel disease heterogeneity across various subject populations and cerebral vascular pathologies, which are supported by current neuroimaging and genetic markers. Dr. Rebecca Gottesman will refer to epidemiologic data, emphasizing shared neuroimaging characteristics and shared risk factors among different small vessel phenotypes. Dr. James Meschia will speak on Mendelian small vessel diseases, including CADASIL, TREX1, CARASIL, and RCVL. Finally, Dr. Peter Kochunov will discuss findings of several research projects that used neuroimaging to parcel out the genetic and environmental risk factors for small vessel damage including hypertension and exposure to hypobaria. The speakers will then have an open discussion with interaction and questions from the audience.

**NeuroNEXT**

**Grand Ballroom 9-10, Third Level**

**Moderator:** Merit E. Cudokowicz, M.D., Massachusetts General Hospital

**Faculty:** Stephen Kolb, M.D., Ph.D., Ohio State University Medical Center

Richard Nowak, M.D., M.S., Yale School of Medicine
NeuroNEXT is a NINDS supported phase II trial biomarker group. It consists of 25 sites and clinical and data coordination centers. Network designed for efficiency with central IRB and master contracts to facilitate study start up. Experienced centers with funded staff ensure on target enrollment and high quality data. Come learn how to apply to run your study in NeuroNEXT. Academics from all sites and pharmaceutical (large or small) all can apply to use the network for their phase II studies.

Meet the Editors*
Dover A-C, Third Level

Moderator: Sudha Seshadri, M.D., Boston University
Faculty: Clifford B. Saper, M.D., Ph.D., Annals of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School
Karen Furie, M.D., M.P.H., Brown Medical School, Rhode Island Hospital, Stroke and JNNP
Bradford B. Worrall, M.D., M.Sc., Neurology, University of Virginia Health System
Roger Rosenberg, M.D., Jama Neurology, University of Texas Southwestern Medical School
Argye Beth Hillis, M.D., Behavioral Neurology, Johns Hopkins University

Editors from the Annals of Neurology, JAMA Neurology, Behavioral Neurology, Neurology, Journal of Neurology, Neurosurgery, & Psychiatry, and Stroke will be available to discuss the submission process, publishing, tips, and other key topics of interest.

*This session is not available for AMA PRA Category 1 Credit™.

1:15 – 3:15 PM
Grand Ballroom 5-6, Third Level

SYMPOSIUM:
NEUROLOGICAL CHALLENGESPOSED BY RECURRING AND NEW VIRAL INFECTIONS

Chairs: Micheline McCarthy, M.D., Ph.D., University of Miami
Avindra Nath, M.D., National Institutes of Health (NIH)

Recurring and new viral infections pose unique neurological challenges in the 21st century. More patients are living with chronic HIV-1 infection due to early diagnosis and use of anti-viral drugs. As these patients age, however, the “living well” may be vulnerable to premature cognitive decline or neuroimmunological complications of chronic infection. Progressive multi-focal leukoencephalopathy (PML) was a complicating opportunistic infection during the era of AIDS. But in this era of managed HIV infection, PML has re-emerged as an insidious complication of the use of immunomodulatory therapies to treat both systemic and neurological auto-immune disease or to prevent organ rejection after transplant. Epidemic flaviviruses, notably West Nile Virus and Dengue, are emerging as recurring causes of neurological disease in regions subject to epidemic viral fevers. Neurological complications of these viruses, as well as yet uncharacterized viral encephalitides may be difficult to diagnose and detect, much less treat. This symposium will discuss current views of the pathogenesis and management of these neurovirological infections, and will also address new molecular microbiological and immunological diagnostic methods that illuminate the role of the microbiome in health and disease.

Learning Objectives: Having completed this symposium, participants will be better prepared to do the following in practice:

1. Identify potentially treatable conditions that may contribute to neurological disease in older HIV+ patients with virologic suppression on antiretroviral therapy.
2. Recognize neurocognitive dysfunction in aging HIV populations
3. Describe the pathophysiology of accelerated aging in HIV-infected patients

1:15 – 1:35 PM
Aging with HIV: Neurological Challenges and Opportunities
Neurological Frontiers in Aging with HIV
Ronald Ellis, M.D., University of California, San Diego

1:40 – 2:00 PM
The Link Between Natalizumab and PML: Putting the Pieces of the Puzzle Together
Eugene O. Major, Ph.D., NINDS, National Institutes of Health (NIH)
2:05 – 2:25 PM  
Raymond D. Adams Lectureship Award Winner  
**Progressive Multifocal Leukoencephalopathy in the Era of Monoclonal Antibodies**  
Joseph R. Berger, M.D., University of Pennsylvania

2:30 – 2:50 PM  
**Neurologic Dengue and Neuroinvasive West Nile Virus Update**  
Larry E. Davis, M.D., University of New Mexico

2:55 – 3:15 PM  
**Small Game Hunting**  
W. Ian Lipkin, M.D., Columbia University

3:15 – 3:30 PM  
**Coffee Break**  
Harborside and Grand Ballroom Foyers, Third and Fourth Levels

3:30 – 5:30 PM  
**Special Interest Group Symposia**

**Multiple Sclerosis**  
*Multiple Sclerosis as a Neurodegenerative Disease: Biomarkers of Progression and Treatment Strategies*  
Grand Ballroom 9-10, Third Level  
**Co-Chairs:** Benjamin M. Segal, M.D., University of Michigan  
Ari Green, M.D., University of California, San Francisco

This section will focus on multiple sclerosis as a neurodegenerative disease. Invited speakers will discuss emerging understanding of the cellular and molecular biology of MS disease progression, clinical methods for assessing risk of progression using biomarkers, state-of-the-art techniques for monitoring disease progression using imaging, and cutting-edge therapeutic efforts aimed at protecting and restoring function in patients with MS. Platform speakers will also be selected from submitted abstracts that address understanding, monitoring or treating progression in MS.

**LEADERS IN THE FIELD PRESENTATIONS:**

3:30 – 3:50 PM  
**Optical Coherence Tomography Versus Magnetic Resonance Imaging for Monitoring MS Disease Progression**  
Shiv Saidha, M.B.B.Ch., Johns Hopkins University

4:00 – 4:20 PM  
**Cervical Spinal Cord Gray Matter Atrophy: A Bio Marker for MS Disease Progression**  
Regina Schlaeger, M.D., University of California, San Francisco

4:30 – 4:50 PM  
**Dysregulation of the IL-23/IL-17 axis in Secondary Progressive MS**  
David Irani, M.D., University of Michigan

**DATA BLITZ PRESENTATIONS:**

5:00 – 5:10 PM  
**The Effect of Glatiramer Acetate Treatment on Mitochondrial Dynamics in Experimental Allergic Encephalomyelitis**  
Christopher T. Bever, M.D., M.B.A., VA Maryland Health Care System

5:10 – 5:20 PM  
**Refining Our Understanding of Prognosis in Progressive Multiple Sclerosis (MS) – Patient Reported Outcomes (PROs) as Part of Composite Predictive Models of Aggressive Disease**  
Vicentiu I Apostu, M.R.C.P., Derriford Hospital

5:20 – 5:30 PM  
**Macromolecular Proton Fraction (MPF) and Magnetization Transfer Ratio (MTR) in Normal Appearing Brain Tissues as Imaging Biomarkers in Multiple Sclerosis (MS)**  
Vasily L. Yarnykh, Ph.D., University of Washington

**Behavioral Neurology**  
*Electrophysiological Recordings in the Awake Human Brain: Promises and Challenges of Electro-Corticography (ECOG)*  
Grand Ballroom 1-2, Third Level  
**Co-Chairs:** Maurizio Corbetta, M.D., Washington University, St. Louis  
Maria Luisa Gorno Tempini, M.D., Ph.D., University of California, San Francisco

This interest group will focus on the new method of electrocorticography (ECOG) to study brain functions and its application in behavioral neurology/neuroscience. Invited speakers will discuss the methodology of ECOG as applied to cognitive neuroscience/behavioral neurology issues; the utilization of ECOG for brain-computer interface and brain stimulation; and ECOG potential for future treatment of neurological disorders. Platform speakers will also be selected from submitted abstracts that relate to the issue of cortical stimulation and network analysis of brain disorders.

**LEADERS IN THE FIELD PRESENTATIONS:**

3:30 – 3:50 PM  
**Intracranial EEG and Electrical Brain Stimulation To Study The Localization of Functions in the Human Brain in Experimental and Real-Life Conditions**  
Josef Parvizi, M.D., Ph.D., Stanford University

4:00 – 4:20 PM  
**More Than the Sum of its Parts: Multimodal Approaches to Language**  
Thomas Thesen, Ph.D., New York University

4:30 – 4:50 PM  
**Cortical Network Dynamics in Human Cognition and Epilepsy from the Perspective of ECoG**  
Nathan E. Crone, M.D., Johns Hopkins University
DATA BLITZ PRESENTATIONS:

5:00 – 5:10 PM
Retinal Nerve Fiber Layer Thinning Is Associated With Medial Temporal Lobe Atrophy And Dysfunction In Otherwise Healthy Older Adults
Michael E. Ward, M.D., Ph.D., University of California, San Francisco

5:10 – 5:20 PM
Natural History of Post-Stroke Apathy during Acute Rehabilitation
Andrew Goldfine, M.D., M.S., Burke Medical Research Institute

5:20 – 5:30 PM
Diagnosing the Cerebellar Cognitive Affective Syndrome
Franziska Hoche, M.D., Harvard Medical School, Massachusetts General Hospital,

Health Services Research
Organizing and Implementing – Tools for Health Services Researchers to Motivate and Mobilize Change on a Broad Scale in Healthcare
Grand Ballroom 3-4, Third Level

Chair: Kevin A. Kerber, M.D., M.S., University of Michigan
Co-Chair: David Newman-Toker, M.D., Ph.D., Johns Hopkins University

There is a wide gap between the goals to deliver efficient care and the reality of practice. In the HSR SIG, information about specific practice gaps and opportunities will be presented and discussed.

LEADERS IN THE FIELD PRESENTATIONS:

3:30 – 3:50 PM
“Starting from Scratch” – Insights from the Diagnostic Errors Movement for Building a Research Program from the Ground Up
David Newman-Toker, M.D., Ph.D., Johns Hopkins University

4:00 – 4:20 PM
Implementation Science – A Transformational Tool for Modern Medicine
Peter J. Pronovost, M.D., Johns Hopkins University

DATA BLITZ PRESENTATIONS:

4:30 – 4:40 PM
Facilitating Early-In-Day Discharge for Multiple Sclerosis Inpatients Treated with Intravenous Methylprednisolone: A Quality Improvement Project
John Probascio, M.D., Johns Hopkins University

4:45 – 4:55 PM
Healthcare Resource Utilization Preceding First Diagnosis for Fragile X Syndrome (FXS)
Tara Nazareth, Novartis Pharmaceuticals Corporation

5:00 – 5:10 PM
Neurologists: Primary Care Providers or Proceduralists?
Lesli E. Skolarus, M.D., M.S., University of Michigan

5:15 – 5:25 PM
PROMIS® Physical and Mental Health Measures across 5 Neurologic Disorders
Lisa M. Shulman, M.D., University of Maryland School of Medicine

Interventional Neurology
Grand Ballroom 7-8, Third Level

Chair: Dileep R. Yavagal, M.D., M.B.B.S., University of Miami Miller School of Medicine
Co-Chair: Sam Zaidat, M.D., Medical College of Wisconsin

Interventional Neurology is a new subspecialty for neurologists focused on catheter based minimally invasive diagnosis and therapy of mainly neuromuscular disorders. The field is rapidly advancing with new therapeutic devices and biological therapies such as stem cells being added to the armamentarium of the interventional neurologist. Scientific data to facilitate evidence based practice has also steadily accumulated for these new therapies. The SIG in interventional neurology will address advances in flow diverter stents for treatment of wide-neck cerebral aneurysms, acute stroke intervention for ischemic stroke, update the audience on results from the recently completed first US intra-arterial stem cell clinical trial for stroke, and address the diagnosis and management of neuromuscular dural arteriovenous fistulas. These topics will substantially address the practice gaps in keeping up with the recent advances in the field for all neurologists.

LEADERS IN THE FIELD PRESENTATIONS:

3:30 – 3:50 PM
Flow Diverters in the Treatment of Complex Intracranial Aneurysms
Tibor Beske, M.D., New York University School of Medicine

4:00 – 4:20 PM
Acute Stroke Endovascular Therapy: Where are we Now?
Sam Zaidat, M.D., Medical College of Wisconsin

4:30 – 4:50 PM
Update on Clinical Trials of Intra-arterial Stem Cell Therapy for Stroke
Dileep R. Yavagal, M.D., MBBS, University of Miami Miller School of Medicine

5:00 – 5:20 PM
Comprehensive Stroke Center Certification: Implications for Interventional Neurology
Jawad Kirmani, M.D., JFK Medical Center
Regulatory Science
Regulatory Issues and Clinical Trials in Rare Neurological Disorders
Essex A-C, Fourth Level

Co-Chairs: Bernard Ravina, M.D., M.S., Voyager Therapeutics
           Merit E. Cudkowicz, M.D., Massachusetts General Hospital

The SIG will focus on The Regulatory Framework and Clinical Trial Design Options for Rare Diseases. There is a knowledge gap in developing therapies for rare diseases. The regulatory pathways and options for clinical trials are different than for other populations. The SIG will directly address these gaps with presentations from regulatory experts and academic clinical researchers/statisticians.

LEADERS IN THE FIELD PRESENTATIONS:

3:30 – 3:40 PM
Common Issues in Clinical Trials for Rare Disorders
Bernard Ravina, M.D., M.S., Voyager Therapeutics and Merit
Cudkowicz, M.D., Massachusetts General Hospital

3:40 – 4:00 PM
Therapeutics Development in Familial ALS
Timothy Miller, M.D., Ph.D., Washington University

4:10 – 4:30 PM
Therapeutics Development for Neurofibromatosis
Jaishri Blakeley, M.D., Ph.D., Johns Hopkins University

4:40 – 5:00 PM
Regulatory Perspectives on Therapeutics Development for Rare Neurological Disorders
Wilson W. Bryan, M.D., Center for Biologics Evaluation and Treatment, Food and Drug Administration

5:10 – 5:30 PM
Panel Discussion
All Faculty & Co-Chairs
Dissect Neural Mechanisms Underlying Differential Pain Acuity of Body Regions

Wenqin Luo, M.D., Ph.D., University of Pennsylvania

It has long been appreciated that the human fingertips are a “fovea” (region of high spatial acuity) for the tactile system due to the small receptive field sizes and high density of mechanoreceptors [1,2]. It was only recently discovered that the fingertips are also a fovea for pain [3,4]. However, skin biopsy studies show that the fingertips have a lower density of nociceptive fibers than other skin areas [4], raising the question of how a region with low receptor density can display high spatial acuity. We recently generated a novel inducible CreERT2 mouse line (MrgD^CreERT2) that induces recombination specifically in non-peptidergic nociceptors, a major type of mammalian nociceptor mediating mechanical pain and beta-alanine triggered itch. Using this line, we used high-density and single-cell level labeling to characterize non-peptidergic nociceptor innervation across the entire body. We found that paw skin features a lower density of non-peptidergic nociceptor terminals when compared to trunk skin, consistent with the human data. In addition, receptive field sizes were comparable for these two skin regions. Surprisingly, the spinal cord terminals of paw-innervating and trunk-innervating nociceptors display distinct morphologies (paw nociceptors have short and round terminals, while trunk nociceptors have long and thin terminals). This finding suggests that pain circuits representing paw and trunk skin are differently organized, possibly explaining the high acuity of the distal limbs for pain stimuli. Future work will dissect the exact differences between paw and trunk non-peptidergic nociceptor circuits, providing the first description of region-specific differences in pain circuit functional organization.


L-serine Supplementation in HSAN1: Overcoming Altered Substrate Selectivity

Florian Eichler, M.D., Harvard Medical School

Hereditary sensory neuropathies are progressive disorders characterized by sensory loss, pain and variable motor symptoms. One of these neuropathies, hereditary sensory neuropathy type 1 (HSAN1), is caused by missense mutations in the SPTLC1 gene encoding a subunit of the enzyme serine palmitoyltransferase. The mutant enzyme shows a shift from its canonical substrate L-serine to the alternative substrate L-alanine. This shift leads to increased formation of neurotoxic deoxysphingolipids (dSL). We found that oral L-serine supplementation is able to inhibit dSL generation in mice and humans, an insight that has led to the first therapeutic clinical trial in this debilitating disorder. In assessing disease mechanisms, we found divergent effects of L-serine and L-alanine upon dendrite development in murine dorsal root ganglia. These observations demonstrate metabolic effects on development that impact neurodegeneration and are not isolated to HSAN1 but are common to a host of disorders involving lipid metabolism. Based on our recent finding that dSL also accumulate in humans and mice with diabetes, we believe there may be a mechanistic link between HSAN1 and diabetic polyneuropathy. Unraveling the impact of genetically-determined aberrations in metabolism may enhance our understanding of basic mechanisms of sensory neuron degeneration.

References:


Chasing Men on Fire: Na Channels and Peripheral Nerve Disease

Stephen G. Waxman, M.D., Ph.D., Yale University School of Medicine and VA Connecticut

As a result of the molecular revolution it is now clear that nine different genes encode nine different subtypes of sodium channels, all sharing a similar overall structure but with slightly different amino acid sequences, and with subtly (or in some case not-so-subtly) different physiological and pharmacological properties. Since non-specific sodium channel blockers have central (e.g. confusion,
sedation, diplopia) and cardiac side-effects, a holy grail of pain research has centered on the question of whether there are “peripheral” sodium channels, with limited expression/ function in the brain and heart, that might be targeted to more effectively treat pain. Three sodium channel subtypes (Nav1.7, Nav1.8, Nav1.9, encoded by genes SCN9A, SCN10A, SCN11A) meeting this criterion as peripheral sodium channels have been identified. While much work on these channels is going on in vitro and in animal models, these models do not effectively predict human response to channel block. Thus there has been substantial interest in human validation.

Here I will discuss molecular genetic studies which have identified and validated Nav1.7, Nav1.8 and Nav1.9 as human pain targets. Nav1.7 was first linked to human pain via studies on very rare families with inherited neuropathic pain (Inherited Erythromelalgia, IEM) due to gain-of-function mutations of Nav1.7, and channelopathy-associated insensitivity to pain due to loss-of-function mutations of Nav1.7. The leap from rare genetic model diseases was made by discovery of Nav1.7 gain-of-function mutations in painful small fiber neuropathy. More recently, Nav1.8 and Nav.9 mutations have been found in small fiber neuropathy. Hopefully these findings will provide a basis for the development of new, more effective pain therapies.

References:

Calcitonin Gene-Related Peptide (CGRP) and Migraine: Gepants and MABs
Peter J. Goadsby, M.D., Ph.D., University of California, San Francisco

Migraine is the most common cause of neurological disability on a worldwide basis 1 and the most common reason for patients to be referred to neurologists. In contrast, primary headache disorders, by any reasonable comparative measure, are the least funded and poorly taught components of neurology. CGRP is a neuropeptide that has emerged as a target for both acute and preventive treatment of migraine and cluster headache 2.

It has been shown that CGRP is released into the cranial circulation during acute severe migraine 3 and that sumatriptan both alleviates an attack and normalises that elevation 4. Based on these and subsequent studies small molecule CGRP receptor antagonists, gepants, have been developed and are effective in acute migraine 5. Several compounds have been developed: olcegepant, telcagepant, MK-3207, BI44370 TA and BMS-927711; each has been shown to be effective in randomized placebo-controlled trials 6. The development of telcagepant and MK-3207 has been stopped with off-target hepatic toxicity. Nevertheless the remaining compounds, without vasoconstrictor effects, and with excellent tolerability would be a boon for acute migraine prevention.

Most recently, monoclonal antibodies to the CGRP peptide, ALD-403 7, LY2951742 8 and LBR-101 9, or to the CGRP receptor, AMG 334 10, have been studied as preventive treatments in episodic migraine. Two studies have been reported, both were positive, and contained a tantalizing group of patients above of about 16% of patients, when compared to placebo, who were 100% migraine free at three months.

Migraine patients need new and better migraine treatments. CGRP-based targets may well usher in a new age of mechanism-based therapies for the most common cause of neurological disability worldwide: migraine.

References:
The sudden unexpected death in epilepsy (SUDEP) is infrequent but catastrophic outcome of epilepsy. It is defined as the sudden unexpected, witnessed or unwitnessed, non-traumatic, and non-drowning death of a patient with epilepsy with or without evidence of a seizure, excluding documented status epilepticus, and in which postmortem examination does not reveal a structural or toxicological cause of death.” (Nashef et al., 1997). SUDEP accounts for up to 18% of all epilepsy related death and symptomatic epilepsy, medically intractable epilepsy, polypharmacy and frequent convulsive seizures are known epidemiological risk factors (Silanpaa and Shinnar, 2010; Hesdorffer et al., 2011). Still, the individual SUDEP risk prediction will need to take into the account emerging knowledge about the SUDEP molecular mechanisms that appear to drive the complex cardio-respiratory compromise often accompanied by postical generalized EEG suppression (PGES). The currently known candidate SUDEP genes are either associated with the control of respiration and arousal or they are the molecules dually expressed within the neuro-cardiac and autonomic pathways (Massey et al. 2014). Mouse and human research indicates complex oligogenic interaction at play in premature epilepsy mortality. Precision molecular diagnostic and prediction of individual SUDEP risk will necessitate research involving complex collaborative network of families, physicians, forensic pathologists, and basic and translational scientists as piloted by the STOP SUDEP registry and genetic repository and by the Center for SUDEP Research sponsored by the National Institute of Neurological Disorders and Stroke (NINDS).

References:

For people with cervical spinal cord injury, pontine stroke, neuromuscular disease including amyotrophic lateral sclerosis, and other neurologic illnesses, currently available assistive and rehabilitation technologies are inadequate. In severe brainstem stroke and advanced ALS, patients may enter a locked-in state of being awake and alert but unable to move or communicate. Through clinical translation based on decades of fundamental neuroscience research, intracortically-based “brain-computer interfaces” are poised to revolutionize our ability to restore lost function. Neurectechnologies to record the individual and simultaneous activities (action potentials, multi-unit activity, and local field potentials) of dozens to hundreds of cortical neurons have yielded new understandings of cortical function in movement, vision, cognition, and memory. This preclinical research, generally performed with healthy, neurologically intact non-human primates, has demonstrated that direct neural control of virtual and physical devices can be achieved. Over the past decade, this exciting research has been translated into initial pilot clinical trials (IDE) of an intracortically-based neural interface system (BrainGate), seeking to determine the feasibility of persons with tetraplegia controlling a computer cursor or other devices simply by imagining movement of their own hand. A variety of methods for decoding brain signals are being tested with the hope of not only restoring communication, but also providing a signal for control of robotic assistive devices or the reanimation of paralyzed limbs. Simultaneously, and through the efforts of extraordinary clinical trial participants, this research provides the opportunity to test fundamental hypotheses about the function of human cortical neuronal ensembles, over a period of years. In related research, early glimpses into the activities of dozens of cortical neurons of people with pharmacologically refractory epilepsy are providing new insights into the neuronal dynamics of seizures, as well as the potential for new diagnostic and therapeutic modalities.

References:
TorsinA Hypofunction Causes Abnormal Twisting Movements and Sensorimotor Circuit Neurodegeneration
Richard Liang, Ph.D., University of Michigan

Lack of a preclinical model of primary dystonia that exhibits dystonic-like twisting movements has stymied identification of the cellular and molecular underpinnings of the disease. The classical familial form of primary dystonia is caused by the DYT1 (ΔE) mutation in TOR1A. We found that conditional deletion of Torla in the CNS or isolated CNS expression of DYT1 mutant torsinA in vivo causes animals to develop perinuclear accumulation of ubiquitin and the E3 ubiquitin ligase HRD1 in discrete sensorimotor regions, followed by neurodegeneration and abnormal twisting movements2. Similar to the neurodevelopmental onset of DYT1 dystonia in humans3, the behavioral and histopathological abnormalities emerged and became fixed during CNS maturation in the murine models. Our research establishes a genetic model of primary dystonia that is overtly symptomatic, and link torsinA hypofunction to neurodegeneration and abnormal twisting movements. These findings provide a cellular and molecular framework for how impaired torsinA function selectively disrupts neural circuits and raise the possibility that discrete foci of neurodegeneration may contribute to the pathogenesis of DYT1 dystonia. Recently, from our in vivo studies on the selective vulnerability suggest that torsinB not only shares functional redundancy with torsinA but also influences the neuropathological changes as a critical determinant of neuronal susceptibility to neurodegeneration.

References:


The ALS/FTD C9ORF72 Hexanucleotide Expansion Disrupts Nucleocytoplasmic Transport
Thomas E. Lloyd, M.D., Ph.D., Johns Hopkins University

Expansion of GGGGCC (G4C2) hexanucleotide repeats in C9ORF72 is the most common genetic cause of ALS/FTD spectrum disorders. Recent evidence suggests that the hexanucleotide expansion likely causes neuronal toxicity via a gain-of-function mechanism and may be mitigated by antisense oligonucleotides (ASOs). Using a recently generated Drosophila model of ALS caused by overexpression of 30 G4C2 repeats (Xu et al, PNAS, 2013), we have identified Ran-GAPI1, a key regulator of nuclear transport, as a potent suppressor of G4C2-mediated neurodegeneration. Interestingly, Ran-GAPI1 binds to the hexanucleotide repeat sequence of C9ORF72 (Donnelly et al, Neuron, 2013), and accumulates within perinuclear punctae in iPS neurons derived from C9ORF72 ALS patients. Importantly, genetic perturbations that inhibit nuclear export also suppress G4C2-mediated neurodegeneration, whereas genetic inhibition of nuclear import dramatically enhances the phenotype. Furthermore, expression of G4C2 blocks nuclear import of coexpressed GFP containing a nuclear localization signal (NLS:GFP). Consistent with these findings, we find that the RNA-binding protein TBPH (Drosophila TDP-43), which normally cycles between the cytoplasm and nucleus, is mislocalized to and accumulates in the cytoplasm. Thus, we hypothesize that generalized nucleocytoplasmic transport defects might underlie the cytoplasmic accumulation of TDP-43 and contribute to the pathogenesis of ALS/FTD.

References:

Adherence to Guidelines: Are Ischemic Stroke Patients Receiving Guideline-Concordant Cardiac Stress Testing?
Jason J. Sico, M.D., VA Connecticut Healthcare System, Yale University School of Medicine

Ischemic stroke and ischemic heart disease (IHD) share many of the same vascular risk factors, especially such atherosclerotic risk factors as hypertension, diabetes, hyperlipidemia, and cigarette smoking. An estimated 20 to 30% of stroke patients have symptomatic IHD, whereas 40% are thought to have silent ischemia. Cardiovascular disease is a common cause of adverse events in the first three months post-stroke, with 2 to 6% of stroke patients dying from vascular causes and 4 to 6% being readmitted with myocardial infarction. While cardiac evaluation in the acute and subacute post-stroke, with 2 to 6% of stroke patients dying from vascular causes and 4 to 6% being readmitted with myocardial infarction. While cardiac evaluation in the acute and subacute
The FCRS uses age, gender, cholesterol and blood pressure values, and cigarette smoking and diabetes status to determine 10-year risk of cardiovascular disease. Stroke patients are more likely to have a ‘high risk’ FCRS compared to demographically matched controls.(3) Previous studies have demonstrated that the FCRS can be reliably calculated from administrative data and the recommendation can feasibly be implemented at discharge for patients with TIA and ischemic stroke. Adherence to cardiac screening among recently discharged ‘high risk’ stroke patients occurs in a minority of patients, with providers citing lack of outcomes data to support the guideline as a reason for not ordering testing.(4) In the absence of a prospective study to guide whether implementation of cardiac screening among post-stroke patients improves outcome or changes patient management, we used administrative data to determine whether post-stroke patients routinely received guideline concordant cardiac stress testing. Further, we evaluated whether screening for asymptomatic IHD improved one year all-cause mortality among ‘high risk’ ischemic stroke patients.

We examined medical records that were abstracted for a sample of 3965 Veterans from 131 Veterans Health Administration (VHA) facilities who were admitted for a confirmed diagnosis of ischemic stroke (fiscal year 2007). Patients with a history of IHD, receipt of cardiac stress testing within 18-months prior to stroke event, and patients who died during the index hospitalization were excluded (n=1628). Administrative data were used to calculate FRS and to determine whether or not cardiac stress testing was performed within 6-months following discharge from the index stroke hospitalization. Among 2337 stroke patients, 28% (n=664) had FCRS 20, and a total of 6% (n=140) had cardiac stress testing within 6-months of discharge. Cardiac stress testing was not more frequently performed among those with ‘high risk’ (5.6%) than those with ‘low risk’ (6.2%) FRS. High risk patients were as likely to have received cardiac stress testing as those with low FCRS (OR = 0.90; CI: 95: 0.61-1.32). High risk patients that received screening also had lower one-year all-cause mortality compared with those that did not receive screening (5% versus 19%; P=0.018).

In conclusion, guideline concordant cardiac screening is underutilized among ischemic stroke patients without evidence of previous cardiac stress testing. Patients at the highest risk of future cardiac events were not more likely to receive cardiac stress testing than patients with lower risk. Further, those at highest risk were likely to have lower mortality when screening was performed. Additional research is required to identify potential barriers to CHD screening, and to determine reasons behind a potential mortality benefit when guideline concordant cardiac screening is performed.

References:


Genome Modification Leads to Ablation of Nuclear RNA Foci in Human DM1 Neural Stem Cells
Guangbin Xia, M.D., Ph.D., University of Florida

Myotonic dystrophy type 1 (DM1) is caused by expanded CTG repeats in the 3’-untranslated region (3’ UTR) of the DMPK gene1. The advancement of induced pluripotent stem (iPS) cell technology has introduced new possibilities for developing cell-based therapies and correcting the mutation in DM1 iPS cells would be an important step towards autologous stem cell therapy. The objective of this study is to demonstrate in vitro genome editing to prevent production of nuclear RNA foci, which accumulate mutant expanded CUG transcripts, in DM1 cells. Genome editing was performed in DM1 neural stem cells derived from human DM1 iPS cells. Integration of a cassette containing Dasher GFP (daGFP) or puromycin selectable marker and SV40/bGH polyA signals upstream of DMPK 3’UTR CTG repeats was mediated by TALEN-induced double-strand break (DSB) and homologous recombination (HR). TALEN has facilitated the site specific integration of the cassette containing poly A signals upstream the CTG repeat expansion. The integration of the poly A signal led to complete disappearance of nuclear RNA foci. We conclude genome modification by integration of exogenous polyA signals upstream of the DMPK CTG repeat expansion prevents the production of toxic RNA. Our data provide proof-of-principle evidence that the genome modification can be used to generate genetically modified progenitor cells as a first step toward autologous cell transfer therapy for DM1.

References:
The Neurexin Enigma – From Synapse Formation to Schizophrenia

Thomas C. Südhof, M.D., Avram Goldstein Chair, Professor of Molecular and Cellular Physiology, and Investigator of the Howard Hughes Medical Institute, Stanford University School of Medicine, 2013 Nobel Laureate in Physiology or Medicine

Neurexins and their ligands are trans-synaptic cell-adhesion molecules that are essential for synapse function, and that shape the properties of synapses such as short- and long-term plasticity. Neurexins are presynaptic cell-adhesion molecules that are encoded by three extraordinarily large genes, each of which generates longer α- and shorter 6-isofoms that are in turn diversified into thousands of alternatively spliced transcripts. Neurexins bind to multiple postsynaptic ligands, including neuroligins, LRRTMs, and the complex of cerebellins with GluR2. The various splice variants of neurexins and the various isofoms of their ligands exhibit strikingly different functional activities and binding affinities; their interactions are likely competitive, and contribute to determining the properties and nature of synapses. Accumulating evidence demonstrates that neurexins and their ligands perform central functions in the assembly and function of neural circuits, but their precise roles and mechanisms of action are only now beginning to emerge. Moreover, many different mutations in neurexin and their ligands have been associated with autism, schizophrenia and intellectual disability, suggesting that the functions of these molecules are relevant for insight into these devastating disorders. In my talk, I will describe our recent studies on how neurexins and their ligands shape synapse properties, and how dysfunction of neurexins and their ligands might predispose to neuropsychiatric disorders.

Gene Discovery and the Emerging Biology of Autism Spectrum Disorders: The Synapse and Beyond

Matthew State, M.D., Ph.D., University of California, San Francisco

The past decade has witnessed a profound shift in the ability to identify the genetic contributors to neurodevelopmental syndromes, including autism spectrum disorders (ASD). While there is convincing evidence that variations that are common in the human population contribute to ASD risk, so far progress in identifying specific genes involved in the biology of autism spectrum disorders has come about instead through the study of rare mutations.

Much of the recent progress, in fact, can be traced to the observation that de novo mutations play a significant role in a substantial minority of ASD cases, particularly those from simplex families, i.e. with only one affected first degree relative (1). Subsequently studies of simplex cohorts have confirmed the contribution of rare de novo copy number variations, submicroscopic alterations in chromosomal structure, and, more recently, of rare de novo point mutations and insertion–deletions mapping to the coding region of the genome (2).

These recent successes in gene discovery have quickly paved the way for novel approaches to integrating genomic, transcriptomic and proteomic data to begin to unravel the complex biology of ASD. Recent analyses have pointed to mid-fetal cortical development as a critical point of vulnerability in ASD (3), and highlighted the role of chromatin modifiers and targets of the Fragile X Mental Retardation Protein (4).

This presentation will review recent genomic and transcriptomic studies of ASD, including comprehensive investigations of the Simons Simplex Collection, the most extensive, publicly available resource for simplex family-based ASD genetic studies. These investigations have clarified the genetic architecture of ASD, identified chromosomal intervals carrying marked risks for the individual, and resulted in the discovery of more than 20 autism genes. They have also established a firm foundation for the elaboration of pathophysiological mechanisms underlying ASD.

References:

Immune Mechanisms Underlying Synaptic Pruning in Development & Disease

Beth Stevens, Ph.D., Boston Children’s Hospital, Harvard Medical School

An early hallmark of Alzheimer’s disease (AD) is a progressive, region-specific degeneration of synapses; however, molecular mechanisms that drive synapse loss and dysfunction in AD remain unclear. Synapse loss in healthy developing nervous system is a normal and
highly regulated process required for proper brain wiring and synaptic connectivity. Recent work has identified unexpected roles for an immune pathway—proteins of classical complement cascade, C1q and C3, and microglia—for elimination and refinement of synaptic connections in postnatal mouse brains (Stevens et al., 2007; Schafer et al., 2012). Interestingly, AD brains have highly increased levels of C1q and downstream complement proteins, and certain complement cascade interactors have emerged as susceptibility genes in AD. Here we hypothesized that mechanisms similar to developmental synapse pruning may be involved to drive synapse loss in early stages of AD pathogenesis. We found a region-specific upregulation and deposition of complement proteins onto synapses well before cognitive and pathological phenotypes in several AD transgenic mice. Moreover, genetic deletion of classical complement cascade components protected against early synapse loss and cognitive impairment in AD mouse models. Together, our results suggest that aberrant reactivation of a normal developmental pruning pathway may work together to mediate early synapse loss in pre-plaque brains, marking an important step in development of AD synaptic pathology. This study has broad therapeutic implications for AD and other age-dependent neurodegenerative diseases involving synaptic loss and dysfunction.

**SYMPOSIUM: BRAIN AND CONNECTOME: INITIATIVES SHAPING THE FUTURE OF CLINICAL NEUROSCIENCE**

**View From Above: The Human Connectomes**

Marcus Raichle, M.D., *Washington University*

Our ability to view the living human brain in health and disease changed dramatically in 1973 when Godfrey Hounsfield announced the invention of X-ray computed tomography. Gone were the days of pneumoencephalography and arteriography for the delineation of brain anatomy, tests that were both difficult to interpret and unpleasant for patients. The invention of X-ray CT also spawned the development of two other imaging techniques, positron emission tomography or PET and magnetic resonance imaging or MRI, both destined to play critical roles in our understanding of human brain function in health and disease.

Functional brain imaging with PET and MRI has followed a long tradition in neuroscience of studying responses to stimuli and task performance. In this work the role of bottom-up versus top-down or feed-forward versus feed-back causality has been frequently discussed reflecting a debate extending back a century or more on the relative importance of intrinsic and evoked activity in brain function. Brain imaging has entered this discussion with information that importantly shaping future research. Rapidly accumulating evidence suggests that intrinsic (ongoing) activity within the brain may be critical in determining brain function.

Accompanying this explosion in human brain imaging has been the realization making the massive amount of accumulating data as widely available as possible is imperative. This has resulted in the highly organized Human Connectome Project as well as a number of other large databases in the United States and abroad. The cumulative effect of the research itself and its wide dissemination should have an increasingly important impact on our understanding of the human brain in health and disease.

**References:**


**What the BRAIN Initiative is About**

Joshua R. Sanes, Ph.D., *Harvard Medical School*

In 2013, President Obama launched the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative to “accelerate the development and application of new technologies that will enable researchers to produce dynamic pictures of the brain that show how individual brain cells and complex neural circuits interact at the speed of thought.” The Director of the NIH then convened a working group to “articulate the short-, mid-, and long-term scientific goals for achieving the vision of the NIH BRAIN Initiative; and develop a scientific plan for achieving these goals.” Aware that a plan advocating everything will end up accomplishing nothing, the group focused somewhat narrowly on the functional analysis of neural circuits as an overarching theme. They were convinced that this area is poised for revolutionary advances and that these advances will, in turn, benefit almost all areas of basic and clinical neuroscience.

The groups consulted with a large number of basic scientists, clinicians and others, then reported back to the Director in May, 2014. They recommended a 10-year plan that begins with an effort to develop multiple transformative technologies; it then shifts gradually to integrating these technologies to make fundamental new discoveries about how the brain works. Highest priority areas are the following:

- Identify and provide experimental access to multiple brain cell types.
- Generate circuit diagrams that vary in resolution from synapses to the whole brain.
- Produce a dynamic picture of the functioning brain through large-scale monitoring of neural activity.
- Link brain activity to behavior with precise interventional tools that affect neural circuits.
- Develop and apply theoretical and data analysis tools to understand the biological basis of mental processes.
- Develop innovative technologies to understand the human brain and treat its disorders, and create integrated human brain research networks to implement these technologies.
• Integrate new technological and conceptual approaches to discover how dynamic patterns of neural activity are transformed into cognition, emotion, perception, and action in health and disease.

Reference:

Microdissecting the Function of Human Brain Circuits...at the Speed of Thought
Edward Chang, M.D., University of California, San Francisco

A major gap in our understanding of human brain function exists because of basic shortcomings in available methodologies for safely measuring spatiotemporal dynamics of neuronal populations. Single neuron recordings are feasible, however they are severely limited by spatial sampling and safety. On the other hand, fMRI and other noninvasive methods are constrained in both temporal and spatial detail, though they provide excellent whole brain coverage. A significant gap exists between the scales of resolution across these modalities.

New methods must be developed that can record direct neural activity at the millimeter (e.g. at the resolution of maps and columns) and millisecond time scale to advance human neuroscience research. Careful investigation in human subjects has several advantages. For example, perception can be directly reported through one’s subjective experience and probed with natural stimuli that are relevant to human behavior. Similar examples exist for studies of motor control, learning, and cognition.

I will discuss how recent advances in clinical intracranial recordings in surgical epilepsy and movement disorder patients are now revolutionizing our approach to fundamental questions in human neuroscience. Through DARPA and the Presidential BRAIN Initiative, next-generation devices for safe and high-throughput recording and stimulation technologies are being innovated now. Such technology will lead to major discoveries about higher-order, emergent brain function in humans, and will have direct implications for brain-machine interfaces and other therapeutic approaches to neurological disability.

References:

Connectomics and the Allen Institute’s MindScope Project
R. Clay Reid, M.D., Ph.D., Allen Brain Institute

The current decade is emerging as golden age of neuroanatomy. Connectomics began was defined a decade ago, mostly as an aspiration for the future, but is likely to emerge as a mature field in this decade. In the first published use of the term (Sporns, Tononi, and Kotter, 2005 PLoS Comp Biol), it was recognized that connectomics should be considered on multiple scales, from the macroscale of entire brains to the microscale of individual synaptic connections between neurons. At the Allen Institute, we have begun a ten-year program to study the cerebral cortex of mice and humans. The mouse program, called MindScope, concentrates on the cortico-thalamic visual system and seeks to examine the computations that lead from visual input to behavioral responses. In this program, there is a strong emphasis on neuroanatomy, or connectomics at a macro- and microscale. Already a large-scale study of mesoscale connectivity in the mouse brain has been completed (Oh et al., 2014 Nature). Future work will include further mesoscale connectivity atlases that concentrate on the mouse visual system, as well as microscale connectivity of local cortical circuits. At a microscale, we have demonstrated that the relationship between structure and synaptic connectivity can be studied in local cortical circuits by combining in vivo physiology with subsequent network anatomy with electron microscopy (Bock et al., Nature, 2011; and subsequent studies), leading towards a functional connectome (Reid, 2012, Neuron). I will examine the near-term and long-term prospects for microscale connectomics and argue that connectomics at all scales must be combined with functional studies to fully exploit its great promise.

References:
Amyotrophic lateral sclerosis (ALS) is a uniformly lethal motor neuron degenerative disorder that sometimes occurs in association with frontotemporal dementia. The advent of next-gen DNA sequencing technologies has accelerated the search for genetic variants that cause or modify the phenotype of this disease. More than 35 ALS genes are now recognized, offering insights into ALS pathogenesis. At least three broad themes are evident, implicating conformational instability of key proteins, perturbations of RNA processing and disturbances of neuronal cytoskeletal elements. Recent studies have emphasized a role for non-neuronal cells in ALS pathogenesis and highlighted the hypothesis that cellular spread of pathology in ALS may entail intercellular migration of misfolded proteins. In the last three years, the field of ALS genetics has been transformed by the finding that the most common cause of familial ALS is an expansion of an intronic hexanucleotide repeat in the gene C9orf72. The pathobiology of the expanded repeat is under intensive investigation, highlighting several models for its neurotoxicity. A direct adverse impact of the large RNA tract has been implicated. Studies have also underscored a role for a striking process of ATG-independent protein production (“RAN translation”) across the repeat domain, initially discovered in the context of SCA8. New cell and animal models of ALS have been generated using many of the ALS genes, allowing in-depth analysis of therapeutic approaches, including both conventional small molecules and innovative biological modalities. These extraordinary developments permit new optimism in the search for meaningful ALS treatments.

References:

C9ORF72: A Tale of Two Neurodegenerative Diseases
Bryan Traynor, M.D., National Institutes of Health (NIH)

Amyotrophic lateral sclerosis (ALS; Lou Gehrig’s disease) is a fatal neurodegenerative disorder that leads to rapidly progressive paralysis and respiratory failure. ALS is the third most common neurodegenerative disease in the Western World, and there are currently no effective therapies. Frontotemporal dementia (FTD) is the most common form of dementia in the population under the age of 65. An overlap between these two clinically distinct neurological diseases has long been recognized, but the molecular basis of this intersection was unknown.

Recently, the Laboratory of Neurogenetics at the National Institute on Aging identified the major genetic cause of both ALS and FTD. To do this, Dr. Traynor organized a worldwide consortium, bringing together groups that had previously been competitors to focus their efforts towards identifying this gene. This was made possible by the next generation sequencing technologies available at the NIH. This innovative approach worked, and his group published the cause of chromosome 9-linked ALS/FTD in the journal Neuron in September 2011. In these cases, the disease is caused by a six base pair segment of DNA that is pathologically repeated over and over again, up to several thousand times. This so-called large hexanucleotide repeat disrupts the C9ORF72 gene located on chromosome 9. This is the most common genetic cause of both ALS and FTD identified to date, accounting for approximately 40% of all familial cases of ALS and FTD in European and North American populations. Further, Dr. Traynor’s group has shown that this mutation underlies about 8% of cases of sporadically occurring ALS and FTD that lack a family history. This represents the first time that a common genetic cause has been identified for the sporadic form of these diseases.

The discovery of the C9ORF72 hexanucleotide repeat expansion is a landmark discovery in our understanding of neurodegenerative disease. It has already greatly effected how these diseases are diagnosed, investigated and perceived, and provides a mechanistic link between two clinically distinct disorders, ALS and FTD. It also provides a distinct therapeutic target for gene therapy efforts aimed at ameliorating the disease, and such efforts are already well underway.

References:
Toxic Peptides from C9ORF72 Expansions
Leonard Petrucelli, M.D., Mayo Clinic, Florida

Our lab has been at the forefront investigating cellular mechanisms causing neurodegeneration in diseases characterized by abnormal protein aggregation, including Alzheimer’s disease, frontotemporal lobar degeneration (FTD) and amyotrophic lateral sclerosis (ALS). In expanding upon our commitment to understanding the causes of such diseases, we are now emphasizing translational research geared toward identifying and developing therapies for treatment and prevention.

A significant portion of patients suffering from ALS and FTD, two diseases commonly seen in comorbidity, carry an expanded non-coding hexanucleotide (GGGGGC) repeat in the C9orf72 gene, a condition commonly referred to as c9FTD/ALS. We recently discovered the RNA structure of GGGGCC and CCGGGG repeats may cause C9orf72-related neurodegeneration via their accumulation into foci and by serving as a template for the synthesis of aggregation-prone “c9RAN proteins” by repeat-associated non-ATG (RAN) translation1,2.

During the symposium, we will explore the significance of RAN translation, specifically in terms of the toxicity that results from RAN translation in various cell models, including models generated from patient-derived fibroblasts, and in vivo systems. We will also discuss how epigenetic events may play a role in disease3. Finally, given no biomarker currently exists for ALS and FTD, we will discuss the use of c9RAN proteins in patient cerebrospinal fluid as a potential biomarker with significant clinical implications4.

References:

Repeat Associated non-ATG (RAN) Translation: New Starts and Directions in Neurological Disease
Laura Ranum, Ph.D., University of Florida

Since their initial discovery more than 20 years ago, microsatellite expansion mutations are now known to cause more than 30 different neurologic diseases. Typically, research for these disorders has focused on understanding the effects of the loss- or gain-of-function effects of a single mutant protein (e.g. Huntington’s disease) or RNA (myotonic dystrophy type 1 (DM1)). Currently there are no effective treatment strategies for any of these disorders.

In 1999 we showed that SCA8 is caused by a CTG•CAG expansion mutation. Over the years our work has led to a number of surprising discoveries. In 2006, we demonstrated that the SCA8 CTG•CAG expansion produces RNAs in both directions1. In 2011, we discovered that one of the basic rules scientists use to predict if a gene can make a protein does not apply for CTG•CAG repeats and that CAG and CUG expansion RNAs can express homopolymeric expansion proteins in all three reading frames without an AUG start codon2. For example, CAGEXP RNAs express polyGln, polyAla, polySer while CUGEXP RNAs express polyLeu, polyAla and polyCys proteins. We showed this repeat associated non-ATG (RAN) translation, is hairpin-dependent, occurs without framesshifting or RNA editing and is observed in SCA8 and DM1 mouse and human tissues2. We and others have also shown RAN translation occurs in C9ORF72 amyotrophic lateral sclerosis/frontotemporal dementia (ALS/FTD9), and fragile X tremor ataxia syndrome (FXTAS)3.

Similar to SCA8, we demonstrated that the C9orf72 ALS/FTD hexanucleotide expansion mutation is expressed in both the sense GGGGCC and antisense GCYCCC directions and that that these RNAs accumulate as nuclear and cytoplasmic foci in patient tissues. Additionally we show that both sense GGGGCC and antisense GCYCCC expansion mutations produce dipeptide expansion proteins with Gly-Ala, Gly-Pro, Gly-Arg, Pro-Arg, Pro-Ala expansion motifs. Cell culture studies show RAN translation of these repeats occurs with as few as 30 repeats and that these proteins are toxic. We have generated several panels of antibodies to detect novel RAN proteins in vivo and show ALS/FTD-dipeptide proteins accumulate as protein aggregates in several regions in C9ORF72 positive but not control autopsy brains. We will discuss recent work on the mechanisms of RAN translation and insights from mouse models.

In summary, the discovery of RAN translation has implications for understanding fundamental mechanisms of protein synthesis and translational control and should now be considered for a broad category of neurological disorders. Additionally, our new understanding that some expansion mutations can express two mutant RNAs and up to six mutant proteins highlights the need to explore therapies that will block the effects of both sense and antisense RNAs and RAN proteins.
References:

SYMPOSIUM: NEUROLOGICAL CHALLENGESPOSED BY RECURRING AND NEW VIRAL INFECTIONS

Aging with HIV: Neurological Challenges and Opportunities
Neurological Frontiers in Aging with HIV
Ronald Ellis, M.D., University of California, San Diego

Learning Objective: Identify potentially treatable conditions that may contribute to neurological disease in older HIV+ patients with virologic suppression on antiretroviral therapy.

Assessment Outcomes: When assessing an older HIV+ individual who is virologically suppressed on ART, important comorbid conditions to consider include: A. myelopathy due to accelerated spondylosis. B. parkinsonism related to anti-HIV medications. C. cerebrovascular disease related to metabolic syndrome disorders

References:
www.cdc.gov/hiv/topics/over50


The Link Between Natalizumab and PML: Putting the Pieces of the Puzzle Together
Eugene O. Major, Ph.D., NINDS, National Institutes of Health (NIH)

The incidence of Progressive Multifocal Leuкоencephalopathy (PML, JC virus induced demyelinating disease) has risen sharply over the last decade due to not only HIV infection but to the use of biological therapies that modulate the immune system. The highest incidence of PML occurs in MS patients treated with natalizumab, a monoclonal antibody directed to the α4 integrin 61 and 7 epitopes, who have a past history of immune suppression, are antibody positive to JCV and received 24 monthly doses or more. The incidence in this patient group is approximately 1:80, slightly higher than in HIV infected individuals. PML is the only significant adverse event in these patients that raises the question of the link between natalizumab and onset of PML. Investigations on the mechanisms of JCV infection in these patients have revealed sites of viral latency in the bone marrow and release of infected
cells into the peripheral circulation, the molecular control of JCV multiplication as cells progress to mature B cells, and trafficking to the brain. The talk will detail the evidence of these steps to explain how and why natalizumab augments the incidence of PML. The prominent risk factors are presence of latent viral DNA in immune cells, rise in antibody titer during course of natalizumab treatment, inadequate CD 4 and CD 8 T cell response to JCV infection, and increased expression of transcription factors in pre B cells that activates JCV multiplication.

References:

Progressive Multifocal Leukoencephalopathy in the Era of Monoclonal Antibodies
Joseph R. Berger, M.D., University of Pennsylvania

With the advent of the HIV/AIDS pandemic in 1981, progressive multifocal leukoencephalopathy, PML, a disease first described in 1958, ceased being a rare disorder. The recognition in 2005 of PML with natalizumab, a monoclonal antibody directed against α4β1 and α4β7 integrin for the treatment of multiple sclerosis (MS) and Crohn's disease, heightened interest which has been further magnified by its appearance with other biological agents (Berger 2010) including, efalizumab, belatacept, rituximab, and alemtuzumab as well as immunomodulatory agents that were not monoclonal antibodies, such as, mycophenolate mofetil.

However, the risk varies very considerably among therapies. Between the ages of 1 and 5 years, approximately 10% of children demonstrate antibody to JCV, by age 10, 40-60%, and in adulthood as many as 79 to 90% of some populations are seropositive and as many as one third are actively secreting JC virus in their urines. No disease has been convincingly associated with acute infection and the mechanism of viral spread remains speculative.

PML can present in variegated fashions with cognitive and behavioral disorders, weakness, gait disorders, visual impairment, and sensory loss among the more commonly observed findings. Seizures and headache have also been reported. Magnetic resonance imaging can be extraordinarily helpful in establishing the diagnosis. Lesions may occur virtually anywhere in the brain and although characteristically multifocal, need not be. The frontal lobes and parieto-occipital regions are the regions that appear to be most commonly affected. Lesions typically appear hyperintense on T2WI and FLAIR and hypointense on T1W1 (Youssry 2012). Contrast enhancement, once thought to be rare, may be seen and is often indicative of the PML- Immune Reconstitution Inflammatory Syndrome (PML-IRIS). CSF examination is most helpful in excluding alternative diagnoses. Demonstrating the presence of JCV DNA in the CSF by PCR enables diagnosis of the disease when coupled by the appropriate clinical and MRI findings (Berger 2013). Brain biopsy reveals a characteristic histopathological triad of demyelination, bizarre astrocytes and enlarged oligodendroglial nuclei (Astrom 1958).

Unfortunately, there are no established therapies for PML; however, based on laboratory data, a number of therapies have been suggested. Survival is dependent on restoration of immune function. Therefore, prognosis is heavily dependent on the underlying condition predisposing to PML. PML due to a drug effect that can be readily reversed, e.g., natalizumab, has a better prognosis than illnesses, e.g., a B cell malignancy predisposing to the disorder.

References:

Neurologic Dengue and Neuroinvasive West Nile Virus Update
Larry Davis, M.D., University of New Mexico

Dengue a flavivirus poses a risk to 1/3rd of the world’s population, and causes 100 million clinical illnesses/year. Dengue virus has 4 serotypes and is transmitted by Aedes aegypti, a mosquito that thrives in warm, moist conditions found in tropical and subtropical regions worldwide. Dengue virus is transmitted to humans through the bite of an infected Aedes mosquito. Dengue can cause a range of illnesses from a mild flu-like illness to a severe and sometimes fatal complication called dengue hemorrhagic fever (DHF). DHF is characterized by symptoms such as fever, headache, muscle pain, vomiting, and a rash. In severe cases, DHF can lead to shock and multi-organ failure, which can be fatal. Prevention of dengue involves avoiding mosquito bites by using insect repellent, wearing long-sleeved clothing, using mosquito nets, and removing standing water to eliminate breeding sites of Aedes mosquitoes.
**aegypti** and **Aedes albopictus** mosquitoes from viremic humans to susceptible humans. Dengue hemorrhagic fever and dengue shock syndrome, although uncommon, cause severe illnesses and occasional deaths. Dengue neurologic disease usually is a subset of the severe disease and manifests as encephalopathy or encephalitis. Clinical features vary from mild encephalopathy to seizures, coma, and paralysis. Cerebral edema and intracerebral hemorrhages are occasionally seen on neuroimaging.

Death may occur with virologic evidence of a CNS dengue infection demonstrated at autopsy. Dengue is diagnosed during the viremia of the fever phase by detection of virus RNA using RT-PCR or NS1 glycoprotein viral antigen in blood. In convalescence, presence of serum IgM antibody is diagnostic of a recent infection. Management of patients with severe dengue is challenging when shock or hemorrhages develop. No antiviral drugs are available and there is no current vaccine approved by the FDA. Unfortunately, infection with one dengue virus serotype does not protect from infection of the other serotypes and second infections may lead to more severe disease.

In the US, 650 cases of dengue develop each year in returning travelers. Since **Aedes** mosquito vectors are present in parts of the Eastern, Southern, and Western states, secondary local spread of dengue is possible. Endemic dengue outbreaks have occurred in Hawaii, Southern Florida, and Southern Texas in the past 10 years, including Miami, Florida in 2014.

West Nile virus (WNV) is also a flavivirus that appeared in New York City in 1999. This arbovirus is a zoonosis that each spring and early summer is transmitted by over 60 species of mosquitoes mainly between birds. In late summer and fall when birds migrate south, humans become most susceptible to the infected mosquitoes. WNV neuroinvasive disease is the most common viral encephalitis in the US.

The virus rapidly spread across the US with a peak in 2003. Human WNV infections are usually asymptomatic in children and young adults. Older adults and individuals with immunosuppression may develop WNV neuroinvasive disease. Clinical manifestations include a meningitis, encephalitis, and occasionally a flaccid paralysis syndrome. In patients with encephalitis, the virus often infections the basal ganglia and brainstem to produce tremors and even Parkinsonism. When the virus infects the spinal cord, it attacks the anterior horn cells producing a polio-like paralysis that often causes permanent limb weakness or death.

Like dengue, there are no antiviral drugs available so management is symptomatic. No human vaccines are FDA approved. However, development of IgG WNV serum antibodies leads to permanent protection from subsequent disease.

**References:**


**Small Game Hunting**

W. Ian Lipkin, M.D., **Columbia University**

The pace of pathogen discovery is increasing dramatically. This reflects not only factors that enable the appearance and globalization of new microbial infections but also improvements in methods for ascertainment. New molecular diagnostic platforms; investments in microbial surveillance in wildlife, domestic animals and humans; and the advent of social media tools that mine the world wide web for clues to outbreaks of infectious disease are proving invaluable in early recognition of threats to public health. Additionally, models of microbial pathogenesis are becoming more complex, providing insights into mechanisms by which microbes can contribute to chronic illnesses like cancer, peptic ulcer disease and mental illness. Here we review methods for microbial surveillance and discovery, recent advances in microbiome research, the use of prospective cohorts to dissect the role of gene-environment interactions in health and disease, strategies and pitfalls in linking discoveries to disease and point to opportunities for improvements in genetic and proteome instrumentation and analysis and the use of social media and medical informatics that will further advance clinical medicine and public health.

**References:**

Thomas Christian Südhof was born in Göttingen in 1955, obtained his M.D. and doctoral degrees from the University of Göttingen in 1982. He performed his doctoral thesis work at the Max-Planck-Institut für biophysikalische Chemie in Göttingen with Prof. Victor P. Whittaker on the biophysical structure of secretory granules. From 1983-1986, Südhof trained as a postdoctoral fellow with Drs. Mike Brown and Joe Goldstein at UT Southwestern in Dallas, TX, and elucidated the structure, expression and cholesterol-dependent regulation of the LDL receptor gene. Subsequently, Südhof served on the faculty of UT Southwestern in Dallas until 2008, where he was founding chair of the Department of Neuroscience. Since 2008, Südhof has been the Avram Goldstein Professor in the School of Medicine at Stanford University. In addition, Südhof has been an Investigator of the Howard Hughes Medical Institute since 1986.

Südhof’s research interests focus on the molecular mechanisms underlying synapse formation and function, in particular on how synapses transmit signals from one neuron to the next, and how they become abnormal during disorders such as Parkinson’s disease, autism, and schizophrenia. His studies have identified and functionally characterized key molecules in synapses, such as synaptotagmins, RIMs, Munc13s, Munc18s, complexins, neurexins, and neuroligins, and studied the role of these molecules in the information processing capacity of the brain. Among others, Südhof’s laboratory found that synaptotagmins generally function as the calcium sensors for exocytosis, including synaptic vesicle exocytosis mediating neurotransmitter release, that RIMs function as central organizers of presynaptic active zones that dock synaptic vesicles and recruit Munc13 priming factors and calcium-channels to active zones, and that neurexins, neuroligins, and LRRTMs function as the central trans-synaptic cell-adhesion molecules at synapses that organize the assembly of synapses into signaling machines. Südhof’s work has been important for understanding neurodegenerative disorders because of his discovery that synucleins, key proteins involved in neurodegeneration, function as chaperones during neurotransmitter release. Moreover, his work has shed light on schizophrenia and autism pathogenesis. Mutations in synaptogenic molecules Südhof discovered predispose to these neuropsychiatric disorders, and mouse models of these gene mutations that Südhof produced mimic features of these disorders.

Südhof is a member of the National Academy of Sciences, the Institute of Medicine, and the American Academy of Arts and Sciences, and is recipient of several awards, including the Kavli Award in Neuroscience, the Alden Spencer Award, the Bristol-Myers Award in Neuroscience, the Passano Award, the Lasker-deBakey Medical Basic Research Award, and the Nobel Prize in Physiology or Medicine.

**2014 AWARD INFORMATION**

**RAYMOND D. ADAMS LECTURESHIP**
This lectureship was established in 2000 to honor Dr. Raymond D. Adams, emeritus Bullard Professor of Neurology at Harvard Medical School and emeritus Chief of the Neurology Service as the Massachusetts General Hospital. An ANA member at the Annual Meeting presents the lectureship.

**Joseph R. Berger, M.D., University of Pennsylvania**
As of July 1, 2014, Dr. Joseph R. Berger is Professor of Neurology and Chief of the Multiple Sclerosis Division of the Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania. Dr. Berger started his professional career at the University of Miami where his research focused on the neurological complications of HIV/AIDS. Between 1995 and 2013, he was the Chair of the Department of Neurology at the University of Kentucky and director of their MS Center. Dr. Berger is particularly interested in the interface between MS and infectious diseases.

**F.E. BENNETT MEMORIAL LECTURESHIP**
Foster Etting Bennett, MD established a lectureship in memory of his son, which has been given to outstanding researchers and educators in neurology since 1979.

**Matthew State, M.D., Ph.D., University of California, San Francisco**
Matthew State received his MD from Stanford University, completed a residency in psychiatry and fellowship in child psychiatry at UCLA and earned a PhD in Genetics from Yale, where he joined the faculty in 2001. In 2013 he moved to UCSF and is now the Oberndorf Family Distinguished Professor and Chair of the Department of Psychiatry. Dr. State's lab studies the genetics and genomics of childhood neuropsychiatric disorders. He co-leads several international genomics collaborations, including the NIH-funded Autism Sequencing Consortium and he has been the recipient of multiple awards and recognition including, his recent induction into the Institute of Medicine.
Soriano Lectureship
The first Soriano lecture was given in 1987 which marked the 40th year of consecutive attendance at ANA meetings by Victor Soriano and his wife. The couple chose to sponsor a lectureship to be given at the ANA, so that in future years the Sorianos would always be linked to all of you, through a brilliant lecture delivered by an outstanding scientist...”

Stephen G. Waxman, M.D., Ph.D., Yale University School of Medicine, VA Connecticut
Stephen Waxman is the Bridget Flaherty Professor of Neurology, Neurobiology, and Pharmacology at Yale University, served as Chairman of Neurology at Yale from 1986 until 2009, and is Director of the Neuroscience & Regeneration Research Center at Yale. His research has defined the ion channel architecture of nerve fibers, demonstrated its importance for axonal conduction, and explicated the role of sodium channels in MS. In translational leaps from laboratory to humans, he carried out molecule-to-man studies combining molecular genetics, molecular biology, and biophysics to demonstrate the contribution of ion channels to human pain, and led an international coalition that identified sodium channel mutations as causes of peripheral neuropathy. A member of the Institute of Medicine of the National Academy of Sciences, Waxman’s many awards include the Tuve Award (NIH), the Distinguished Alumnus Award (Albert Einstein College of Medicine), the Dystel Prize and Wartenberg Award (American Academy of Neurology), and the Middleton Award and Magnuson Award of the Veterans Administration. He has been honored in Great Britain with The Physiological Society’s Annual Prize, an accolade that he shares with Nobel Prize laureates Andrew Huxley, John Eccles, and Alan Hodgkin.

He has received international recognition for his research, which uses tools from the “molecular revolution” to find new therapies that will promote recovery of function after injury to the brain, spinal cord, and peripheral nerves.

Derek Denny-Brown Neurological Scholar Award
Selected by the Membership Advisory Committee, this award is given to newly elected members of the Association who have achieved a significant stature in neurological research and who promise to continue making major contributions to the field of Neurology.

Derek Denny-Brown Neurological Scholar Award in Basic Science:

Alica M. Goldman, M.D., PhD., Baylor College of Medicine
Dr. Alica Goldman is a neurologist specialized in the treatment of patients with epilepsy. She obtained her medical degree at the Medical School of the Comenius University in Slovakia and completed her neurology residency and epilepsy fellowship training at the University of Texas-Houston.

In parallel with medical training, she pursued scientific training in molecular biology and genetics initially at the Slovak Academy of Sciences and later at the Institute for Microbiology and Genetics at the University of Vienna in Austria and at the Institute for Molecular Genetics at Baylor College of Medicine in Houston. There she worked on the development of a mouse model for myotonic dystrophy and on a clinical translational project related to the genetic screening of female carriers of Duchenne muscular dystrophy. Dr. Goldman received a masters degree in clinical investigation through the Baylor Clinical Scientist Training Program led by Morrey L. Raymond.

Dr. Goldman joined the faculty at the Department of Neurology at Baylor College of Medicine in 2004 with the goal to apply her training in genetics to translational epilepsy research. Under the mentorship of Dr. Jeffrey L. Noebels, she became interested in the molecular underpinnings of sudden unexpected death in epilepsy (SUDEP) which led to the discovery of the first SUDEP risk gene, the KCNQ1 ion channel, as investigated in a genetic mouse model. Her subsequent research has been focused on human translational research of SUDEP genetics. In collaboration with professional colleagues and families nationally and internationally, she established the SUDEP Tissue Donation Program (STOP). The Program entails a SUDEP registry, genetic repository, and research with ongoing active recruitment of families affected by SUDEP. Applied epilepsy genetics, genetic testing, and its clinical utility have remained Dr. Goldman’s overarching clinical and research interests. In addition to her research, Dr. Goldman is an active clinical epileptologist with responsibilities in Baylor Comprehensive Epilepsy Program. The scientific development of Dr. Goldman was critically influenced by exceptional mentors, such as Doc.Dr. Viera...
The research work of Dr. Goldman was made possible initially due to funding from the Epilepsy Foundation of America/American Epilepsy Society and CURE, the Christopher Donnalty Award for SUDEP Research. These awards paved the way towards NINDS funding through the K08 Mentored Clinical Scientist Training Award and later an R01 NIH grant.

**Derek Derek Denny-Brown Neurological Scholar Award in Clinical Science:**

Leigh R. Hochberg, M.D., Ph.D., F.A.A.N., F.A.N.A., Massachusetts General Hospital, Harvard Medical School/ Brown University, Providence VA Medical Center

Leigh Hochberg received his Bachelors in Science with Honors in Neural Science at Brown University. During his M.D. and Ph.D. at Emory University he studied motor cortical plasticity, and during his graduate research was the first to use cortical recordings from chronically implanted electrodes to drive a robot wrist. After residency and chief residency in Neurology at Massachusetts General Hospital/Brigham and Women’s Hospital/Harvard Medical School, Dr. Hochberg stayed on as a fellow in Stroke and Neurocritical Care. Currently Dr. Hochberg has appointments as Neurologist, Massachusetts General Hospital, where he attends in the NeuroICU and on the Acute Stroke service; Associate Professor, School of Engineering and Institute for Brain Science, Brown University; Associate Director, Center for Neurorestoration and Neurotechnology, Providence VA Medical Center; and Senior Lecturer in Neurology at Harvard Medical School. Dr. Hochberg also directs the Neurotechnology Trials Unit for MGH Neurology, where he received his M.D. and later, an M.M.Sc. in clinical investigation. Dr. Hochberg has been a reviewer for journals in the field of myelin biology, neurodegeneration and inherited peripheral nerve diseases.

**Wolfe Neuropathy Research Prize**

The Wolfe Neuropathy Research prize was established in 2009 by Winston Wolfe and the ANA. The award was designed to honor an outstanding investigator who has identified a new cause or treatment of axonal peripheral neuropathy.

Jun Li, M.D., Ph.D., Vanderbilt University

Dr. Jun Li received his medical degree from Anhui Medical University and PhD from Drexel University College of Medicine. He completed his neurology residency training at Ohio State University and neuromuscular fellowship training at University of Utah. Dr. Li is a current tenured Associate Professor in Department of Neurology at Vanderbilt University. He was a recipient of NIH K08 ward. His laboratory has been funded by NIH and Muscular Dystrophy Association. He has published over 50 articles in peer-reviewed journals. Dr. Li has been elected to the editorial board of Experimental Neurology, the Journal of the Peripheral Nervous System and Neural Regeneration Research. He has been a member in the scientific advisory board of the Muscular Dystrophy Association and the study section of the National Institutes of Health. He has been a reviewer for journals in the field of neuropathy.

**The Grass Foundation – ANA Award in Neuroscience**

The Grass Foundation – ANA Award in Neuroscience was established in 2007 to honor outstanding young investigators doing research in basic or clinical neuroscience.

Joshua M. Shulman, M.D., Ph.D., Baylor College of Medicine

Joshua M. Shulman MD, PhD is an Assistant Professor of Neurology, Molecular and Human Genetics, and Neuroscience at Baylor College of Medicine and an Investigator in the Jan and Dan Duncan Neurological Research Institute at Texas Children’s Hospital. He received an A.B. in Biochemical Sciences from Harvard College, and his Ph.D. in Genetics from Cambridge University. He subsequently studied at Harvard Medical School and the Massachusetts Institute of Technology, Division of Health Sciences and Technology, where he received his M.D. and later, an M.M.Sc. in clinical investigation. Dr. Shulman completed his residency and fellowship training in the Harvard/Partners Neurology Program at the Brigham & Partners Neurology Program at the Harvard & Partners Neurology Program at the Brigham & Women’s Hospital and the Massachusetts General Hospital in Boston, MA. Before moving to Houston in August 2012, Dr. Shulman was
Associate Neurologist at the Brigham & Women’s Hospital and Assistant Professor in Neurology at Harvard Medical School. Dr. Shulman’s current research focuses on the genetic mechanisms of susceptibility for and pathogenesis of neurodegenerative disorders, including Parkinson’s disease and Alzheimer’s disease. His work integrates genetic investigation in human subject cohorts with functional experiments in fruit fly models relevant to disease. Dr. Shulman continues to see patients with Parkinson’s disease and related disorders within the Parkinson’s Disease Center and Movement Disorders Clinic at Baylor College of Medicine. Among his previous honors, Dr. Shulman has received a Career Award for Medical Scientists from the Burroughs Wellcome Fund and the C.W. Cotterman Award from the American Society of Human Genetics.

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