92ND ANNUAL MEETING

June 16-19, 2016

The Hyatt Regency Baltimore on the Inner Harbor

American Association of Neuropathologists

American Association of Neuropathologists 92ND ANNUAL MEETING

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS, INC.

June 16 - 19, 2016

Hyatt Regency at the Inner Harbor
Baltimore, Maryland

This activity is provided by the American Association of Neuropathologists.

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The American Association of Neuropathologists, Inc.
5575 S. Sycamore St., Suite 235
Littleton, Colorado 80120
Phone: 720-372-0888; Fax: 303-568-0406
Email: aanp@aoeconsulting.com

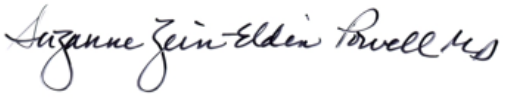
Dear Colleagues:

I would like to personally welcome each of you to the 92nd Annual Meeting of the American Association of Neuropathologists. It's an exciting time for AANP as we continue to grow and adapt, remaining always curious, motivated and responsive. It is important to meet and bring inspired people together in forums like this, to ensure our association remains at the cutting edge.

I'd like to give you an idea of what you can expect over the next few days. This year's meeting application (www.eventmobi.com/aanp2016) outlines a scheduled program of events that encompasses a wide variety of relevant topics, ranging from frontotemporal dementia to TBI in the military population. By the end of this year's annual meeting, we hope to cite new information on the underlying causes and mechanisms of neurologic diseases, discuss research findings related to genetics and molecular mechanisms to better understand disorders of brain neoplasia, CNS trauma, and neurodegeneration, and incorporate new knowledge into improving everyday clinical practice and teaching of neuropathology.

Thank you for attending our conference and bringing your expertise to our gathering. Throughout this conference, I ask you to stay engaged, keep us proactive, and help us shape the future of neuropathology. My personal respect and thanks goes out to all of you.

Sincerely,



Suzanne Z. Powell, MD
President
The American Association of Neuropathologists

Save the Date!

93RD ANNUAL MEETING

June 8-11, 2017 / Hyatt Regency Orange County

94TH ANNUAL MEETING

June 7-10, 2018 / Hyatt Regency Louisville

95TH ANNUAL MEETING

June 6-9, 2019 / Grand Hyatt Atlanta

All meetings to be held the second weekend of June

American Association of Neuropathologists

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

AANP OFFICE
5575 S. Sycamore St., Suite 235, Littleton, CO 80120
Phone: 720-372-0888; Fax: 303-568-0406
Email: aanp@aoeconsulting.com

OFFICERS

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Thomas J. Montine, MD, PhD, *University of Washington*

ARCHIVIST

Michael N. Hart, MD, *University of Wisconsin School of Medicine*

OFFICIAL JOURNAL

Journal of Neuropathology and Experimental Neurology
Raymond A. Sobel, MD, Editor-in-Chief
Eileen S. Healy, Managing Editor
E-mail: jnen@pathology.wisc.edu
Home page: http://www.jneuropath.com

DIAGNOSTIC SLIDE SESSION

Caterina Giannini, MD, PhD and Rebecca Folkerth, MD, *Managers*

AANP COMMITTEES

Awards Committee
Sandra Camelo-Piragua, MD (Chair)
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Ewa Borys, MD
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Cynthia Hawkins, MD, PhD
Cheng-Ying Ho, MD, PhD, FRCPC
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Jamie Jacobsohn, MD
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Quinwen Mao, MD, PhD
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Jennifer Baccon, MD

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Steven Carroll, MD, PhD
Andreana Rivera, MD

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Arie Perry, MD
Arnulf H. Koeppen, MD
E. Tessa Hedley-Whyte, MD
Goerge Perry, PhD

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Roberta Seidman, MD
Bret Mobley, MD

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Raymond A. Sobel, MD

Professional Affairs Committee
Kathy L. Newell, MD (Chair)
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Robert E. Mrak, MD, PhD
Marie Rivera Zengotita, MD
Eileen H. Bigio, MD
Dan J. Brat, MD, PhD
William H. Yong, MD
Mariarita Santi-Vicini, MD, PhD
Steven Dubner, MD
Doug Anthony, MD, PhD
Bradley Miller, MD, PhD

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Thomas Beach, MD
Ivana Delalle, MD
Charles Specht, MD
Miguel Guzman, MD
Mike Lawlor, MD
Adenkunle Adesina MD, PhD
Han Lee, MD
Anne Hiniker, MD, PhD
Richard Perrin, MD, PhD
Julie Kofler, MD
Amanda Fisher-Hubbard, MD
Michelle Madden Felicella, MD
Brent Orr, MD, PhD

Website Committee (Ad Hoc of Professional Affairs)
Douglas Anthony, MD, PhD (Chair)
John Crary, MD, PhD
Luis F. Gonzalez-Cuyar, MD
Jingxin Qiu, MD, PhD
Henry G. Brown, MD, PhD
Sonika Dahiya, MD
Kar-Ming Fung, MD, PhD
Charles L. White, III, MD
William McDonald, MD
Mark Cohen, MD
Murat Gokden, MD
Edward Lee, MD
Brian Moore, MD
Hilary Nickols, MD

CME INFORMATION

TARGET AUDIENCE

The educational design of AANP's Annual Meeting addresses the needs of physicians and scientists in the field of neuropathology who are involved in the diagnosis and/or treatment of patients with neurological disorders.

STATEMENT OF NEED

The purpose of this activity shall be to advance medical and scientific knowledge, understanding, and competence in the practice of neuropathology. The practice of neuropathology is understood to include diagnosis of diseases of the nervous system, scientific investigation into their causes, and teaching of neuropathology principles to colleagues and trainees.

LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

I. Cite new information on the underlying causes and mechanisms of neurologic diseases.

II. Discuss research findings related to genetics and molecular mechanisms to better understand disorders of brain neoplasia, CNS trauma, and neurodegeneration.

III. Incorporate new knowledge into improving everyday clinical practice and teaching of neuropathology.

DISCLAIMER

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented is this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed in this activity should not be used by clinicians without evaluation of patient conditions and possible contraindications on dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

PHYSICIAN ACCREDITATION STATEMENT

The American Association of Neuropathologists is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

PHYSICIAN CREDIT DESIGNATIONS

The American Association of Neuropathologists designates this live educational activity for a maximum of 24.50 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

CME INFORMATION (Continued)

CME CREDIT

Instructions to Receive Credit

In order to receive credit for this activity, the participant must complete the CME evaluations and credit applications for sessions attended, which are made available through the AANP Meeting App (**http://eventmobi.com/aanp2016**).

The chart below outlines which sessions are offered for CME credit and the maximum number of credit hours a physician can earn for each educational activity being certified for *AMA PRA Category 1 Credit™* at this year's Annual Conference.

Activity	CME Credit Hours
Special Course	6.75
Scientific Sessions	8
Korey Lecture	1
DeArmond Lecture	1
Parisi Lecture	1
Moore Lecture	1
Diagnostic Slide Session	3
Presidential Symposium	2.75
Total	**24.5**

For any questions regarding the accreditation of this meeting, please contact AANP's CME Coordinator, Sarah Schott, via e-mail at: sschott@aoeconsulting.com, or via phone at: 303-557-0859 x84.

DISCLOSURE INFORMATION

Disclosure of Commercial Support:
"In-kind" support through the donation of microscopes is being provided by Morrell Instruments.

Disclosure of Unlabeled Use:
This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The American Association of Neuropathologists does not recommend the use of any agent outside of the labeled indications.

The opinions expressed in this educational activity are those of the faculty and do not necessarily represent the views of any organization associated with this activity. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings.

Disclosure of Conflict of Interest:
The American Association of Neuropathologists requires instructors, planners, managers and other individuals who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by AANP for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis for content, and appropriateness of patient care recommendations. Complete disclosure information will be provided to learners on-site.

Planners and Managers

*The following planners and managers have **nothing to disclose**:*

Adenkunle **Adesina**, Doug **Anthony**, Jennifer **Baccon**, Eileen **Bigio**, Dan **Brat**, Sandra **Camelo-Piragua**, Ivana **Delalle**, Steven **Dubner**, Amanda **Fisher-Hubbard**, Matthew **Frosch**, Miguel **Guzman**, Anne **Hiniker**, Craig **Horbinski**, Eric **Huang**, Alexander **Judkins**, Julia **Kofler**, Jesse **Kresak**, Edward **Lee**, Han **Lee**, Michelle **Madden Felicella**, Quinwen **Mao**, Maria **Martinez-Lage**, Rupal **Mehta**, Thomas **Montine**, Brian **Moore**, Robert **Mrak**, Peter **Nelson**, Kathy **Newell**, Brent **Orr**, Cheryl **Palmer**, Richard **Perrin**, Arie **Perry**, Edward **Plowey**, Suzanne **Powell**, Peter **Pytel**, R. Ross **Reichard**, Marie **Rivera Zengotita**, Fausto **Rodriguez**, Mariarita **Santi**-**Vicini**, Raymond **Sobel**, Charles **Specht**, Susan **Staugaitis**, Anat **Stemmer-Rachamimov**, Mario **Suva**, Jane **Uyehara-Lock**, Sriram **Venneti**, Karen **Weidenheim**, Cindy **Welsh**, Charles **White III**, Anthony **Yachnis**, Gabrielle **Yeaney**, William **Yong**

The following **planners/managers** reported the following financial relationships or relationships to products or devices they or their spouse/ partner have with commercial interests related to the content of this CME Activity.

Thomas Beach	**Consultant/Independent Contractor:** GE Healthcare, Avid Radiopharmaceuticals **Grant/Research Support:** Navidea Biopharmaceuticals, Avid Radiopharmaceuticals, Janssen Research and Development
Michael Lawlor	**Consultant/Independent Contractor:** Sarepta Therapeutics **Grant/Research Support:** Audentes Therapeutics, Solid GT **Honoraria**: Audentes Therapeutics **Other:** Scientific Advisory Board Member – Audentes Therapeutics
Jack Lee	**Consultant/Independent Contractor:** UpToDate **Other:** Joint Patents with Corenelli Consulting and others - Drug for AD and anti-anxiety effects
Bradley Miller	**Stock Shareholder:** Eli Lilly and Company **Other:** Eli Lilly and Company

DISCLOSURE INFORMATION (Continued)

Faculty

*The following faculty have **nothing to disclose:***

Maram **Abdaljaleel**, Malak **Abedalthagafi**, Stephanie **Adams**, Homa **Adle-Biassette**, Heather **Ames**, Tejus **Bale**, Jill **Bayliss**, W. Robert **Bell**, Eileen **Bigio**, Daniel **Brat**, David **Brody**, Nigel **Cairns**, Neil **Cashman**, Emily **Chan**, Leila **Chemelli**, Rati **Chkheidze**, Matthew **Cykowski**, Dennis **Dickson**, Charles **Eberhart**, David **Ellison**, Rebecca **Folkerth**, Matthew **Frosch**, Christine **Fuller**, Maria-Magdalena **Georgescu**, Bernardino **Ghetti**, Caterina **Giannini**, Pallavi **Gopal**, Brian **Harding**, Kimmo **Hatanpaa**, Cynthia **Hawkins**, Lili-Naz **Hazrati**, Marco **Hefti**, Craig **Horbinski**, Eric **Huang**, David **Irvin**, Heather **Jarrell**, Kasthuri **Kannan**, Joseph **Kellum**, Elaine **Keung**, Bette **Kleinschmidt-DeMasters**, Julia **Kofler**, Walter **Koroshetz**, Boleslaw **Lach**, Caitlin **Latimer**, Mirna **Lechpammer**, Edward **Lee**, Norman **Lehman**, Benjamin **Liechty**, David **Louis**, James **Mandell**, Quinwen **Mao**, Ann **McKee**, Ian **Mckenzie**, Steven **Moore**, Melissa **Murray**, MacLean **Nasrallah**, Peter **Nelson**, Amber **Nolan**, Derek H. **Oakley**, Brent **Orr**, Angelica **Oviedo**, Dan **Perl**, Richard **Perrin**, Edward **Plowey**, Suzanne **Powell**, Michael **Punsoni**, Amyn **Rojiani**, Jiri **Safar**, Peyman **Samghabadi**, Katherine **Schwetye**, Matija **Snuderl**, Raymond **Sobel**, David **Solomon**, Thor **Stein**, Trevor **Steve**, William **Stewart**, Mario **Suva**, Masaki **Takao**, Vivian **Tang**, Andrew Franklin **Teich**, Cheddhi Jahan **Thomas**, Rachael **Vaubel**, Erik **Williams**, Angela **Wu**, Ming **Yuan**

The following **faculty** reported the following financial relationships or relationships to products or devices they or their spouse/ partner have with commercial interests related to the content of this CME Activity.

Ted Dawson	**Consultant/Independent Contractor:** Inhibikase Therapeutics, Dong-A ST **Grant/Research Support:** Abbvie, Inc., Inhibikase Therapeutics **Stock Shareholder:** Valted L.L.C.
Brittany Dugger	**Research Support:** Daiichi Sankyo
Michael Lawlor	**Consultant/Independent Contractor:** Sarepta Therapeutics **Grant/Research Support:** Audentes Therapeutics, Solid GT **Honoraria**: Audentes Therapeutics **Other:** Scientific Advisory Board Member: Audentes Therapeutics

GENERAL INFORMATION

LOCATION

Hyatt Regency Baltimore – Inner Harbor
300 Light Street
Baltimore, MD 21202

All meeting sessions will be held at the Hyatt Regency Baltimore.

All platform presentations and general sessions (Special Course, Korey Lecture, DeArmond Lecture, Parisi Lecture, Moore Lecture, Business Meetings, Diagnostic Slide Session, and Presidential Symposium) will be held in **Constellation CDEF** of the hotel on the second floor.

All poster sessions will be held in **Atrium/Harborview** on the second floor.

REGISTRATION DESK

Constellation Foyer	
Wednesday, June 15	4:00 pm – 8:00 pm
Thursday, June 16	7:00 am – 5:00 pm
Friday, June 17	7:00 am – 5:00 pm
Saturday, June 18	7:00 am – 5:00 pm
Sunday, June 19	7:00 am – 12:00 pm

PRE-REGISTRATION PICK-UP

Attendees pre-registered and pre-paid for the Meeting will have their name badge, program booklet, and June 2016 issue of *JNEN* with abstracts ready for pick-up at the AANP Registration Desk, located in the foyer area outside of **Constellation CDEF** on the second floor. On-site registration and additional tickets for the Annual Reception will be available at the registration desk. Registration receipts are available upon request.

NAME BADGE REQUIREMENT

Your name badge is required for admittance to any function of the Association, including the Special Course, all Friday, Saturday and Sunday sessions, and the Friday evening reception.

MICROSCOPE VIEWING ROOM

Multi-headed microscopes will be available in **Charles** on the third floor of the hotel.

Location: Charles Room	
Thursday, June 16	7:00 am – 7:30 pm
Friday, June 17	7:00 am – 7:30 pm
Saturday June 18	7:00 am – 7:30 pm
Sunday, June 19	7:00 am – 12:00 pm

GENERAL INFORMATION (Continued)

SPECIAL MEETINGS BY INVITATION

Day/Date	Meeting	Time/Location
Wednesday, June 15	**NP Program Directors Meeting**	4:30 pm – 6:30 pm **Pratt/Calvert**, 3rd Floor
	Education Committee Meeting	6:30 pm – 9:30 pm **Annapolis/Baltimore**, 2nd Floor
Thursday, June 16	**Awards Committee Meeting #1**	5:30 pm – 6:00 pm **Pratt/Calvert**, 3rd Floor
	Executive Council Meeting	6:00 pm – 9:00 pm **Lombard**, 3rd Floor
Friday, June 17	**Trainee Luncheon*** ***Open to all Trainees**	11:45 am – 2:00 pm **Columbia/Frederick**, 2nd Floor
	Website Committee Meeting	12:30 pm – 1:30 pm **Pratt/Calvert**, 3rd Floor
	Awards Committee Meeting #2	5:30 pm – 6:30 pm **Pratt/Calvert**, 3rd Floor
	Professional Affairs Committee Meeting	5:30 pm – 7:00 pm **Lombard**, 3rd Floor
Saturday, June 18	***JNEN* Editorial Board Meeting**	7:00 am – 8:00 am **Columbia**, 2nd Floor
	Awards Committee Meeting #3	6:00 pm – 8:00 pm **Pratt/Calvert**, 3rd Floor
	Presidential Reception	6:00 pm – 9:00 pm **Columbia**, 2nd Floor
Sunday, June 19	**DSS Founders Breakfast**	7:00 am – 8:00 am **Columbia**, 2nd Floor

ANNUAL RECEPTION

The annual reception will be held 6:30 pm to 8:30 pm, Friday June 17 in **Pisces** on the 15th floor of the Hyatt Regency. Registrants and guests of the AANP are welcome to attend. Additional tickets are $20 each for guests of AANP attendees, and may be purchased at the time of registration or at the door.

Pisces – 15th Floor	
Friday, June 17, 2016	6:30 pm – 8:30 pm

TRAINEE LUNCHEON

Trainees are invited to attend the 2016 Trainee Luncheon on Friday, June 17 in **Columbia**, hosted by Dr. B.K. DeMasters. Lunch will be provided, followed by dessert. The agenda is posted below.

2016 Trainee Luncheon Agenda

I. 11:45 am – 12:15 pm: Welcome & Lunch
II. 12:15 pm – 12:20 pm: JNEN Overview: Dr. Ray Sobel
III. 12:15pm – 1:00 pm: Dr. Peter Burger and Dr. Barbara Crain: Reflections on Successful Careers--What Might be Helpful to Trainees
IV. 1:00 pm – 1:15 pm: Travel Awards Recognition
V. 1:15 pm – 1:20 pm: Book Raffle Results
VI. 1:20 pm – 1:45 pm: Dessert and Mingle with Executive Council

SPONSORS & DONORS

This meeting is sponsored in part by generous contributions from several sponsors and donors. Please visit their displays and exhibits in the Constellation Foyer. Thank you to all our sponsors and donors!

Location: Constellation Foyer	
Thursday, June 16	12:00 pm – 5:30 pm
Friday, June 17	7:00 am – 5:30 pm
Saturday, June 18	7:00 am – 5:30 pm

MEETING EXHIBITORS
ARUP Laboratories, Inc.
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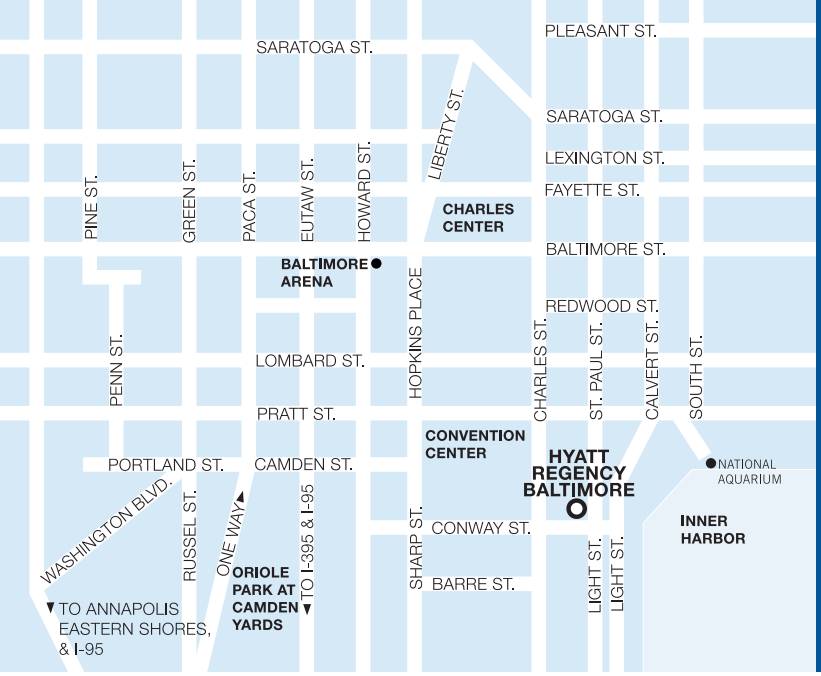
Wolters Kluwer Health

MEETING DONORS
Copies of the June Edition of the JNEN is being provided by Oxford Press.
"In-kind" support through the donation of microscopes is being provided by Morrell Instruments.

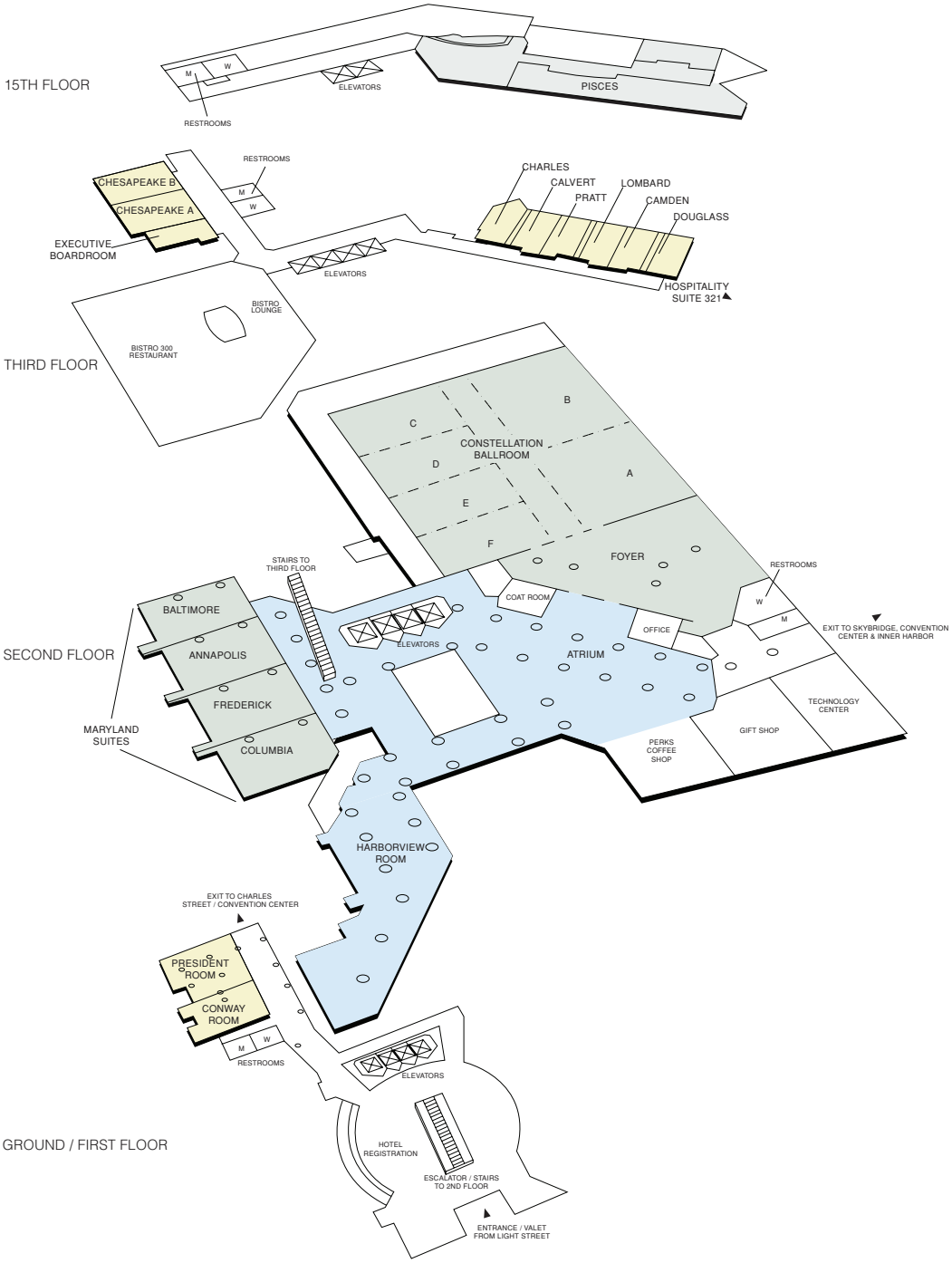


Hyatt Regency Baltimore

On The Inner Harbor

DIRECTIONS

From Baltimore Washington International Airport (12 miles): Take I-295 North Baltimore-Washington Pkwy. I-295 becomes Russell Street (Oriole Park is on right). Turn right on Pratt Street. Proceed six blocks to Light Street and turn right. Hotel is ½-block on right.



2016 MEETING AT A GLANCE

2016 SPECIAL COURSE

Updated WHO Classifications of Tumors and Chronic Traumatic Encephalopathy

Directors: Matthew P. Frosch, MD, PhD, and Rebecca D. Folkerth, MD

Thursday, June 16, 2016	
Time:	**Constellation CDEF**
7:00 am – 8:00 am	**CONTINENTAL BREAKFAST**
8:00 am – 8:10 am	*Welcome and CME Pre-test* Matthew P. Frosch, MD, PhD Massachusetts General Hospital, Boston, MA
8:10 am – 8:50 am	*NINDS and Neuropathology* Walter J. Koroshetz, MD National Institute of Neurological Disorders and Stroke, Bethesda, MD
8:50 am – 9:30 am	*Radiological Pathological Correlations in Traumatic Axonal Injury* David Brody, MD, PhD Washington University in St. Louis, St. Louis, MO
9:30 am – 10:20 am	*CTE 2016: What We Know, What We Need to Know* Ann C. McKee, MD Boston University, Boston, MA
10:20 am – 10:50 am	**REFRESHMENT BREAK**
10:50 am – 11:30 am	What Every Neuropathologist Needs to Know: *Diffuse Glioma Diagnosis in the 2016 CNS WHO* David N. Louis, MD Massachusetts General Hospital, Boston, MA
11:30 am – 12:20 pm	What Every Neuropathologist Needs to Know: *Pediatric Tumors* Cynthia Hawkins, MD, PhD, FRCPC Hospital for Sick Children, Toronto, Canada
12:20 pm – 1:30 pm	**LUNCH ON OWN**
1:30 pm – 2:15 pm	*The Neuropathology of Traumatic Brain Injury (TBI) Among Military Personnel* Daniel P. Perl, MD Uniformed Services University of the Health Sciences, Bethesda, MD
2:15 pm – 3:00 pm	*Pathophysiology of TBI to CTE and Approaches to Study* William Stewart, MD, PhD University of Glasgow, Glasgow, Scotland
3:00 pm – 3:30 pm	**REFRESHMENT BREAK**
3:30 pm – 5:00 pm	*Chronic Traumatic Encephalopathy Round Table* Rebecca D. Folkerth, MD (Moderator) Ann C. McKee, MD Daniel P. Perl, MD William Stewart, MD, PhD
5:00 pm – 5:10 pm	*Closing Remarks* Matthew P. Frosch, MD, PhD Massachusetts General Hospital, Boston, MA

2016 MEETING AT A GLANCE

2016 ABSTRACTS AND NAMED LECTURES, DAY 1

Director: Suzanne Z. Powell, MD

<table>
<tr><th colspan="4">Friday, June 17, 2016</th></tr>
<tr><td>7:00 am – 8:00 am</td><td colspan="2">CONTINENTAL BREAKFAST
Constellation Foyer</td><td>Atrium/Harborview</td></tr>
<tr><td></td><td>Constellation CDEF</td><td>Constellation A</td><td rowspan="15">Posters #33-88
Friday, June 17
8:00 am – 4:30 pm</td></tr>
<tr><td>8:00 am – 10:00 am</td><td>PLATFORM 1

Developmental, Pediatric, Infectious

Abstracts #1-8</td><td>PLATFORM 2

Tumors: Glial

Abstracts #9-16</td></tr>
<tr><td>10:00 am – 10:15 am</td><td colspan="2">REFRESHMENT BREAK
Constellation Foyer</td></tr>
<tr><td></td><td colspan="2">Constellation CDEF</td></tr>
<tr><td>10:15 am – 11:15 am</td><td colspan="2">PARISI LECTURE
CNS White Matter Disorders with Viral Causation and Association

Bette Kleinschmidt-DeMasters, MD
University of Colorado Anschutz Medical Campus, Aurora, CO</td></tr>
<tr><td>11:15 am – 11:30 am</td><td colspan="2">MERITORIOUS AWARD
Honoring Dennis W. Dickson, MD
Presented by Melissa E. Murray, PhD</td></tr>
<tr><td>11:30 am – 12:15 pm</td><td colspan="2">BUSINESS MEETING I
All Members Welcome</td></tr>
<tr><td>12:15 pm – 1:30 pm</td><td colspan="2">LUNCH ON OWN</td></tr>
<tr><td></td><td>Constellation CDEF</td><td>Constellation A</td></tr>
<tr><td>1:30 pm – 3:30 pm</td><td>PLATFORM 3

Neurodegeneration: Alzheimer’s Disease

Abstracts #17-24</td><td>PLATFORM 4

Tumors: Nonglial

Abstracts #25-32</td></tr>
<tr><td>3:30 pm – 4:30 pm</td><td colspan="2">POSTER VIEWING & REFRESHMENT BREAK
Atrium and Constellation Foyer</td></tr>
<tr><td></td><td colspan="2">Constellation CDEF</td></tr>
<tr><td>4:30 pm – 5:30 pm</td><td colspan="2">DEARMOND LECTURE
FTD and ALS: Genes, Circuits and Therapeutic Targets

Eric J. Huang, MD, PhD,
University of California San Francisco, San Francisco, CA</td></tr>
<tr><td></td><td colspan="2">Pisces – 15th Floor</td></tr>
<tr><td>6:30 pm – 8:30 pm</td><td colspan="2">ANNUAL RECEPTION
All Attendees Welcome</td></tr>
</table>

2016 MEETING AT A GLANCE

2016 ABSTRACTS AND NAMED LECTURES, DAY 2

Director: Suzanne Z. Powell, MD

<table>
<tr><th colspan="4">Saturday, June 18, 2016</th></tr>
<tr><td>7:00 am – 8:00 am</td><td colspan="2">CONTINENTAL BREAKFAST
Constellation Foyer</td><td>Atrium/Harborview</td></tr>
<tr><td></td><td>Constellation CDEF</td><td>Constellation A</td><td rowspan="17">Posters #121-178
Saturday, June 18
8:00 am – 4:30 pm</td></tr>
<tr><td>8:00 am – 10:00 am</td><td>PLATFORM 5

Tumors: Pediatric

Abstracts #89-96</td><td>PLATFORM 6

Neurodegeneration, Trauma, Prions

Abstracts #97-104</td></tr>
<tr><td>10:00 am – 10:15 am</td><td colspan="2">REFRESHMENT BREAK
Constellation Foyer</td></tr>
<tr><td></td><td colspan="2">Constellation CDEF</td></tr>
<tr><td>10:15 am – 11:15 am</td><td colspan="2">KOREY LECTURE
The FTLD-ALS Connection
Eileen H. Bigio, MD
Northwestern University, Chicago, IL</td></tr>
<tr><td>11:15 am – 11:30 am</td><td colspan="2">MERITORIOUS AWARD
Honoring Barbara J. Crain, MD, PhD
Presented by Michael N. Hart, MD</td></tr>
<tr><td>11:30 am – 12:15 pm</td><td colspan="2">BUSINESS MEETING II
All Members Welcome</td></tr>
<tr><td>12:15 pm – 1:30 pm</td><td colspan="2">LUNCH ON OWN</td></tr>
<tr><td></td><td>Constellation CDEF</td><td>Constellation A</td></tr>
<tr><td>1:30 pm – 3:30 pm</td><td>PLATFORM 7

Peripheral Nerve and Muscle

Abstracts #105-112</td><td>PLATFORM 8

Neurodegeneration: FTD, Lewy Body and Other

Abstracts #113-120</td></tr>
<tr><td>3:30 pm – 4:30 pm</td><td colspan="2">POSTER VIEWING & REFRESHMENT BREAK
Atrium and Constellation Foyer</td></tr>
<tr><td></td><td colspan="2">Constellation CDEF</td></tr>
<tr><td>4:30 pm – 5:30 pm</td><td colspan="2">MOORE LECTURE
Unlocking the Secrets of Parkinson’s
Ted M. Dawson, MD, PhD
John Hopkins Medicine, Baltimore, MD</td></tr>
<tr><td></td><td colspan="2">Constellation CDEF</td></tr>
<tr><td>8:00 pm – 11:00 pm</td><td colspan="2">DIAGNOSTIC SLIDE SESSION
10 Cases Moderated by Caterina Giannini, MD, PhD and Rebecca D. Folkerth, MD</td></tr>
</table>

2016 MEETING AT A GLANCE

2016 PRESIDENTIAL SYMPOSIUM

Amyotrophic Lateral Sclerosis

Director: Suzanne Z. Powell, MD

Sunday, June 19, 2016	
Time:	**Constellation CDEF**
7:00 am – 8:00 am	**CONTINENTAL BREAKFAST**
8:00 am – 8:05 am	*Introduction of Presidential Symposium* Suzanne Z. Powell, MD Houston Methodist Hospital, Houston, TX
8:05 am – 8:35 am	*What Every Neuropathologist Needs to Know About the JNEN** Raymond A. Sobel, MD Editor-in-Chief, *Journal of Neuropathology and Experimental Neurology* **This session is not offered for CME Credit*
8:35 am – 8:50 am	*CME Pre-test* Suzanne Z. Powell, MD Houston Methodist Hospital, Houston, TX
8:50 am – 9:40 am	*Neuropathological Assessment of ALS* Ian R. Mackenzie, MD FRCPC University of British Columbia & Vancouver Coastal Health, Vancouver, Canada
9:40 am – 10:00 am	**AANP AWARDS PRESENTATIONS**
10:00 am – 10:15 am	**REFRESHMENT BREAK**
10:15 am – 11:00 am	*Seeding and Propagation of SOD1 Misfolding in Amyotrophic Lateral Sclerosis* Neil Cashman, MD University of British Columbia, Vancouver, Canada
11:00 am – 11:45 am	*Next-Generation Neuropathology: The Molecular Biology of TDP-43 Proteinopathies* Edward B. Lee, MD, PhD University of Pennsylvania, Philadelphia, PA
11:45 pm – 12:00 pm	**INSTALLATION OF NEW OFFICERS AND ADJOURNMENT**

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Special Course

Thursday, June 16, 2016

Learning Objectives:

1. *Cite the 2016 updates to the WHO classification of tumors of the central nervous system.*
2. *Discuss the neuropathological manifestations of traumatic brain injuries.*
3. *Articulate the pathologic complexities of chronic traumatic encephalopathy (CTE).*

SPECIAL COURSE

NINDS and Neuropathology

Time: 8:10 am – 8:50 am

Walter J. Koroshetz, MD, *Director, NINDS/NIH*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Discuss the neuroscience research portfolio at NIH.
2. Explain the research portfolio at NINDS.
3. Cite of the role of neuropathology in NINDS funded research and the mission of NINDS.

II. Abstract & Relevant References

A large proportion (5.4 billion) of NIH resources are appropriated to fund neuroscience. The mission of the NINDS is to increase the understanding of the nervous system and to develop this knowledge to reduce the burden of illness to due neurological disorders and stroke. Attenuating the Neuropathology remains the holy grail for much of NINDS's disease research. Development of biomarkers that track neuropathological processes whether by imaging, electrophysiological techniques, fluid or tissue assays is perhaps the greatest challenge in tying advances in neuroscience to neurological disorders. Relevant advances are coming including the *Clarity* method of examining brain in 3-D, a major project to identify the many different types of neurons and glia as part of the *BRAIN initiative*, the use of diffusion MRI tractography to understand pathology in the white matter as the end product of the *human connectome project*, *molecular imaging, exosomes, proteomics,* all of which need to be validated by pathology. NINDS is also very interested in the research training of neuropathologists and has an R25 program to fund research during neuropathology fellowship that we hope will incentivize research career development afterwards.

References:

1. http://www.humanconnectomeproject.org/
2. http://www.braininitiative.nih.gov/funding/celltypes-xml.htm
3. http://med.stanford.edu/news/all-news/2013/04/getting-clarity-hydrogel-process-creates-transparent-brain.html
4. http://www.ninds.nih.gov/funding/r25_institutions.htm

III. Faculty Biography

Walter Koroshetz is the Director of the National Institute of Neurological Disorders and Stroke (NINDS). He works to advance the mission of the Institute, to improve fundamental knowledge about the brain and the nervous system, and to use that knowledge to reduce the burden of neurological disorders. He joined NINDS as the Deputy Director in 2007. Before coming to NIH Dr. Koroshetz was a Harvard Professor of Neurology, Vice Chair of Neurology at the Massachusetts General Hospital, director of Stroke and Neurointensive Care, and a member of the Huntington's disease unit. His research activities spanned basic neurobiology to clinical trials. He directed Neurology training at MGH for 16 years. A graduate of Georgetown University and University of Chicago Medical School Dr. Koroshetz specialized in Internal Medicine and Neurology.

SPECIAL COURSE

Radiological Pathological Correlations in Traumatic Axonal Injury

Time: 8:50 am – 9:30 am

David L. Brody, MD, PhD

I. Learning Objectives

At the end of this activity learners should be able to:

1. Discuss the difficulty in interpreting non-invasive imaging findings in suspected traumatic axonal injury.
2. List quantitative coregistration methods for direct radiological pathological correlations.
3. Assess the evidence favoring the use of advanced diffusion MRI methods for traumatic axonal injury.

II. Relevant References

References:

1. Mac Donald, C.L., Song, S.K., Bayly, P.V. Holtzman, D.M., and **Brody, D.L**. "Detection of Traumatic Axonal Injury with Diffusion Tensor Imaging in a Mouse Model of Traumatic Brain Injury," Experimental Neurology 2007: 205, 116-131.
2. C. L. Mac Donald, K. Dikranian, P. V. Bayly, D. M. Holtzman, and **D. L. Brody** "Diffusion Tensor Imaging Reliably Detects Experimental Traumatic Axonal Injury and Indicates Approximate Time of Injury" Journal of Neuroscience 2007: 27, 11869-11876.
3. C.L. Mac Donald, A.M. Johnson, D. Cooper, E. C. Nelson, N. J. Werner, J. S. Shimony, A. Z. Snyder, M. E. Raichle, J. R. Witherow, R. Fang, S. F. Flaherty, and **D. L. Brody**, "Detection of Blast-Related Traumatic Brain Injury in US Military Personnel." New England Journal of Medicine 2011: 364: 2091-2100. PMC3146351

III. Faculty Biography

Research in the Brody Laboratory and collaborative group is focused traumatic brain injury (TBI), neurodegenerative diseases, and the relationship between TBI and later neurodegeneration. TBI is a major cause of morbidity and mortality in the United States and worldwide (CDC report), and a major risk factor for the development of Alzheimer's Disease (Plassman et al, Neurology 2000; Gardner et al, JAMA Neurology 2014). Repeated concussive TBI's can lead to a distinct neurodegenerative condition called Chronic Traumatic Encephalopathy (McKee et al, JNEN 2009).

There are three major lines of research in the laboratory. The first is focused on uncovering mechanisms underlying amyloid-beta and tau pathologies following traumatic brain injury. The second major line of research is focused on the detection of traumatic axonal injury using advanced MRI methods such as Diffusion Tensor Imaging (DTI), Diffusion Kurtosis Imaging (DKI) and Generalized Q-sampling Imaging (GQI). The third major line of research involves purification and characterization of amyloid-beta oligomers from human brain tissue.

SPECIAL COURSE

CTE 2016: What We Know, What We Need to Know

Time: 9:30 am – 10:20 am

Ann C. McKee, MD

I. Learning Objectives

At the end of this activity learners should be able to:

1. Describe the classical neuropathological lesions of chronic traumatic encephalopathy (CTE).
2. Discuss the common co-morbidities associated with CTE and how the pathology of CTE progresses in severity.
3. Discuss how CTE differs from concussion and post-concussion syndrome.

II. Abstract & Relevant References

Chronic traumatic encephalopathy (CTE) is a latent neurodegenerative disease associated with repetitive minor head trauma, including concussion and subconcussion. CTE was first recognized in boxers nearly a century ago as "dementia pugilistica" but has been recently identified in athletes who played a variety of contact sports, including American football, ice hockey, soccer, baseball, rugby, boxing and wrestling as well as in military veterans exposed to blast and concussive injuries. *Like many other neurodegenerative diseases, CTE is diagnosed with certainty only by neuropathological examination of brain tissue.* Significant advances have been made over the past decade in classifying and characterizing the neuropathological and immunohistochemical features of CTE. CTE is a tauopathy; it is characterized by the accumulation of hyperphosphorylated tau (p-tau) as neurofibrillary tangles (NFTs), astrocytic inclusions and dotlike neurites in a unique pattern around small blood vessels in the cortex, with a striking tendency to occur in clusters at the sulcal depths. Recently, a consensus panel of expert neuropathologists defined the neuropathological criteria for the diagnosis of CTE, outlined supportive but non-specific pathological features, and recommended a minimum blocking and staining scheme for the pathological evaluation for CTE. The pathology of CTE appears to progress through a predictable 4-stage sequence of severity that is significantly associated with age of the subject at death as well as duration of exposure to repetitive head impacts. Symptoms of CTE include behavioral and mood changes that often begin in middle age. In advanced disease, memory loss, executive dysfunction, cognitive impairment and dementia are common. Most individuals *develop symptoms years after exposure to trauma, although* 20% develop symptoms while still active in sports*. Criteria for the diagnosis of clinical diagnosis of CTE have been proposed. Many fundamental questions remain to be answered regarding CTE; w*e are not able to diagnose CTE during life and *we do not know how common it is*. *We also do not know if there are* genetic risk and susceptibility factors. M*ulti-center, prospective research efforts are currently underway* to develop operational biomarkers for CTE and to improve the sensitivity and specificity of the clinical diagnostic criteria. Additional large scale, longitudinal, epidemiological, genetic and animal studies will be required in order to develop effective ways to diagnose, monitor and treat the disorder during life.

References:

1. McKee AC, Cantu RC, Nowinski CJ, Hedley-Whyte ET, Gavett BE, Budson AE, Santini VE, Lee H-Y, Kubilus CA, Stern RA. Chronic Traumatic Encephalopathy in Athletes: Progressive Tauopathy following Repetitive Head Injury. J Neuropath Exp Neurol, 2009 68(7): 709-735.
2. McKee AC, Stein TD, Nowinski CJ, Stern RA, Daneshvar DH, Alvarez VE, Lee H-S, Hall GF, Wojtowicz SM, Baugh CM, David O. Riley DO, Kubilus CA, Cormier KA, Jacobs MA, Martin BR, Abraham CR, Ikezu T, Reichard RR, Wolozin BL, Budson AE, Goldstein LE, Kowall NW, Cantu RC. The Spectrum of Disease in Chronic Traumatic Encephalopathy, Brain 2013, Jan;136(Pt 1):43-64. doi: 10.1093/brain/aws307.
3. Bieniek KF, Ross OA, Cormier KA, Walton RL, Soto-Ortolaza A, Johnston AE, DeSaro P, Boylan KB, Graff-Radford NR, Wszolek ZK, Rademakers R, Boeve BF, McKee AC, Dickson DW. Chronic traumatic encephalopathy pathology in a neurodegenerative disorders brain bank. Acta Neuropathol. 2015 Dec;130(6):877-89. doi: 10.1007/s00401-015-1502-4. Epub 2015 Oct 30.
4. McKee AC, Stein TD, Alvarez VE.The Neuropathology of Chronic Traumatic Encephalopathy. Brain Pathology 2015 May;25(3):350-64. doi: 10.1111/bpa.12248.

5. McKee AC, Cairns NJ, Dickson DW, Folkerth RD, Keene CD, Litvan I, Perl DP, Stein TD, Stewart W, Vonsattel JP, Tripodis Y, Alvarez VE, Bieniek KF, Crary J, Dams-O'Connor K, Gordon W and the TBI/CTE group. The First NINDS/NIBIB Consensus Meeting to Define Neuropathological Criteria for the Diagnosis of Chronic Traumatic Encephalopathy. Acta Neuropathol. 2016 Jan;131(1):75-86. doi: 10.1007/s00401-015-1515-z.

III. Faculty Biography

My research focuses on understanding pathogenetic mechanisms of neurodegeneration, including Chronic Traumatic Encephalopathy (CTE), Alzheimer's disease (AD) motor neuron disease, and frontotemporal degeneration. I direct multiple highly successful brain banks focused on AD, aging (Framingham Heart Study (FHS), amyotrophic lateral sclerosis (ALS), CTE and traumatic brain injury (TBI). The CTE and TBI brain tissue repositories are the largest in the world devoted to understanding posttraumatic neurodegeneration, and hold the largest collection of cases of CTE (>200 neuropathologically confirmed cases). Work from my laboratory over the past decade pioneered the expanding field of CTE and was instrumental in changing the awareness and acute management of mild repetitive brain injury, including concussion, subconcussion and blast related injury.

SPECIAL COURSE

What Every Neuropathologist Needs to Know: *Diffuse Glioma Diagnosis in the 2016 CNS WHO*

Time: 10:50 am – 11:30 am

David N. Louis, MD, *Pathologist-in-Chief, Massachusetts General Hospital; Benjamin Castleman Professor of Pathology, Harvard Medical School*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Discuss classification differences between 2007 and 2016 WHO CNS tumor classifications.
2. List practical approaches to the classification of diffuse gliomas according to the 2016 WHO CNS tumor classification.

II. Abstract & Relevant References

The 2016 World Health Organization Classification of Tumors of the Central Nervous System is both a conceptual and practical advance over its 2007 predecessor. For the first time, the WHO classification of CNS tumors uses molecular parameters in addition to histology to define many tumor entities, thus formulating a concept for how CNS tumor diagnoses should be structured in the molecular era. As such, the 2016 CNS WHO presents major restructuring of the diffuse gliomas, medulloblastomas and other embryonal tumors, and incorporates new entities that are defined by both histology and molecular features, including glioblastoma, IDH-wildtype and glioblastoma, IDH-mutant; diffuse midline glioma, H3 K27M–mutant; RELA fusion–positive ependymoma; medulloblastoma, WNT-activated and medulloblastoma, SHH-activated; and embryonal tumour with multilayered rosettes, C19MC-altered. The 2016 edition has added newly recognized neoplasms, and has deleted some entities, variants and patterns that no longer have diagnostic and/or biological relevance. Other notable changes include the addition of brain invasion as a criterion for atypical meningioma and the introduction of a soft tissue-type grading system for the now combined entity of solitary fibrous tumor/haemangiopericytoma—a departure from the manner by which other CNS tumors are graded. Overall, it is hoped that the 2016 CNS WHO will facilitate clinical, experimental and epidemiological studies that will lead to improvements in the lives of patients with brain tumors.

References:

1. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK (eds.). World Health Organization Histological Classification of Tumours of the Central Nervous System. Lyon: International Agency for Research on Cancer, 2016 (in press).
2. Tanboon J, Williams EA, Louis DN. The diagnostic use of immunohistochemical surrogates for signature molecular genetic alterations in gliomas. J Neuropathol Exp Neurol (in press).
3. Louis DN. Perry A, Burger P, Ellison DW, Reifenberger G, von Deimling A, Aldape K, Brat D, Collins VP, Eberhart C, Figarella-Branger D, Fuller GN, Giangaspero F, Giannini C, Hawkins C, Kleihues P, Korshunov A, Kros JM, Lopes MB, Ng HK, Ohgaki H, Paulus W, Pietsch T, Rosenblum M, Rushing E, Soylemezoglu F, Wiestler O, Wesseling P. International Society of Neuropathology-Haarlem consensus guidelines for nervous system tumor classification and grading. Brain Pathol 24:429-435, 2014.
4. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW. The 2016 WHO classification of tumours of the central nervous system: a summary. Acta Neuropathol (in press).
5. Cancer Genome Atlas Research N, Brat DJ, Verhaak RG, Aldape KD, Yung WK, Salama SR, Cooper LA, Rheinbay E, Miller CR, Vitucci M, et al. Comprehensive, Integrative Genomic Analysis of Diffuse Lower-Grade Gliomas. The New England journal of medicine 372: 2481-2498, 2015.
6. Reuss DE, Sahm F, Schrimpf D, Wiestler B, Capper D, Koelsche C, Schweizer L, Korshunov A, Jones DT, Hovestadt V, et al. ATRX and IDH1-R132H immunohistochemistry with subsequent copy number analysis and IDH sequencing as a basis for an "integrated" diagnostic approach for adult astrocytoma, oligodendroglioma and glioblastoma. Acta neuropathologica 129: 133-146, 2015.

7. Sahm F, Reuss D, Koelsche C, Capper D, Schittenhelm J, Heim S, Jones DT, Pfister SM, Herold-Mende C, Wick W, et al. Farewell to oligoastrocytoma: in situ molecular genetics favor classification as either oligodendroglioma or astrocytoma. Acta neuropathologica 128: 551-559, 2014
8. Wiestler B, Capper D, Sill M, Jones DT, Hovestadt V, Sturm D, Koelsche C, Bertoni A, Schweizer L, Korshunov A, et al (2014) Integrated DNA methylation and copy-number profiling identify three clinically and biologically relevant groups of anaplastic glioma. Acta neuropathologica 128: 561-571, 2014.

III. Faculty Biography

David N. Louis, MD, is the Benjamin Castleman Professor of Pathology at Harvard Medical School and pathologist-in-chief at Massachusetts General Hospital. Pathology at MGH has nearly 100 faculty members, over 100 trainees and over 700 employees, and performs about 12 million laboratory tests as well as 80,000 surgical pathology evaluations, 400,000 microbiology analyses, and 50,000 cytologies each year. Dr. Louis' own clinical neuropathology practice and research focuses on brain tumors, with an emphasis on the molecular basis of malignant gliomas and the application of molecular diagnostics to glioma classification. He has published close to 300 original articles, as well as numerous reviews, chapters and books. His laboratory was the first to demonstrate that molecular approaches could be used to subdivide malignant gliomas in a biologically relevant manner, and that molecular approaches could be used to predict the response of particular malignant gliomas to specific therapies. This work has contributed to worldwide adoption of molecular testing for the management of patients with these tumors. Dr. Louis has received a number of prestigious awards for his work in brain tumors and was lead editor of the 2007 and 2016 World Health Organization Classification of Central Nervous System Tumors. Dr. Louis served as President of the American Association of Neuropathologists in 2009-2010, gave the Saul Korey Lecture at the 2008 meeting and the Matthew Moore Lecture at the 2014 meeting, and has participated in many committees.

SPECIAL COURSE

What Every Neuropathologist Needs to Know: *Pediatric Tumors*

Time: 11:30 am – 12:20 pm

Cynthia Hawkins, MD, PhD, FRCPC, *Hospital for Sick Children, Toronto*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Apply the 2016 update to the WHO classification to the diagnosis of pediatric brain tumors.
2. Approach the diagnosis of pediatric brain tumors using a combination of morphologic and molecular diagnostic techniques.
3. Integrate morphologic and molecular results into a comprehensive pathology report.

II. Abstract & Relevant References

The last decade has seen numerous major discoveries about the genetics of pediatric brain tumors. The recent revision of the WHO classification of brain tumors is aimed at incorporating this new molecular information into clinical diagnostic practice. In this lecture I will review the changes to the WHO classification, its implications for pediatric brain tumor diagnosis, and how this can be practically implemented.

References:

1. Horbinski C: To BRAF or not to BRAF: is that even a question anymore? J Neuropathol Exp Neurol 72:2-7, 2013
2. Horbinski C, Nikiforova MN, Hagenkord JM, et al: Interplay among BRAF, p16, p53, and MIB1 in pediatric low-grade gliomas. Neuro Oncol 14:777-89, 2012
3. Parker M, Mohankumar KM, Punchihewa C, et al: C11orf95-RELA fusions drive oncogenic NF-kappaB signalling in ependymoma. Nature 506:451-5, 2014
4. Khuong-Quang DA, Buczkowicz P, Rakopoulos P, et al: K27M mutation in histone H3.3 defines clinically and biologically distinct subgroups of pediatric diffuse intrinsic pontine gliomas. Acta Neuropathol 124:439-47, 2012
5. Schwartzentruber J, Korshunov A, Liu XY, et al: Driver mutations in histone H3.3 and chromatin remodelling genes in paediatric glioblastoma. Nature 482:226-31, 2012
6. Sturm D, Bender S, Jones DT, et al: Paediatric and adult glioblastoma: multiform (epi)genomic culprits emerge. Nat Rev Cancer 14:92-107, 2014
7. Tabori U, Baskin B, Shago M, et al: Universal poor survival in children with medulloblastoma harboring somatic TP53 mutations. J Clin Oncol 28:1345-50, 2010
8. Zhukova N, Ramaswamy V, Remke M, et al: Subgroup-specific prognostic implications of TP53 mutation in medulloblastoma. J Clin Oncol 31:2927-35, 2013
9. Ellison DW, Dalton J, Kocak M, et al: Medulloblastoma: Clinicopathologic correlates of SHH, WNT and non-SHH/WNT molecular subgroups. Acta Neuropathol 121:381-96, 2011
10. Taylor MD, Northcott PA, Korshunov A et al: Molecular subgroups of medulloblastoma: the current consensus. Acta Neuropathol 123:465-72, 2012

III. Faculty Biography

Dr. Cynthia Hawkins is a Neuropathologist and Senior Scientist at the Hospital for Sick Children and a Professor of Laboratory Medicine and Pathobiology at the University of Toronto, in Toronto, Canada. Her research focuses on molecular pathogenesis and therapeutics for pediatric astrocytomas as well as identification and clinical implementation of novel prognostic and therapeutic markers for pediatric brain tumors.

SPECIAL COURSE

The Neuropathology of Traumatic Brain Injury (TBI) Among Military Personnel

Time: 1:30 pm – 2:15 pm

Daniel P. Perl, MD, *Uniformed Services University of the Health Sciences, Professor of Pathology*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Explain the extent of TBI on military personnel and the impact of the acute and long-term effects of these episodes.
2. Discuss the ways in which TBI of military personnel differ from those seen in civilian life.
3. Summarize and recognize unique neuropathologic features of blast-related TBI.

II. Abstract & Relevant References

Members of the Armed Services commonly suffer from traumatic brain injury (TBI). The majority of such incidents relate to accidents that are identical to those seen in civilian populations, such as motor vehicle accidents, falls, fights and participation in contact sports. However, following the introduction of high explosives into warfare in World War I, thousands of Service Members have also suffered from blast exposures, with accompanying traumatic brain injuries (TBIs). Since 2001 approximately 2.5 million U.S. service members have deployed overseas, in addition to hundreds of thousands from countries of the European Union and the world. During these current conflicts, coalition troops frequently encountered attacks with high explosives, which caused at least 60% of combat casualties. The majority of these blast exposures have been classified as mild (concussion). The effects of blast exposure on the human brain remains largely unknown since the medical literature offers few studies characterizing acute or chronic neuropathological sequelae. Even though conventional neuroimaging for mild TBI typically shows no brain abnormalities, military personnel can suffer from persistent post-concussive symptoms, such as headache, sleep disturbance, concentration impairment, memory problems, depression, and anxiety, suggesting structural damage below standard resolution levels. With symptoms but no biomarkers, these TBIs became colloquially termed “invisible wounds.”

High explosives were introduced into warfare in World War I, primarily in the protracted artillery exchanges of the lengthy trench battles on the western front. High explosives have been a major component of all subsequent conflicts. Remarkably, there have been a very small number of neuropathologic studies of TBI among military personnel, especially to characterize the acute and long-term effects on the human brain of exposure to high explosives. During World War I, Frederick Mott, a pioneering British neurologist/neuropathologist, reported postmortem findings in brains of three soldiers who died acutely following blast exposure. Examination of these brains revealed multiple petechial hemorrhages (mostly within the white matter of the centrum semiovale, corpus callosum, and internal capsule) and extravasation of blood into the subarachnoid space, with no physical evidence of external trauma to the head. Mott suggested that blast exposure could directly damage the brain, in the absence of other traumatic complications. From World War II, several publications provided only cursory descriptions of postmortem brains, describing mostly hemorrhagic complications. No other literature emerged until 2011, with the case report of a deceased 27-year-old veteran exposed to multiple blasts during Operation Iraqi Freedom (Omalu, et al.). At autopsy, the brain displayed neurofibrillary tangles (NFTs) in neuroanatomical areas consistent with chronic traumatic encephalopathy (CTE), a neurodegenerative tauopathy associated with repeated mild TBIs from contact sports. Shortly thereafter, four additional CTE cases were reported in deceased veterans with blast exposures during deployments (Goldstein, et al. 2012, McKee, et al. 2014). Lastly, unlike these other studies, another postmortem brain study of six veterans failed to reveal tauopathy, but rather provided evidence of axonal damage (Ryu, et al. 2014).

Recently, we performed detailed neuropathologic examination of brain specimens from deceased US Service Members who were exposed to blast who suffered post-concussive sequelae or who died shortly after the attacks from severe

injuries. We then compared these tissues to brain specimens from civilians with impact TBI (without blast exposure). These specimens were obtained from archival brain tissue collections at the Joint Pathology Center (JPC), University of Maryland Brain and Tissue Bank and the Center for Neuroscience and Regenerative Medicine (CNRM) Brain Tissue Repository. In these studies, we identified a distinct and previously undetected pattern of damage to the human brain in all of the blast-exposed cases. The civilian cases, with or without history of impact traumatic brain injury, did not demonstrate similar pathologic changes as the blast exposure cases. The details of these new findings will be presented and discussed.

References:

1. Shively, SB, Perl, DP Traumatic brain injury, shell shock and post-traumatic stress disorder in the military - past, present and future. J. Head Trauma Rehabil. 27: 234-239, 2012.
2. Cernak I, Noble-Haeusslein LJ. Traumatic brain injury: an overview of pathobiology with emphasis on military populations. J Cereb Blood Flow Metab 2010; 30: 255-66.
3. Rosenfeld JV, McFarlane AC, Bragge P, Armonda RA, Grimes JB, Ling GS. Blast-related traumatic brain injury. Lancet Neurol 2013; 12: 882-93.
4. Jones, E, Wessely, S. Shell Shock to PTSD: Military Psychiatry from 1900 to the Gulf War, Psychology Press, 2005, pp. 1-300.

III. Faculty Biography

Dr. Daniel Perl was born and raised in New York City and received his undergraduate degree from Columbia and his medical training at the State University of New York, Downstate Medical Center. He then took postgraduate training in Anatomic Pathology and Neuropathology at Yale University, following which he served for two years as a pathologist in the US Public Health Service, stationed at the Centers for Disease Control in Atlanta, Georgia. In subsequent years he served on the faculty of the Brown University Medical School and then the University of Vermont College of Medicine. It was at Vermont that he began working on Alzheimer's disease and other age-related neurodegenerative disorders. In 1986, Dr. Perl was recruited to the Mount Sinai School of Medicine in New York where for 24 years he served as Director of the Neuropathology Division and was Professor of Pathology, Psychiatry and Neurosciences.

Dr. Perl has authored over 300 peer-reviewed publications and book chapters and is co-author with Prof. Margaret Esiri, of Oxford University, of the 3rd edition of Oppenheimer's Diagnostic Neuropathology. He is highly regarded for his work on various aspects of the neuropathology of age-related neurodegenerative disorders, especially the role of environmental factors in their induction. He is a leading authority on the pathology of the fascinating complex of neurodegenerative disorders occurring among the native population living on Guam.

SPECIAL COURSE

Pathophysiology of TBI to CTE and Approaches to Study

Time: 2:15 pm – 3:00 pm

William Stewart, MD, PhD, *University of Glasgow, Scotland*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Discuss how neurodegenerative pathologies associated with TBI are NOT unique to sport or repetitive mild injury or military personnel.
2. Explain and appreciate that CTE, the neurodegenerative pathology of TBI survival, is a complex pathology featuring tau, amyloid beta, TDP-43, axonal degeneration, neuroinflammation, neuronal loss, white matter degradation, blood brain barrier disruption and glial pathology.
3. List putative links between acute TBI pathology and late neurodegeneration.
4. Summarize limitations in current clinical and pre-clinical research in TBI and its outcomes.

II. Abstract & Relevant References

Traumatic brain injury (TBI) represents one of the strongest risk factors for dementia. Almost a century ago the first clinical account of the 'punch drunk' syndrome emerged, describing chronic neurologic and neuropsychiatric sequelae of former boxers. Thereafter, throughout the 20th century, further reports added to our understanding of the neuropathological consequences of a career in boxing, leading to descriptions of a distinct neurodegenerative pathology termed dementia pugilistica. In the past decade, growing recognition of this pathology in autopsy studies in non-boxer athletes exposed to repetitive mild traumatic brain injury (TBI) or in individuals exposed to single moderate or severe TBI has led to an awareness that it is exposure to TBI that carries risk neurodegeneration, not the sport or circumstance in which the injury is sustained. Further, the neuropathology of this post-TBI neurodegeneration, now termed chronic traumatic encephalopathy (CTE), is acknowledged as a complex polypathology featuring abnormalities in tau, amyloid beta and TDP-43, in addition to axonal degradation, blood brain barrier disruption, neuroinflammation and glial pathologies. In contrast to wider studies in neurodegeneration timing of the initiating insult, TBI, is known for CTE. As a consequence, CTE offers an unrivalled opportunity to study the temporal evolution of pathologies leading to dementia, but only if limitations in current pre-clinical and clinical research are recognised.

References:

1. Hay, J, Johnson, VE, Smith, DH, Stewart, W (2016). Chronic traumatic encephalopathy: the neuropathological legacy of traumatic brain injury. *Ann Rev Pathol*, DOI: 10.1146/annurev-pathol-012615-044116
2. McKee, A, Cairns, NJ, Dickson, DW, Folkerth RD, Keene, CD, Litvan, I, Perl, DP, Stein, TD, Vonsattel, J-P, Stewart, W, Tripodis, Y, Crary, JF, Bieniek, KF, Dams-O'Connor, K, Alvarez, VE, Gordon, WA (2016). The first NINDS/NIBIB consensus meeting to define neuropathological criteria for the diagnosis of chronic traumatic encephalopathy. *Acta Neuropathol,* 131, 75-86 PMC4698
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4. Johnson, VE, Meaney, DF, Cullen, DK, Smith, DH (2015). Animal models of traumatic brain injury. *Handb Clin Neurol,* 127, 115-128
5. Johnson VE, Stewart W**,** Smith DH (2013). Axonal Pathology in Traumatic Brain Injury. *Exp Neurol,* 246, 35-43.
6. Smith DH, Johnson VE, Stewart W. 2013. Chronic neuropathologies of single and repetitive TBI: substrates of dementia? *Nat Rev Neurol* 9: 211-21
7. Johnson, VE, Stewart, JE, Begbie, FD, Trojanowski, JQ, Smith, DH, Stewart, W (2013). Inflammation and white matter degeneration persist for years after a single traumatic brain injury. *Brain*, 136, 28-42
8. Johnson VE, Stewart W, Smith DH. 2012. Widespread Tau and Amyloid-Beta Pathology Many Years After a Single Traumatic Brain Injury in Humans. *Brain Pathol* 22: 142-49

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III. Faculty Biography

Dr. Stewart is a Consultant and Lead Neuropathologist at the Southern General Hospital, Glasgow, and holds honorary Associate Professor status at the University of Glasgow (Institute of Neuroscience & Psychology) and the University of Pennsylvania (Department of Neurosurgery). Dr Stewart's research in TBI utilises the unique Glasgow TBI Archive to characterise the complex pathologies of human TBI, with particular focus on the link between TBI and late neurodegenerative disease. This work attracts research funding from a variety of agencies, including the US NIH and Department of Defense, NHS Research Scotland and the European Community. Reflecting his insight into the biology and pathology of TBI Dr Stewart acts as an external advisor to multiple national and international sports and government organisations.

SPECIAL COURSE

Chronic Traumatic Encephalopathy Round Table

Time: 3:30 pm – 5:00 pm

Rebecca D. Folkerth, MD (Moderator)
Ann C. McKee, MD, *Boston University, Boston, MA*
Daniel P. Perl, MD, *Uniformed Services University of the Health Sciences, Bethesda, MD*
William Stewart, MD, PhD, *University of Glasgow, Glasgow, Scotland*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Cite clinical and neuropathologic features of CTE, blast injury, and other forms of traumatic brain injury.
2. Summarize new research techniques, gaps in knowledge, and potential resources in the field of traumatic brain injury.

II. Faculty Biographies

Ann C. Mckee, MD

My research focuses on understanding pathogenetic mechanisms of neurodegeneration, including Chronic Traumatic Encephalopathy (CTE), Alzheimer's disease (AD) motor neuron disease, and frontotemporal degeneration. I direct multiple highly successful brain banks focused on AD, aging (Framingham Heart Study (FHS), amyotrophic lateral sclerosis (ALS), CTE and traumatic brain injury (TBI). The CTE and TBI brain tissue repositories are the largest in the world devoted to understanding posttraumatic neurodegeneration, and hold the largest collection of cases of CTE (>200 neuropathologically confirmed cases). Work from my laboratory over the past decade pioneered the expanding field of CTE and was instrumental in changing the awareness and acute management of mild repetitive brain injury, including concussion, subconcussion and blast related injury.

Daniel P. Perl, MD

Dr. Daniel Perl was born and raised in New York City and received his undergraduate degree from Columbia and his medical training at the State University of New York, Downstate Medical Center. He then took postgraduate training in Anatomic Pathology and Neuropathology at Yale University, following which he served for two years as a pathologist in the US Public Health Service, stationed at the Centers for Disease Control in Atlanta, Georgia. In subsequent years he served on the faculty of the Brown University Medical School and then the University of Vermont College of Medicine. It was at Vermont that he began working on Alzheimer's disease and other age-related neurodegenerative disorders. In 1986, Dr. Perl was recruited to the Mount Sinai School of Medicine in New York where for 24 years he served as Director of the Neuropathology Division and was Professor of Pathology, Psychiatry and Neurosciences.

William Stewart, MD, PhD

Dr. Stewart is Consultant and Lead Neuropathologist at the Southern General Hospital, Glasgow, and holds honorary Associate Professor status at the University of Glasgow (Institute of Neuroscience & Psychology) and the University of Pennsylvania (Department of Neurosurgery). Dr Stewart's research in TBI utilises the unique Glasgow TBI Archive to characterise the complex pathologies of human TBI, with particular focus on the link between TBI and late neurodegenerative disease. This work attracts research funding from a variety of agencies, including the US NIH and Department of Defense, NHS Research Scotland and the European Community. Reflecting his insight into the biology and pathology of TBI Dr Stewart acts as an external advisor to multiple national and international sports and government organisations.

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AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Overview: Scientific Sessions

All abstracts of the papers presented in this program are published in the June 2016 issue of the *Journal of Neuropathology and Experimental Neurology.*

FRIDAY PLATFORMS 1 & 2

	Platform Session 1: ***Developmental, Pediatric, Infectious*** **Constellation CDEF** **Chairs: Alexander Judkins, MD; Peter Pytel, MD**	**Platform Session 2:** ***Tumors: Glial*** **Constellation A** **Chair: Fausto Rodriguez, MD; Brent A. Orr, MD, PhD**
8:00 am – 8:15 am	**1** **Early neuropathological findings in congenital Zika virus infection** Heather Ames, Fausto Rodriguez, D Hill, Cheng-Ying Ho	**9** **Diagnostic and Prognostic Utility of H3K27M Immunohistochemistry in Adult Spinal Tumors** Marco Hefti, George Zanazzi, Heather Bell, Peter Canoll, Nadejda Tsankova
8:15 am – 8:30 am	**2** **Neuropathological aspects of congenital Zika virus infection in Brazil** Leila Chimelli, Adriana S O Melo, Fernanda Tovar-Moll, Patricia S Oliveira-Szejnfeld, Aline H S Camacho, Giovanna C Gomes, Fabiana O Melo, Alba G M Batista, Heloisa N Machado, Elizabeth Awad, Thales A Ferreira, Rodrigo D Andrade, Roberto J V Mello, Monica B Arruda, Rodrigo M Brindeiro, Rodrigo Delvechio, Amilcar Tanuri	**10** **Clinical, Pathological and Molecular Characteristics of Infiltrating Astrocytomas of the Spinal cord** Cheddhi Thomas, Eveline Hidalgo, Yosef Dastagirzada, Jonathan Serrano, Shiyang Wang, Kasthuri Kannan, David Capper, Volker Hovestadt, Stefan Pfister, David Jones, Martin Sill, Andreas von Deimling, Adriana Heguy, Sharon Gardner, Jeffrey Allen, David Zagzag, Matthias Karajannis, Matija Snuderl
8:30 am – 8:45 am	**3** **Truncating Mutations in Citron-Kinase: a Cause of Micro-Lissencephaly with Multinucleated Neurons.** Brian Harding, Amanda Moccia, Stephanie Bielas	**11** **Targeted next-generation sequencing panel (GlioSeq) provides comprehensive genetic profiling of central nervous system tumors** Craig Horbinski, Abigail Wald, Melissa Melan, Somak Roy, Shan Zhong, Ronald Hamilton, Frank Lieberman, Jan Drappatz, Nduka Amankulor, Ian Pollack, Yuri Nikiforov, Marina Nikiforova
8:45 am – 9:00 am	**4** **Impact of Germinal Matrix Hemorrhage on Human Interneuron Development** Vivian Tang, Jennifer Cotter, Tiffany Hong, Mercedes Paredes, Eric Huang	**12** ***Drosophila* Brat and human ortholog TRIM3 maintain stem cell equilibrium and suppress brain tumorigenesis by attenuating Notch signaling** Daniel Brat, Subhas Mukherjee, Monica Chau, Changming Zhang, Carol Tucker-Burden, Kenneth Moberg, Renee Read, Costas Hadjipanayis
9:00 am – 9:15 am	**5** **Neonatal Hypoxic Ischemic Brain Injury Upregulates Cystathione β-synthase and mTOR Signaling Pathway** Mirna Lechpammer, Yen Tran, Pia Wintermark, Veronica Martínez-Cerdeño, Konstantin Shatalin, Robert Berman, Frances Jensen, Evgeny Nudler, David Zagzag	**13** **Molecular profiling of low grade glioma and glioneuronal tumors identifies miR-487b as a microRNA relevant to gliomagenesis** Ming Yuan, Heather Ames, Fausto Rodriguez
9:15 am – 9:30 am	**6** **Multiple radial glial subtypes and progenitors with distinct neurogenic potentials in human fetal, healthy adult and Alzheimer hippocampi** Homa Adle-Biassette, Sara Cipriani, Jeannette Nardelli, Catherine Verney, Fabien Guimiot, Pierre Gressens	**14** **Large-scale single-cell RNA-seq reveals a developmental hierarchy in oligodendrogliomas** Itay Tirosh, Andrew S. Venteicher, Christine Hebert, Leah Escalante, Cyril Neftel, Brian V. Nahed, Will T. Curry, Dan P. Cahill, Matthew P. Frosch, David N. Louis, Aviv Regev, Mario L. Suva
9:30 am – 9:45 am	**7** **ARID1A, member of the SWI/SNF chromatin remodeling complex, guides early neuron development in the human cerebral cortex** Emily Chan, Jennifer Cotter, Vivian Tang, Eric Huang	**15** **Cell of Origin and Initiating Mutations Influence Glioma Pathogenesis** David Irvin, Robert McNeill, Ryan Bash, C. Miller
9:45 am – 10:00 am	**8** **Abnormal Neuronal Migration and Complex Neurological Phenotypes in Mitochondrial DNA Cytochrome b Gene Mutation** Boleslaw Lach, Janet Simson, Samantha Marin, Lauren Mac Neil, Steve Sommer, Mark Tarnopolsky	**16** **A study of 82 glioblastoma autopsies including subset evaluation of PD-1 and PDL-1** Maram Abdaljaleel, Masoud Movassaghi, Seyed Amin Hojat, Randy Tashjian, Shino Magaki, Negar Khanlou, Harry Vinters, Phioanh Nghiemphu, Albert Lai, Linda Liau, Timothy Cloughesy, William Yong

FRIDAY PLATFORMS 3 & 4

	Platform Session 3 ***Neurodegeneration: Alzheimer's Disease*** **Constellation CDEF** **Chair: Julia Kofler, MD; Edward Lee, MD**	**Platform Session 4** ***Tumors: Nonglial*** **Constellation A** **Chairs: Mario L. Suva, MD, PhD; Sriram Vennetti, MD, PhD**
1:30 pm – 1:45 pm	**17** **NIA-AA Guidelines for the Neuropathologic Evaluation of Alzheimer's Disease applied to the Nun Study and the Honolulu-Asia Aging Study** Caitlin Latimer, C. Keene, Laura Hemmy, Lon White, Thomas Montine	**25** **Molecular Genetics Pathology of Pituitary Adenomas** Malak Abedalthagafi, Wenya Linda Bi, Peleg Horowitz Horowitz, Pankaj Agarwalla, William Gibson, Edward Laws Jr, Rameen Beroukhim, Sandro Santagata
1:45 pm – 2:00 pm	**18** **Protein Expression of Low Hippocampal Volume Risk Allele Candidates *MSRB3* and *LEMD3* in Human CA1 Region During Progression of Alzheimer's Disease** Stephanie Adams, Kathy Tilton, Tim Norman, Sudha Seshadri, Ivana Delalle	**26** **Histopathologic correlates of newly defined brain tumor entities identified through molecular classification** Brent Orr, Dominik Sturm, Umut Toprak, Volker Hovestadt, David Jones, David Capper, Paul Northcott, Sariah Allen, Joanna Phillips, Arie Perry, Bret Mobley, Matthew Schniederjan, Mariarita Santi, Anna Buccoliero, Sonika Dahiya, Matija Snuderl, Amar Gajjar, Kenneth Aldape, Andreas von Deimling, Stefan Pfister, David Ellison, Andrey Korshunov, Marcel Kool
2:00 pm – 2:15 pm	**19** **Impaired TDP-43 Repression of Nonconserved Cryptic Exons in Alzheimer's Disease** W. Robert Bell, Mingkuan Sun, Katherine LaClair, Jonathan Ling, Olga Pletnikova, Juan Troncoso, Phillip Wong, Liam Chen	**27** **Molecular and histologic features of a series of sporadic and familial schwannomas** Erik Williams, James Kim, Alona Muzikansky, John Iafrate, Scott Plotkin, Anat Stemmer-Rachamimov
2:15 pm – 2:30 pm	**20** **Beclin 1/BECN1 sorts cell-surface amyloid precursor protein for lysosomal degradation.** Edward Plowey, Wan Zhu, Gayathri Swaminathan	**28** **Global Loss of Histone H3K27 Trimethylation in Atypical and Anaplastic Meningiomas** Benjamin Liechty, Leah Katz, Girish Fatterpekar, Rajeev Sen, Joshua Silverman, John Golfinos, Chandra Sen, David Zagzag, Matija Snuderl
2:30 pm – 2:45 pm	**21** **Dementia associated with the *PSEN2* R71W variant** Bernardino Ghetti, Adrian Oblak, Rose Richardson, Francine Epperson, Holly Garringer	**29** **Transcriptome sequencing analysis of four psammomatous meningiomas** Peyman Samghabadi, Erna Forgó, Robert West, Hannes Vogel Vogel
2:45 pm – 3:00 pm	**22** **Advanced tau in the hippocampus, but not initial tau or β-amyloid differ across pathologically-defined subtypes of Alzheimer's disease** Melissa E. Murray, Neill R. Graff-Radford, Kelly M. Ross, Ranjan Duara, and Dennis W. Dickson	**30** **Spontaneous necrosis is associated with higher recurrence and mortality rates in atypical meningioma treated with radiation therapy** Joseph Kellum, Kimmo Hatanpaa, Jack Raisanen, Dennis Burns, Charles White, Chunyu Cai
3:00 pm – 3:15 pm	**23** **ZCCHC17 is a potential driver of synaptic dysfunction in Alzheimer's Disease** Andrew Teich, Zeljko Tomljanovic, Mitesh Patel	**31** **NHERF1/EBP50 immunohistochemistry reveals microlumens in chordoid meningioma - diagnostic utility in meningioma** Maria-Magdalena Georgescu, Adriana Olar, Ping Shang, Jack Raisanen
3:15 pm – 3:30 pm	**24** **LR11/SorLA Expression Is Modulated By APOE Genotype And Increased In Sporadic Alzheimer Disease** Richard Perrin, Chengjie Xiong, Anne Fagan, Nigel Cairns, Hideaki Bujo	**32** **Exome Sequencing Reveals Activation of STAT3 Pathway in non-VHL Tumors in Hemangioblastoma** Kasthuri Kannan, Matija Snuderl, Elad Mashiach, Rabaa Baitalmal, Olga Aminova, Paul Zappile, Matthias Karajannis, Adriana Heguy, David Zagzag

FRIDAY POSTERS #33-#51

Friday, June 17, 2016		
Time:	**Poster #:**	**Atrium/Harborview**
8:00 am – 4:30 pm	33	**Absence of Alzheimer disease neuropathologic changes in eyes of subjects with Alzheimer disease** Erik Williams, Declan McGuone, Matthew Frosch, Brad Hyman, Anat Stemmer-Rachamimov
	34	**A Relative Lack of Aβ and Tau Immunoreactivity in the Choroid Plexus of Alzheimer Disease** Mari Perez-Rosendahl, Ronald Kim, Edwin Monuki
	35	**ZO*om*^{3}: A three-dimensional super-resolution technique to map brain connectivity from millimeters to molecules** Carol Miller, Farshid Sepehrband, Celia Williams, Alexander Talishinsky, Shagun Mehta, Michael Bienkowski, Clio Gonzalez-Zacarias, Samuel Barnes, Russell Jacobs, Arthur Toga, Hongwei Dong, Kristi Clark
	36	**The Spectrum of Preclinical Alzheimer's Pathological Changes and its Modulation by ApoE Genotype** Olga Pletnikova, Gay Rudow, Yusuke Kageyama, Katherine LaClair, David Fowler, Lee Martin, Juan Troncoso
	37	**Utilizing Cytoskeleton Stabilizing Drugs for Alzheimer's Disease Treatment** Maya Rukshin, Julia Ferro, Josephine Blaha, Camelia Prodan
	38	**Intraneuronal Accumulation of ß-Amyloid. Case report.** Miguel Riudavets, Jorge Campos, Ezequiel Surace, Ana Lia Taratuto, Gustavo Sevlever
	39	**Phenotypic Characterization of Early-Onset Familial Alzheimer Disease Associated with a PSEN1 L418F Mutation** Kathy Newell, Jean Paul Vonsattel, Jill Murrell, Pierluigi Gambetti, Bernardino Ghetti
	40	**Phospho-MAPT neuropathology in the fornix and basal forebrain nuclei in Alzheimer disease: an immunohistochemical study.** Edward Plowey, Jennifer Ziskin
	41	**Emerging Prion Paradigm of Alzheimer Disease Diversity: Implications for Diagnostic and Therapeutic Strategies** Jiri Safar
	42	**Age-related Neuropathology helps distinguish Autosomal Dominant from Late-onset Alzheimer Disease** Nigel Cairns, Richard Perrin, Erin Franklin, Benjamin Vincent, Michael Baxter, John Morris
	43	**The establishment of the Biobank- Brain Bank for Aging Research, Tokyo Japan** Shigeo Murayama, Renpei Sengoku, Daita Kaneda, Yasushi Nishina, Yuta Nakano, Junko Fujigasaki, Yuko Saito
	44	**A rapidly progressive frontotemporal lobar degeneration- yet another ubiquitinated pathology?** Abeer Tabbarah, Olga Pletnikova, Argye Hillis-Trupe, Juan Troncoso, Liam Chen
	45	**Pathology of ALS with Dementia** Yasushi Nishihira, Qinwen Mao, Sandra Weintraub, Nailah Siddique, Teepu Siddique, M-Marsel Mesulam, Eileen Bigio
	46	**Mutational Status of IDH1 in Uveal Melanoma** Patrick Cimino, Patrick Cimino, Yungtai Kung, Shu-Hong Chang, C. Keene
	47	**Congenital Myopathy a Prominent Feature in the York Platelet Syndrome** Cheryl Palmer, Nicholas Johnson, Joy Roman, Russell Butterfield
	48	**A Novel Desmin Gene Mutation Associated with Distal Myopathy and Cardiomyopathy – A Case Report** Annie Daniel, Charles Whitaker, Jared Woods, Rebecca Flugrad, Qian Wu
	49	**Severe OPMD Phenotype Associated with a Double Mutation of the Poly (A) Binding Protein Nuclear 1 (PABPN1) Gene – A Case Report** Jared Woods, Annie Daniel, Charles Whitaker, Howard Yang, Qian Wu
	50	**Histological and Immunohistochemical Studies of Excised Olfactory Mucosae in Patients with Phantosmia** Hajime Miyata, Haruko Yoshimoto, Tomokatsu Hori
	51	**Mitochondrial Myopathy Potentially Due to Environmental Arsenic Exposure** Marco Hefti, Susan Morgello, Susan Shin, Lan Zhou

Posters are not offered for CME credit

FRIDAY POSTERS #52-#69

Friday, June 17, 2016		
Time:	**Poster #:**	**Atrium/Harborview**
8:00 am – 4:30 pm	52	**Novel *PTCH1* Mutation in an Infant with Gorlin Syndrome and Desmoplastic/Nodular Medulloblastoma** Andrea Gilbert
	53	**Human Herpesvirus Multiplex ddPCR Detection in Brain Tissue from Low- and High-Grade Astrocytoma Cases and Controls** Major Cheng-Te Lin, Emily Leibovitch, M. Isabel Almira-Suarez, Steven Jacobson
	54	**Olfactory ensheathing cell tumors: a case report and review of the literature with comparison to olfactory groove schwannomas.** William Harrison, Thomas Cummings
	55	**A case of Glioneuronal Tumor with Neuropil Like Islands (GTNI), a rare entity with intriguing molecular profile.** Avneesh Gupta, Sriram Venneti, Noah Brown, Sandra Camelo-Piragua
	56	**A Subset of Cells in Glioblastoma Multiforme Express Multiple Stem Cell Markers** Nelli Lakis, Alexander Brodsky, Tyler Smith, Dongfang Yang, Ian Wong, Douglas Anthony
	57	**Secondary Gliosarcoma With Rapid Progression** William Borch, Kristen Natale, Daniel Cordaro, Patrick Malafronte
	58	**Signaling of ghrelin and its functional receptor, the growth hormone secretagogue receptor, promote tumor growth in gliomas** Yasuo Sugita, Koichi Ohshima, Yosuke Okada, Satoshi Komaki, Junko Miyoshi, Motohiro Morioka
	59	**Cerebellar pleomorphic xanthoastrocytoma in 11-year-old girl** Yasuo Sugita, Koichi Ohshima, Junko Miyoshi, Satoshi Komaki, Motohiro Morioka
	60	**The Notch Target HES1 Is Expressed in Normal Pituicytes and in Pituicytoma: An Immunohistochemical Study** Yang Liu, Antoinette Price, Abeer Tabbarah, Charles Eberhart
	61	**Automated analysis of chromosome 9p status by FISH identifies a subgroup of high-risk oligodendroglial tumours** Peter Gould, Céline Duval, Marie de Teyrac, Karine Michaud, Stéphan Saikali
	62	**T Cells Redirected to EGFRvIII with a Chimeric Antigen Receptor Engraft, Traffic and Mediate Antigen Loss in Patients with EGFRvIII+ Glioblastoma** MacLean Nasrallah, Maria Martinez-Lage, Donald O'Rourke, Arati Desai, Jennifer Morrissette, Steven Brem, Eileen Maloney, Angela Shen, Keith Mansfield, Suyash Mohan, Sumei Wang, Gaurav Verma, Simon Lacey, Jan Melenhorst, Jean-Marc Navenot, Zhaohui Zheng, Bruce Levine, Hideho Okada, Carl June, Marcela Maus
	63	**Infrequent IDH1 or IDH2 mutation in Glioblastoma** Zhe Piao, Vaninder Chhabra, Vartan Tashjian, Todd Goldenberg
	64	**Clinicopathologic Characteristics of Esophageal Adenocarcinoma Metastatic to the Pineal Region** Margaret Flanagan, Margaret Flanagan, Peter Chiarelli, Richard Ellenbogen, Patrick Cimino
	65	**CAMTA1 Positive Immunoperoxidase In A Dural-Based Epithelioid Hemangioendothelioma, A Case Report** Henry Brown, Juan Alzate, Heather Leeper
	66	**Intracerebellar Crystal-Storing Histiocytosis** Gordana Juric-Sekhar, Margaret Flanagan, Christopher Keene, David Louis, Gordana Juric-Sekhar
	67	**Unsuspected lymphoma presenting as Tolosa-Hunt syndrome. A case report and review of literature** David Priemer, Marwah Abdulkader, Dean Hawley, Jose Bonnin
	68	**Primary Bone ALK-negative Anaplastic Large Cell Lymphoma (ALCL) Presenting with Spinal Cord Compression** Soumya Pandey, Ginell Post, Ryan Fitzgerald, Murat Gokden
	69	**Malignant Transformation in Neurocutaneous Melanosis** Andrew Guajardo, Christopher VandenBussche, D Ashley Hill, Miguel Reyes-Mugica, Cheng-Ying Ho

Posters are not offered for CME credit

FRIDAY POSTERS #70-#88

Friday, June 17, 2016		
Time:	**Poster #:**	**Atrium/Harborview**
8:00 am – 4:30 pm	70	**Light Chain Deposition Disease Limited to the CNS – Case Report and Literature Review** Juan Mercado, James Markert, William Meador, Philip Chapman, James Hackney
	71	**Localized Crystal-Storing Histiocytosis Associated with Vertebral Compression Fracture** Alexander Feldman, Mamerhi Okor, James Hackney
	72	**Histopathologic Review of Pineal Parenchymal Tumors Identifies Novel Morphologic Subtypes and Prognostic Factors for Outcome** David Solomon, David Raleigh, Shane Lloyd, Ann Lazar, Michael Garcia, Penny Sneed, Jennifer Clarke, Michael McDermott, Mitchel Berger, Daphne Haas-Kogan, Tarik Tihan
	73	**Secretagogin Expression in the Peripheral Blood of Stroke Patients** Ang Eng Tat, Raymond Seet, Vanessa Lim
	74	**Amyloid Beta Related Angiitis with associated meningoencephalitis. Morphologic and immunohistochemical evaluation of six patients** Osama Elkadi, Marjorie Grafe, Randall Woltjer
	75	**Alpha-Endosulfine (ARPP-19e) Expression in Experimental Rat Stroke** Rupal Mehta, Svetlana Ivanova, Vladimir Gerzanich, J Marc Simard
	76	**Neurosarcoidosis of the Spinal Cord** Ibrahim Robadi, Walid Radwan, Sanjay Bhatia, Kymberly Gyure
	77	**IgG4-Related Hypophysitis Associated with a Rathke's Cleft Cyst** H. Brent Clark
	78	**Optic neuritis: Clinical and pathological findings in a 73 year-old female.** Bartholomew White, Michael Wilkinson, Charles Specht
	79	**Neuropathology of Neuroserpin Encephalopathy Associated with the *SERPINI1* S52R Mutation** Bernardino Ghetti, Adrian Oblak, Martin Farlow, Jill Murrell, Rose Richardson, Francine Epperson, Shannon Risacher, Andrew Saykin, Holly Garringer
	80	**Histological Validation of High Field MRI of the Human Brainstem** Karin Mente, Govind Nair, Daniel Reich, Abhik Ray-Chaudhury, Drew Pratt, Nancy Edwards, Silvina Horovitz, Mark Hallett
	81	**Amphetamine-induced hallucinations in an invertebrate** Anne Lee, Cindy Brandon, Jean Wang, William Frost
	82	**Neuropathology instruction using online methodologies coupled with live coaching: implications for the next generation of medical students** Brian Moore, Heeyoung Han
	83	**Preventing 'Freezing' Artifacts in Neuropathological Frozen Sections** Douglas Miller, Troy Leewright
	84	**EBV-Associated B-Cell Lymphoproliferative Disorder of the CNS in Systemic Lupus Erythematosus with Mycophenolate Immunosuppression** Nicholas Coley, Mirna Lechpammer, Mingyi Chen
	85	**BK Virus Encephalopathy and Sclerosing Vasculopathy in a Patient with Hypohidrotic Ectodermal Dysplasia and Immunodeficiency** Armine Darbinyan, Eugene Major, Susan Morgello, Mary Fowkes, Thomas Naidich, Steven Holland, Joanna Malaczynska, Caroline Ryschkewitsch, Maria Chiara Monaco, Joshua Bederson, Fei Ye, Ronald Gordon, Charlotte Cunningham-Rundles, Abhik Ray-Chaudhury, Nadejda Tsankova
	86	***Balamuthia* Amebic Encephalitis Occuring in a Healthy Middle-Aged Woman** Dibson Gondim, Kristen Partyka, Mercia Gondim, Andrew Koivuniemi, Dean Hawley, Bryan Schmitt, Ryan Relich, Eyas Hattab
	87	**Neurosarcoidosis: does *Propionibacterium* acnes have a role?** Guang Yang, Yoshinobu Eishi, Anwar Raza, Kenneth De Los Reyes, Adina Achiriloaie, Ravi Raghavan
	88	**Brain and liver pathology and amyloid deposition among older HIV-positive patients in the late HAART era** Isaac Solomon, Umberto De Girolami, Sukrutha Chettimada, Vikas Misra, Elyse Singer, Dana Gabuzda

Posters are not offered for CME credit

SATURDAY PLATFORMS 5 & 6

	Platform Session 5 ***Tumors: Pediatric*** **Constellation CDEF** **Chairs: Maria Martinez-Lage, MD; Craig Horbinski, MD, PhD**	**Platform Session 6** ***Neurodegeneration, Trauma, Prions*** **Constellation A** **Chair: Richard Perrin, MD; Rupal Mehta, MD**
8:00 am – 8:15 am	**89** **Building new medulloblastoma models from human neural progenitors with *in silico* analysis to identify novel therapeutic targets** Charles Eberhart, Allison Hanaford, Tenley Archer, Pablo Tamayo, Scott Pomeroy, Eric Raabe	**97** **Immunohistochemical and Gene Expression Patterns in Osmotic Demyelination Syndrome** R Kersting, Ravindra Kolhe, Ashis Mondal, Mumtaz Rojiani, Amyn Rojiani
8:15 am – 8:30 am	**90** **Tumor and germline sequencing of pediatric brain tumor patients at first diagnosis: the UCSF experience** David Solomon, Cassie Kline, Theodore Nicolaides, Sabine Mueller, Anuradha Banerjee, Joseph Torkildson, David Samuel, Mariam Aboian, Soonmee Cha, Nalin Gupta, Corey Raffel, Alejandra de Alba Campomanes, Nancy Joseph, James Grenert, Jessica van Ziffle, Iwei Yeh, Boris Bastian, Tarik Tihan, Andrew Bollen, Joanna Phillips, Arie Perry	**98** **Contribution of the Neuropathology laboratory at Indiana University to the study of Gerstmann-Sträussler-Scheinker disease: 1976-2016** Bernardino Ghetti, Stephen Dlouhy, Brenda Dupree, Francine Epperson, Jill Murrell, Adrian Oblak, Pedro Piccardo, Rose Richardson, Salvatore Spina, Masaki Takao
8:30 am – 8:45 am	**91** **Lowered H3K27me3 and DNA hypomethylation define poorly prognostic pediatric posterior fossa ependymomas** Jill Bayliss, Piali Mukherjee, Chao Lu, Siddhant U. Jain, Daniel Martinez, Ashley S. Margol, Melike Pekmezci, Chan Chung, Richard C McEachin, Marcin Cieslik, Benjamin A. Garcia, Benita Tamrazi, Gaspare La Rocca, Mariarita Santi, Peter W. Lewis, Ari Melnik, C. David Allis, Craig B. Thompson, Arul M. Chinnaiyan, Alexander R. Judkins, Sriram Venneti	**99** **New Ultrasensitive Tests for Diagnosis and Differentiation of Human Prion Diseases** Jiri Safar, Aaron Foutz, Brian Appleby, Mark Cohen, Jianxin Xiao, Clive Hamlin, Yvonne Cohen, Wei Chen, Janis Blevins, Pierluigi Gambetti, Andrew Hughson, Lawrence Schonberger, Byron Caughey
8:45 am – 9:00 am	**92** **The Genetic And Clinical Landscape Of Pediatric Low Grade Gliomas** Cynthia Hawkins, Michal Zapotocky, Alvaro Lassaletta, Scott Ryall, Anthony Arnoldo, M. Mistry, Ana Guerreiro-Stucklin, Natalyia Zhukova, V. Ramaswamy, Eric Bouffet, Uri Tabori	**100** **Hippocampal sclerosis of aging: genetics and neuroimaging experiments in ADNI** Peter Nelson, Kwangsik Nho, Andrew Saykin, Ai-Ling Lin, Eseosa Ighodaro
9:00 am – 9:15 am	**93** **Genetic alterations in uncommon low-grade neuroepithelial tumors – frequent *BRAF*, *FGFR1*, and *MYB/MYBL1* mutations align with morphology** David Ellison, Wilda Orisme, Ji Wen, Jim Dalton, Bo Tang, Kelly Haupfear, Kirti Gupta, Daniel Brat, Sonika Dahiya, Hilary Nickols, Arie Perry, Ruth Tatevossian	**101** **Immune Cell Infiltrates in Hippocampal Sclerosis: Correlation of CD8+ Cytotoxic T-cells with Neuronal Loss** Trevor Steve, Douglas Zochodne, Matt Wheatley, Donald Gross, Jian-Qiang Lu
9:15 am – 9:30 am	**94** **Recurrent Genetic Alterations in Classic and Anaplastic Pleomorphic Xanthoastrocytoma: characterization of 36 cases by SNP array** Rachael Vaubel, Alissa Caron, Seiji Yamada, Fausto Rodriguez, Amulya NageswaraRao, Daniel Lachance, Ian Parney, Robert Jenkins, Caterina Giannini	**102** **Repetitive Head Impacts are Associated with Microglial Activation in Chronic Traumatic Encephalopathy** Thor Stein, Jonathan Cherry, Yorghos Tripodis, Victor Alvarez, Bertrand Huber, Jesse Mez, Ann McKee
9:30 am – 9:45 am	**95** **Neuropathological features of astroblastoma, including $BRAF^{V600E}$ mutations, suggest an ontological relationship to other pediatric gliomas.** Norman Lehman, Eyas Hattab, Bret Mobley, Aisulu Usubalieva, Matthew Schniederjan, Roger McLendon, Werner Paulus, Elisabeth Rushing, Maria-Magdalena Georgescu, Marta Couce, Mohanpal Dulai, Mark Cohen, Christopher Pierson, Jack Raisanen, Sarah Martin, Trang Lehman, Eric Lipp, Jose Bonnin, Mousa Al-Abbadi, Kara Kenworthy, Kevin Zhao, N. Mohamed, G. Zhang, John Zhao	**103** **Spatial Analysis of Tau-immunoreactive Lesions in Eleven Cases of Chronic Traumatic Encephalopathy** Nigel Cairns, Ann McKee, Thor Stein, Victor Alvarez, Richard Armstrong
9:45 am – 10:00 am	**96** **Endothelium-Independent Primitive Myxoid Vascularization Creates Invertebrate-like Channels to Maintain Blood Supply in Optic Gliomas** Matija Snuderl, Guoan Zhang, Pamela Wu, Tara Jennings, Seema Shroff, Valerio Ortenzi, Rajan Jain, Benjamin Cohen, Jason Reidy, Mitchell Dushay, Jeffrey Wisoff, David Harter, M. Karajannis, David Fenyo, Thomas Neubert, David Zagzag	**104** **Infants with Repetitive Non-accidental Trauma and Chronic Traumatic Encephalopathy: A Study of 14 Cases** Heather Jarrell

SATURDAY PLATFORMS 7 & 8

	Platform Session 7 ***Peripheral Nerve and Muscle*** **Constellation CDEF** **Chairs: Sandra Camelo-Piragua, MD; Mariarita Santi, MD, PhD**	**Platform Session 8** ***Neurodegeneration: FTD, Lewy Body and Other*** **Constellation A** **Chair: Edward Plowey, MD; Peter Nelson, MD**
1:30 pm – 1:45 pm	**105** **Clinicopathologic features of lipid myopathy with multiple acyl dehydrogenase deficiency (MADD): a brief case series.** Tejus Bale, David Meredith, Adam Chen, Anthony Amato, Umberto De Girolami	**113** **Sensitivity and specificity of Consortium for DLB neuropathologic criteria In the Mayo Clinic Jacksonville brain bank** Dennis Dickson
1:45 pm – 2:00 pm	**106** **Morin Stain Detects Aluminum-Containing Macrophages in Macrophagic Myofasciitis with High Sensitivity and Specificity** Rati Chkheidze, Dennis Burns, Charles White, Chunyu Cai	**114** **Enteric Manifestations of Alpha-Synucleinopathies** Michael Punsoni, Joseph Friedman, Murray Resnick, John Donahue, DongFang Yang, Edward Stopa
2:00 pm – 2:15 pm	**107** **Upregulation of Chromosome 14q32 Cluster microRNAs in Inclusion Body Myositis** James Mandell, Yoshiyuki Shibata, Anindya Dutta	**115** **Truncated α-synuclein May Link Lewy Body Diseases And Tauopathies** Kimmo Hatanpaa, Sarah Gough, Chandrasekhar Sundarrajan, Reza Amanipour, Margaux Schwartzstein, Vamsidhara Vemireddy, Chan Foong, Dennis Burns, Charles White
2:15 pm – 2:30 pm	**108** **Muscle Contractures Can Be Modeled in the Mouse Through Limb Immobilization During Early Life, Allowing the Evaluation of Therapeutic Strategies** Michael Lawlor, Jennifer Tinklenberg, James Bain, Margaret Beatka, Hui Meng, Danny Riley	**116** **Spinal Cord And Brain Neuropathology In ALS: The Spectrum of TDP-43 Pathology And Its Relationship To Clinical Parameters** Matthew Cykowski, Suzanne Powell, Hidehiro Takei, Joan Appel, Andreana Rivera, Stanley Appel
2:30 pm – 2:45 pm	**109** **Mutations in ER-Golgi trafficking genes lead to hypoglycosylation of alpha-dystroglycan and muscular dystrophy** Steven Moore, Austin Larson, Mary Cox, Jacqueline Lekostaj, Aaron Stence, Aaron Bossler, Jennifer Mueller, Miroslav Milev, Keshika Prematilake, Michael Sacher, Peter Baker II, Charles Williams, Perry Shieh	**117** **Distribution of granulins in FTLD-TDP and normal brains** Qinwen Mao, Kimmo Hatanpaa, Yanqing Li, Jayson Wilson, Sandra Weintraub, Haibin Xia, Charles White, Marsel Mesulam, Eileen Bigio
2:45 pm – 3:00 pm	**110** **Gastric Dysmotility in Duchenne Muscular Dystrophy: Distribution of Dystrophin and Utrophin in Gastric Musculature** Christine Fuller, Brenda Wong, Karen Shellenbarger, Jamie Reuss, Christopher Hackett, Daniel Leino, Ajay Kaul	**118** **Distinct liquid-like properties of axonal TDP-43 RNP granules** Pallavi Gopal, Jeffrey Nirschl, Eva Klinman, Erika Holzbaur
3:00 pm – 3:15 pm	**111** **Congenital myopathy with selective muscle atrophy, necklace-like fibres/central cores and craniosynostosis associated with recessive mutations in *SCN4A*.** Maryam El-Murshed, Hernan Gonorazy, Christian R. Marshall, Lili-Naz Hazrati, Roope Männikkö, Peter N. Ray, Grace Yoon	**119** **Aging-related tau astrogliopathy (ARTAG) of three supercentenarian brains.** Masaki Takao, Hiroaki Kimura, Ban Mihara, Michiyasu Arai, Nobuyoshi Hirose, Masaru Mimura
3:15 pm – 3:30 pm	**112** **Neuropathologic Findings in a Long-term Survivor of Krabbe's Disease with Umbilical Cord Blood Transplantation** Julia Kofler, Paul Szabolcs, Maria Escolar	**120** **Tau Immunohistochemistry in Peripheral Tissues of Progressive Supranuclear Palsy, Corticobasal Degeneration, and Alzheimer's Disease** Brittany Dugger, Brittany Hoffman, Alex Scroggins, Geidy Serrano, Thomas Beach

SATURDAY POSTERS #121-#140

Saturday, June 18, 2016		
Time:	**Poster #:**	**Atrium/Harborview**
8:00 am – 4:00 pm	121	**Aging-related tau astrogliopathy in the Einstein Aging Study** Kevin Bieniek, Sunhee Lee, Karen Weidenheim, Mindy Katz, Richard Lipton, Dennis Dickson
	122	**Chronic traumatic encephalopathy pathology in multiple system atrophy** Shunsuke Koga, Kevin Bieniek, Dennis Dickson
	123	**Chronic Traumatic Encephalopathy with prominent dentate gyrus TDP-43 proteinopathy** Heather Ames, Jason Denney, Liam Chen
	124	**A Pathologic and Cognitive Comparison of Primary Age-Related Tauopathy (PART) to Alzheimer's Disease** William Bell, Olga Pletnikova, Yang An, Yusuke Kageyama, Barbara Crain, Gay Rudow, Abhay Moghekar, Madhav Thambisetty, Marilyn Albert, Susan Resnick, Peter Rabins, Juan Troncoso
	125	**Correlating tauopathy and TDP-43 pathology in aged brains** Vanessa Smith, Eseosa Ighodaro, Erin Abner, Peter Nelson
	126	**Role of autophagy in hereditary ferritinopathy** Jose Irimia, Holly Garringer, Ruben Vidal
	127	**Diagnosis of Chronic Traumatic Encephalopathy in an Exhumed Brain Four Years After Burial.** Ronald Hamilton
	128	**Progressive Atrophy in Neuroserpin Encephalopathy Associated with the *SERPINI1* S52R Mutation** Shannon Risacher, John West, Eileen Tallman, Adrian Oblak, Francine Epperson, Martin Farlow, Andrew Saykin, Bernardino Ghetti
	129	**A Case of Adult-Onset Leukoencephalopathy with Spheroids and Pigmented Glia** Jose Velazquez Vega, Stewart Neill, Matthew Schniederjan, Stephen Hunter, Jonathan Glass, Marla Gearing
	130	**Neuropathologic Phenotype Associated with a *UBQLN2* P497L Mutation in 3 Affected Women from 3 Generations** Kathy Newell, Jill Murrell, Bernardino Ghetti, Christine Seidman, Donald Harter
	131	**Neuropathologic evaluation of Adenylate Cyclase 5 related dyskinesia** Caitlin Latimer, Marie Davis, Dong-Hui Chen, Wendy Raskind, Thomas Bird, C. Keene
	132	**Absence of PHF-Tau Neuropathology in Remote Traumatic Brain Injury.** Shannon Rose, Desiree Marshall, Nadia Postupna, Natalie Coleman, Kayla Ritchie, Leanne Hellstern, Eugene Chau, Allison Beller, Paul Crane, Eric Larson, Thomas Montine, C. Keene
	133	**Results of NINDS/NIBIB CTE neuropathology screening in an ADRC cohort.** Desiree Marshall, Shannon Rose, Samantha Rice, Allison Beller, Elaine Peskind, C Keene
	134	The Aging Vervet as a Model of Alzheimer's Disease **Caitlin Latimer, Jay Kaplan, Carol Shively, J Cline, Rachel Andrews, Matthew Jorgensen, Suzanne Craft, Thomas Montine, C. Keene**
	135	**Isolated myofibrillar myopathy with alpha-B crystallin mutation (c.460G>A; p.G154S): Clinical and pathological findings.** Bartholomew White, Matthew Wicklund, Charles Specht
	136	**Xanthomatous Neuropathy: A Rare Neuropathy Associated with Primary Biliary Cirrhosis** Saed Sadeghi, BT Harris, MS Ongkeko, WW Campbell
	137	**Sarcoplasmic Hyaline Inclusion Bodies in a Case of Adult-Onset Acid-Maltase Deficiency. Report of a Case and Review of the Literature** Dibson Gondim, Jose Bonnin
	138	**Lobulated Fiber Myopathy Associated With *GAA* (Acid Alpha Glucosidase) Mutation** Luis Gonzalez-Cuyar, Margaret Flanagan, Catlin Latimer, Jamila Madhani, Leo Wang, Patrick Cimino
	139	**Treating acute traumatic spinal cord injury with combination therapy of thyrotropin releasing hormone, selenium and vitamin E** Barbara Gwardjan, Seth Nitin, Farah Masood, John Sledge, Douglas Rosene, Susan Westmoreland, Shiela Macri, Ervin Sejdic, Amber Hoggatt, Heather Simmons, Hussein Abdullah, Shanker Nesathurai
	140	**Structural characterization of perivascular lesions in chronic traumatic encephalopathy** Bertrand Huber, Kerry Cormier, Katharine Babcock, Victor Alvarez, Thor Stein, Ann McKee

Posters are not offered for CME credit

SATURDAY POSTERS #141-#160

Saturday, June 18, 2016		
Time:	**Poster #:**	**Atrium/Harborview**
8:00 am – 4:30 pm	141	**Regression of a H3K27M Mutation Positive Midbrain Tectal Glioma** Marco Hefti, Saadi Ghatan, Kambiz Nael, Mary Fowkes, John Crary
	142	**Clinicopathologic Features Of A Pleomorphic Pituicytoma.** Adelita Vizcaino, Kaisorn Chaichana, Fausto Rodriguez
	143	**Precision Neuropathology: Experience at Weill Cornell Medical College through the Englander Institute of Precision Medicine** David Pisapia, Rohan Ramakrishna, Theodore Schwartz, Prajwal Rajappa, Michael Kluk, Olivier Elemento, Andrea Sboner, Himisha Beltran, Howard Fine, Jeffrey Greenfield, Juan Miguel Mosquera, Mark Rubin
	144	**Molecularly-Defined Secondary and "Stealth" Glioblastomas: An Institutional Experience** Vivian Snyder, Deirdre Amaro, Irene Thung, Karra Jones
	145	**Breaking Bad: Chromothripsis and Malignancy in CNS tumors** Deirdre Amaro, Karra Jones
	146	**Pediatric pilocytic astrocytoma with de-novo atypical features: histologic and molecular characteristics** Suash Sharma, Ravindra Kolhe, Mumtaz Rojiani, Ian Heger, Amyn Rojiani
	147	**49 Year Old Male Presenting with Rare Primary Intracranial and Spinal High-Grade Gliomas within 18 Months** Darshan Trivedi, Clifford Crutcher, Frank Culicchia, Bart Farris
	148	**Differential Innate and Adaptive Immune Infiltration Across Glioblastoma Subtypes** Aivi Nguyen, Timothy Lynch, Sharmistha Pal, Ramana Davuluri, Donald O'Rourke, Nadia Dahmane, Maria Martinez-Lage
	149	**Astrocytoma Morphology and IDH Mutation Status: What Did We Miss?** Jose Velazquez Vega, Jun Kong, Daniel Brat
	150	**Alterations of chromosomes 1 and 19 in glial tumors** Armine Darbinyan, Russell McBride, Ryan Rhome, Vesna Najfeld, Sheryl Green, Isabelle Germano, Mary Fowkes
	151	**An Unusual Case of Astroblastoma in a Patient with Ameloblastoma: Is There a Connection?** Joy King, Mark Anderson, Anna Mathew
	152	**Modeling Cost-Effectiveness of IDH1 Testing in Glioma** John DeWitt, David Louis, Jochen Lennerz
	153	**Glioblastoma (GB) Arising in a Multiple Sclerosis (MS) Patient During Treatment** James Nix, Ryan Fitzgerald, Murat Gokden
	154	**Primary intra-cranial epithelioid angiosarcoma, a rare tumor and great mimicker.** Jiang Qian, Sungeun Kim, Tyler Kenning, Jiang Qian
	155	**A Rare Intracranial Presentation of Angiomatoid Fibrous Histiocytoma** Michael Paolini, Karen Fritchie, Ajay Rawal, Joseph Parisi, Mark Jentoft
	156	**Orbitocranial Ganglioneuroma with Adenocarcinoma Component** Mercia Gondim, Dibson Gondim, Aaron Kamer, Jose Bonnin
	157	**Primary Melanoma of the Pineal Gland: A Case Report** Christine Rupcich, Yahya Al-Ghamdi, Lorenzo Munoz, Leonidas Arvanitis, Sukriti Nag
	158	**High-grade neuroepithelial neoplasm with EWSR1 rearrangement in a pediatric patient** Woon Chow, Paisit Paueksakon, Fausto Rodriguez, David Ellison, Hilary Nickols
	159	**Angiogenesis and Immune Checkpoint Ligands in Melanoma Brain Metastases Prognosis** Dimitri Trembath, Ronald Hamilton, Nana Nikolaishvilli-Feinberg, Shanti Rao, Daniel Zedek, Matthew Ewend, Stergios Moschos
	160	**Sellar Atypical Teratoid/Rhabdoid Tumors (AT/RTs): Review of Reported Cases** Michael Paolini, Benjamin Kipp, William Sukov, Aditya Raghunathan, Emily Barr Fritcher, Derick Aranda, Karen SantaCruz, Sadeq Al-Dandan, Pete Fisher, William McDonald, Grant Van Dyke Darkow, Charles Bondurant, Caterina Giannini, Joseph Parisi, Mark Jentoft

Posters are not offered for CME credit

SATURDAY POSTERS #161-#178

Saturday, June 18, 2016		
Time:	**Poster #:**	**Atrium/Harborview**
8:00 am – 4:30 pm	161	**Hodgkin lymphoma of the central nervous system: a report of two cases** Shih-Hsiu Wang, Phyllis Faust
	162	**Glomus Tumor of the Brachial Plexus Carrying a *BRAF* p.V600E Mutation** Michal Raz, Allan Belzberg, Lysandra Voltaggio, Fausto Rodriguez
	163	**A case of intracranial tufted angioma in a 69 year-old man** George Zanazzi, Gunnar Hargus, Phyllis Faust
	164	**Elucidating Subtypes and Risk Factors of Brain Arteriolosclerosis** Eseosa Ighodaro, Erin Abner, Sarah Monsell, Walter Kukull, Janna Neltner, Vanessa Smith, David Fardo, Peter Nelson
	165	**Radiation-induced cerebral vascular malformations at biopsy** Bette Kleinschmidt-DeMasters, Kevin Lillehei
	166	**Adult-onset Leukoencephalopathy with Cerebral Calcifications and Cysts (Labrune Syndrome): A Case With Novel Copy Number Abnormalities** Jose Velazquez Vega, Stewart Neill, Matthew Schniederjan, Stephen Hunter, Daniel Brat, Debra Saxe, Michael Rossi, Chad Holder, Jeffrey Olson
	167	**Friedreich Cardiomyopathy is a Disease of Intercalated Discs** Arnulf Koeppen, Alyssa Becker, Joseph Mazurkiewicz, Paul Feustel, Benjamin Gelman
	168	**Prevalence and Risk Factors for Neural Tube Defects In the US from 2005-2013. A Population Based Study** Ahmed Gilani, Zainab Siddiq, Jenny Libien
	169	**A Case Study of Craniosynostosis Associated with Hemorrhage and Vascular Lesions in Two Infants** Ran Wang, Murat Gokden, Ju Liu, Rongsheng Cai
	170	**Gene Expression Profiling in Serotonergic Neurons in Human Infant Medulla** Emma Giles, Hannah Kinney, Elisabeth Haas, Othon Mena, Susan Dymecki, Ben Okaty
	171	**A Potential Biomarker of a Subset of Infants Dying of Sudden Infant Death Syndrome** Robin Haynes, Andrew Frelinger, Hoa Tran, Emma Giles, Elisabeth Haas, Othon Mena, Richard Goldstein, Hannah Kinney
	172	**Novel Brain Findings in Osteogenesis Imperfecta Patient with Previously Unreported *COL1A2* Mutation** Amanda Tchakarov, Rebecca Collins, Jamie Walker, Anita Sengupta, Veena Rajaram
	173	**Expression of GATA-3 in Human Pituitary Adenomas and Other Sellar and Parasellar Neoplasms** Amber Wang, Alexander Gill, Maria Martinez-Lage
	174	**A rare case of infantile hemangioma involving a lumbosacral fibrous stalk with intradural extension and without a cutaneous hemangioma component** Andrea Gilbert, Jonathan Sellin, Andrew Jea, Carrie Mohila
	175	**CNS Manifestations of Mycoplasma pneumoniae: Case report.** Esther Jack, Jane Cryan, Declan O'Rourke, Joanne O'Gorman, Darach Crimmins
	176	**Cryptococcoma (*C. gattii*) mimicking cerebellar neoplasia in a patient from Florida** Meggen Walsh, Shawn Lockhart, Anthony Yachnis
	177	**A histopathologic review of post-herpes simplex virus encephalitis with neurologic relapse** Masoud Movassaghi, Yalda Naeini, Paul Krogstad, Gary Mathern, Harry Vinters
	178	**The Selective Association between Hypertension and Diabetes on Delusions in Alzheimer's disease is not mediated by Vascular Pathology** Julia Kim, Tom Schweizer, Corinne Fischer, David Munoz

Posters are not offered for CME credit

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Endowed Lectureships

Friday, June 17, 2016

I. Parisi Lecture
II. DeArmond Lecture

Saturday, June 18, 2016

I. Saul R. Korey Lecture
II. Matthew T. Moore Lecture

ENDOWED LECTURESHIP

PARISI LECTURE

The *Parisi Lecture* was established in 2007. The lecture was named the *Parisi Lectureship* in honor of one of the American Association of Neuropathologists' exceptional members, Dr. Joseph E. Parisi. He has published seminal neuropathological studies on a wide range of diseases affecting the nervous system, with particular focus on neurodegenerative diseases and multiple sclerosis. He has held virtually every office of the Society, including President, and has served on several AANP committees. In 2006, his dedication and generosity were recognized with the Award for Meritorious Contributions to Neuropathology. He is considered by many the heart and soul of the association and a man worth emulating.

We are pleased to have **Bette Kleinschmidt-DeMasters** join our list of distinguished speakers.

2008	Claudia Lucchinetti	The Spectrum of CNS Inflammatory Demyelinating Diseases: *From Pathology to Pathogenesis*
2009	Hans Lassmann	Inflammation Induced Mitochondrial Injury: A Major Mechanism of Neurodegeneration
2010	Joseph Dalmau	Autoimmune Synaptic Encephalitis
2011	Steven S. Scherer	Molecular Pathologies at the Nodes of Ranvier
2012	Bruce D. Trapp	Neuronal Damage in Multiple Sclerosis
2013	Albee Messing	GFAP: Friend or Foe
2014	Clayton Wiley	Human Parechovirus Encephalitis
2015	Bruce T. Lamb	The Role of Innate Immunity in Neurodegenerative Disease Pathogenesis
2016	Bette Kleinschmidt-DeMasters	CNS White Matter Disorders with Viral Causation and Association

PARISI LECTURE

CNS White Matter Disorders with Viral Causation and Association

Time: 10:15 am – 11:15 am

Date: Friday, June 17, 2016

Bette Kleinschmidt-DeMasters, MD, *Professor and Head of Neuropathology, University of Colorado*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Discuss the basic biology of JC virus of progressive multifocal leukoencephalopathy and varicella zoster virus.
2. Explain which drug is more strongly associated with the development of progressive multifocal leukoencephalopathy: natalizumab or fingolimod.
3. Explain which drug allows one to predict better when PML will develop, ie after a certain number of doses: natalizumab or fingolimod.
4. Note whether the VZV infections that follow fingolimod are more likely to affect cutaneous or CNS sites.

II. Abstract & Relevant References

The central nervous system white matter is affected by several productive lytic viral infections that have been identified in patients with severe immunocompromising disorders including those with human immunodeficiency virus infection, transplant recipients, and hematological malignancies, but have re-emerged in patients treated with immunomodulatory drugs. The latter include cases of progressive multifocal leukoencephalopathy (PML) and varicella zoster virus encephalitis (VZV) in patients treated with natalizumab, fingolimod, and rituximab. These drugs involve different risks for these two infections, both in terms of incidence but also in terms of whether the onset of infection can be predicted temporally after a given number of drug doses, or not. In addition, immune reconstitution inflammatory syndrome (IRIS) after removal of natalizumab in patients who develop PML remains a challenging condition.

References:

1. Steiner I, Berger JR. Update on progressive multifocal leukoencephalopathy. Curr Neurol Neurosci Rep. 2012;12(6):680-6. doi: 10.1007/s11910-012-0313-4.
2. Carruthers RL, Berger J. Progressive multifocal leukoencephalopathy and JC virus-related disease in modern neurology practice. Mult Scler Relat Disord. 2014;3(4):419-30. doi: 10.1016/j.msard.2014.01.005. Epub 2014 Feb 8.
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4. Gilden DH, Kleinschmidt-DeMasters, BK, LaGuardia JJ, Mahalingam R, Cohrs RJ. Neurologic complications of the reactivation of Varicella-Zoster virus. N Engl J Med. 2000;342-635-645. doi: 10. 1056/NEJM200003023420906.
5. Kleinschmidt-DeMasters BK, Gilden DH. Varicella-Zoster virus infections of the nervous system: clinical and pathologic correlates. Arch Pathol Lab Med. 2001;125(6):770-80
6. Cohen JA, Chun J. Mechanisms of fingolimod's efficacy and adverse effects in multiple sclerosis. Ann Neurol. 2011;69(5):759-77. Doi: 10.1002/ana.22426
7. Kleinschmidt-DeMasters BK, Miravalle A, Schowinsky J, Corboy J, Vollmer T. Update on PML and PML-IRIS occurring in multiple sclerosis patients treated with natalizumab. J Neuropathol Exp Neurol. 2012;71(7):604-17. doi: 10.1097/NEN.0b013e31825caf2c.
8. Wüthrich C, Popescu BFGh, Gheuens S, Marvi M, Ziman R, Pojen Deng S, Tham M, Norton E, Parisi JE, Dang X, Lucchinetti CF, Koralnik IJ. Natalizumab-associated progressive multifocal leukoencephalopathy in a patient with multiple sclerosis: a post mortem study. J Neuropathol Exp Neurol. 2013;72(11):1043-1051. doi:10.1097/NEN.0000000000000005.
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10. multifocal leukoencephalopathy immune reconstitution inflammatory syndrome supports treatment with the CCR5 inhibitor maraviroc. Acta Neuropathol (2015) 129:467–468. doi: 10.1007/s00401-015-1391-6

III. Faculty Biography

Bette DeMasters is a tenured Professor in the Departments of Pathology, Neurology, and Neurosurgery, at the University of Colorado at Denver and Health Sciences Center. Dr. DeMasters received her M.D. from the University of Wisconsin, Madison, her AP/CP pathology training at the University of Colorado Health Sciences Center, and her neuropathology training under the late John J. Kepes at the University of Kansas and Dr. Michael Norenberg, then at UCHSC. She has served as past president of the AANP, as Program Committee chair for AANP, and is a recipient of the Meritorious Service Award. She has been a member of the Residency In-Service Training Exam committee (RITE) for the American Academy of Neurology, the faculty at Pathobiology of Cancer/Edward A. Smuckler Memorial Workshop of the AACR, and the American Board of Pathology. Over the years, she has given several short courses for the United States and Canadian Academy of Pathology and been a member of numerous USCAP Diagnostic Neuropathology night panels. She has been the reference neuropathologist for one of the largest multiple sclerosis brain banks in North America since 1999. Dr. DeMasters' diverse research interests include central nervous systems infections, brain tumors, radiation-induced secondary brain tumors, pituitary adenomas, and iatrogenic drug and radiation-induced disorders. She is the recipient of local and national teaching awards and is currently on the editorial boards of 4 journals: Archives of Pathology and Laboratory Medicine, American Journal of Surgical Pathology, Brain Pathology, and Journal of Neuropathology and Experimental Neurology. She is married and the mother of 3 children and 3 grandchildren.

ENDOWED LECTURESHIP

DEARMOND LECTURE

The *DeArmond Lecture* was established in recognition of Stephen J. DeArmond's excellent leadership and organization of the scientific program for the 2006 International Congress of Neuropathology. This successful meeting garnered significant support intended for the future advancement of the mission of the American Association of Neuropathologists. To continue these intended goals and recognize Dr. DeArmond's contributions, the American Association of Neuropathologists has honored him by establishing the *DeArmond Lecture*. Dr. DeArmond is a leading authority on prion disease, where his work has been fundamental in demonstrating mechanisms of transmission and routes to therapeutics. The DeArmond Lecture focuses on honoring those making major advances in the field of neurodegeneration and aging with a particular emphasis on translating these findings to patient care.

We are pleased to have **Eric J. Huang** join our list of distinguished speakers.

2008	Virginia M. –Y. Lee	TDP-43, A New Class of Proteinopathies in Neurodegenerative Diseases
2009	Rudy Tanzi	Decoding Alzheimer's Disease Gene by Gene
2010	Todd Golde	Alzheimer's Disease: Models and Therapeutics
2011	Beverley L. Davidson	Emerging Therapies for Neurogenetic Diseases
2012	Krystof Bankiewicz	New Therapies for Parkinson Disease
2013	Stanley Prusiner	A Unifying Role for Prions in Neurodegenerative Diseases
2014	Dale Bredesen	Prionic Loops, Dependence Receptors, and a New Approach to Alzheimer's Disease
2015	William W. Seeley	Frontotemporal Dementia: Onset and Spread
2016	Eric J. Huang	FTD and ALS: Genes, Circuits and Therapeutic Targets

DEARMOND LECTURE

FTD and ALS: Genes, Circuits and Therapeutic Targets

Time: 4:30 pm – 5:30 pm

Date: Friday, June 17, 2016

Eric J. Huang, MD, PhD, Professor of Pathology, *University of California San Francisco & Attending Pathologist, San Francisco VA Medical Center*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Discuss the genetic underpinnings that have been causally linked to patients with familial forms of frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS).
2. Summarize the latest research using animal models to understand the pathogenesis and identify disease pathways for FTD and ALS.
3. Explain how to translate research from animal models and human disease into potential therapeutic targets for FTD and ALS.

II. Abstract & Relevant References

Frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) are two neurodegenerative diseases that share overlapping clinico-pathological features. However, the mechanisms contributing to the pathogenesis of FTD and ALS remain poorly characterized. The 2016 DeArmond Lecture will focus on the role of progranulin (PGRN [protein]; Grn [gene]) in regulating microglial function and how PGRN deficiency contributes to FTD. Microglia maintain homeostasis in the brain, but whether aberrant microglial activation can cause neurodegeneration remains controversial. To test this, we use transcriptome profiling to demonstrate that deficiency in PGRN leads to an age-dependent, progressive up-regulation of lysosomal and innate immunity genes, increased complement production, and enhanced synaptic pruning in microglia. During aging, Grn-/- mice show profound microglia infiltration and preferential elimination of inhibitory synapses in the ventral thalamus, which lead to hyperexcitability in the thalamocortical circuits and obsessive-compulsive disorder (OCD)-like grooming behaviors. Remarkably, deleting C1qa gene significantly reduces synaptic pruning by Grn-/- microglia, and mitigates neurodegeneration, behavioral phenotypes and premature mortality in Grn-/- mice. Together, these results uncover a previously unrecognized role of progranulin in suppressing aberrant microglia activation during aging. These results represent an important conceptual advance that complement activation and microglia-mediated synaptic pruning are major drivers, rather than consequences, of neurodegeneration caused by progranulin deficiency.

References:

1. Martens et al., Progranulin deficiency promotes neuroinflammation and neuron loss following toxin-induced injury. J Clin Invest. 2012 Nov 1;122(11):3955-9.
2. Qiu et al., ALS-associated mutation FUS-R521C causes DNA damage and RNA splicing defects. J Clin Invest. 2014 Mar 3;124(3):981-99.
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4. Lee and Huang, Modeling ALS and FTD with iPSC-derived neurons. Brain Res. 2015 Oct 14.
5. Shang and **Huang**, Mechanisms of FUS mutations in familial amyotrophic lateral sclerosis. Brain Res. 2016 Mar 28.
6. Lui et al., Progranulin deficiency promote circuit-specific synaptic pruning by microglia and complement activation. Cell 2016 May 5.

III. Faculty Biography

Dr. Eric Huang received his MD from the National Taiwan University School of Medicine in 1986 and PhD in Molecular Biology from Cornell University/Sloan Kettering Institute in New York City in 1993. He received his combined AP/NP clinical training in the Department of Pathology at UCSF from 1993 to 1997, and postdoctoral

training in Developmental Neurobiology at the Howard Hughes Medical Institute and UCSF from 1997 to 2000. In 2000, he was recruited to a joint appointment at the Department of Pathology at UCSF and the San Francisco VA Medical Center. He is currently a Professor of Pathology at UCSF.

Dr. Huang is the recipient of the following awards: 1997-99, Postdoctoral Research Fellowship for Physicians (Howard Hughes Medical Institute); 1998, Weil Award for the best paper in Experimental Neuropathology (AANP Annual Meetings); 2000-05, Presidential Early Career Award for Scientists and Engineers (PECASE); 2002-07, Independent Scientist Award (NINDS/NIH); 2009-14, Mid-career Investigator Award in Mouse Pathobiology, NCRR/NIH.

There are two general areas of research in Dr. Huang's laboratory, both supported by extramural funding. The first area focuses on trophic factor signaling mechanisms that regulate neural circuit development and function. Another major area of research focuses on the molecular mechanisms of neurodegenerative diseases, including frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS). Dr. Huang and his colleagues have developed several mouse models that greatly improve our understanding of the diverse disease mechanisms for FTD and ALS. To connect his basic science research with human diseases, Dr. Huang and his colleagues have spearheaded the efforts to establish two major brain tissue banking systems at UCSF, namely the Alzheimer's Disease Research Center (ADRC) Brain Bank and the UC Pediatric Neuropathology Consortium. The success of these endeavors is underscored by our extensive collaborations with colleagues within and outside UCSF, which lead to many high profiles publications in *Cell*, *Nature*, *Neuron*, *Nature Neuroscience*, etc. Most importantly, these studies revealed previously unrecognized role of neural circuit dysfunctions in neurodevelopmental and neurodegenerative diseases, and re-define our approaches toward investigating the molecular and cellular pathways in these devastating diseases.

ENDOWED LECTURESHIP

SAUL R. KOREY LECTURE

The *Korey Lecture* was established by Dr. Robert D. Terry in honor of Dr. Saul R. Korey, the founder and first Chair of the Department of Neurology at Albert Einstein College of Medicine. Dr. Korey's vision of an interdisciplinary approach to the study of neurological diseases by basic and clinical scientists has inspired generations of colleagues and trainees. Dr. Terry, a close collaborator and colleague of Dr. Korey, was the first recipient of the prestigious *Potamkin Prize for Pick's and Alzheimer's Disease* in 1988, in recognition of his seminal observations of the pathological changes in Alzheimer disease. Dr. Terry generously contributed a portion of the prize funds to endow the *Korey Lectureship*, to be administered by the American Association of Neuropathologists, with the lecturer to be chosen annually by the President in conjunction with the Nominating Committee and the Chair of the Program Committee. Dr. Terry has summarized the qualities of the Korey lecturer as someone who has "…been an active member of the Association…a working MD or MD/PhD neuropathologist…responsible for diagnostic work as well as teaching and research. The lecture should be aimed at the members of the Association, and the lecturer might well serve as a role model for younger members."

We are pleased to have **Eileen H. Bigio** join our list of distinguished speakers.

Year	***Lecturer***	***Title***
1989	Nicholas K. Gonatas	MG-60, a Novel Sialoglycoprotein of Medial Cisternae of the Neuronal Golgi Apparatus: Implications and Applications
1990	Henry M. Wisniewski	Amyloidosis in Alzheimer's Disease and the Spongiform Encephalopathies
1991	Robert D. Terry	Alzheimer's Disease as Seen by a Lucky Morphologist
1992	Henry de Forest Webster	Formation and Regeneration of Myelin
1993	Kunihiko Suzuki	Molecular Genetics of Tay-Sachs and Related Disorders: The Legacy of Saul Korey
1994	*No Lecture*	*XIIth International Congress (Toronto)*
1995	Blas Frangione	Amyloid Genes and Chaperones in Alzheimer Disease
1996	Floyd Gilles	The 3R's of Neuro-oncology – Recording, Reliability and Reporting
1997	Donald L. Price	The Role of Neuropathologists in the Analyses of Models of Neurodegenerative Disease
1998	Sandra H. Bigner	Molecular Genetics of Medulloblastoma
1999	William F. Hickey	Key Participants in the Initiation of Inflammation in the Central Nervous System
2000	Mary E. Case	Neuropathology and Forensic Pathology: A Natural Synergism
2001	Paul H. Kleihues	Molecular Biology of Brain Tumors
2002	James E. Goldman	Astrocytes, Intermediate Filaments, Cellular Stress and Neuropathology
2003	Samuel K. Ludwin	Pathology and Pathogenesis in Multiple Sclerosis
2004	James M. Powers	The Road Not Taken
2005	Bernardino Ghetti	Deciphering Hereditary Presenile Dementias: Neuropathology at the Crossroads of Neuropsychiatry and Molecular Genetics
2006	Donna M. Ferriero	Molecular Mechanisms of Hypoxic-Ischemic Injury in the Developing Nervous System
2007	Dennis W. Dickson	Neuropathology and Genetics of Parkinsonism
2008	David N. Louis	Brain Tumor Classification: Little Steps and Big Jumps

2009	Stephen J. DeArmond	Mechanisms of Neurodegeneration in Prion Disease Originating from the Neuronal Plasma Membrane
2010	Peter C. Burger	A Long-Term Perspective on Pediatric CNS Tumors
2011	Hans H. Goebel	Protein Aggregate Myopathies
2012	Michael Norenberg	Astrocyte Pathobiology
2013	Harry Vinters	Gain and Pain from Cerebral Microvessels – Adventures in Vascular Neuropathology
2014	Thomas J. Montine	Alzheimer's Disease and Related Dementias
2015	Matthew Frosch	Working at the Crossroads of Neurodegeneration and Cerebrovascular Disease
2016	Eileen H. Bigio	The FTLD-ALS Connection

SAUL R. KOREY LECTURE

The FTLD-ALS Connection

Time: 10:15 am – 11:15 am
Date: Saturday, June 18, 2016
Eileen H. Bigio, MD, *Northwestern University, Chicago, IL*

I. Learning Objectives

At the end of this activity learners should be able to:

1. State the molecular FTLD neuropathology most often seen in brains of ALS patients with dementia.
2. Name the gene most commonly mutated in both familial ALS and familial FTD patients.
3. Describe the main types of abnormal TDP-43 deposits seen in the cortex of the FTLD-TDP pathologic subtypes and know which one is most often seen in FTLD-ALS.

II. Abstract & Relevant References

Twenty years ago it was thought that amyotrophic lateral sclerosis (ALS) patients were free from dementia, but it is now known that up to 50% of ALS patients have cognitive impairment consistent with frontotemporal dementia (FTD), and a fair proportion of patients with FTD develop ALS. The connection between clinical ALS and FTD was strengthened with the key discovery that the major protein component of the inclusions in frontotemporal lobar degeneration with ubiquitinated inclusions (FTLD-U) and most cases of ALS was Transactive Response (TAR) DNA-binding protein of 43 kD (TDP-43). Pathologically, at autopsy, some patients with ALS but no cognitive impairment have the pathology not only of ALS, but also of FTLD-TDP, and some patients with only FTD have not only the pathology of FTLD-TDP, but also of ALS. With regard to genetics, 20 years ago the only gene known to have a mutation in familial ALS (FALS) was *SOD1*, and there were no known gene mutations in familial FTD. Now there are numerous known gene mutations in FALS and familial FTD, and many of them are shared by both ALS and FTD, including mutations in *TARDBP*, *UBQLN2*, *SIGMAR1*, *OPTN*, *SQSTM1*, *CHMP2B*, *C9orf72*, and most recently, *TBK1*. Interestingly, mutations in some genes seem to be found in ALS and not FTD, and vice versa, but obviously, a significant number of genes have mutations in both ALS and FTD, or in combined ALS-FTD. These and other connections between ALS and FTLD will be discussed.

References:

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3. Bigio EH, Lipton AM, White CL III, et al. Frontotemporal and motor neurone degeneration with neurofilament inclusion bodies: additional evidence for overlap between FTD and ALS. Neuropathol Appl Neurobiol 29:239-253, 2003
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6. DeJesus-Hernandez M, Mackenzie IR, Boeve BF, et al. Expanded GGGGCC hexanucleotide repeat in non-coding region of *C9ORF72* causes chromosome 9p-linked FTD and ALS. Neuron 2011;72:245-256
7. Gitcho MA, Balch RH, Chakraverty S, et al. *TDP-43* A315T mutation in familial motor neuron disease. Ann Neurol 63:535-538;2008
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9. Mackenzie IRA, Bigio EH, Ince PG, et al (2007) Pathological TDP-43 distinguishes sporadic amyotrophic lateral sclerosis from amyotrophic lateral sclerosis with *SOD1* mutations. Ann Neurol 61:427-434

10. Mackenzie IRA, Neumann M, Baborie A, et al. A harmonized classification system for FTLD-TDP pathology. Acta Neuropathol (2011) 122:111-113
11. Mackenzie IRA, Neumann M, Bigio EH, et al. Nomenclature and nosology for neuropathologic subtypes of frontotemporal lobar degeneration: an update. Acta Neuropathol (2010) 119:1-4
12. Neumann M, Sampathu DM, Kwong LK, et al (2006) Ubiquitinated TDP-43 in frontotemporal lobar degeneration and amyotrophic lateral sclerosis. Science 314:130-133
13. Renton AE, Majounie E, Waite A, et al. A nexanucleotide repeat expansion in C9ORF72 is the cause of chromosome 9p21-linked ALS-FTD. Neuron 2011;72:257-268

III. Faculty Biography

Dr. Bigio graduated from the University of Michigan in 1975 with a degree in Medical Technology. She worked as a medical technologist until she decided to go to medical school and graduated from the University of Texas Medical Branch (UTMB) in 1985. She did a residency in Pathology and a year as Chief Resident at UTMB, and subsequently trained in Neuropathology with Dr. Charles L White III, MD at UT Southwestern Medical School. From the beginning of her neuropathology training, her focus has been on neurodegenerative disorders. After fellowship she became a faculty member at UT Southwestern where she rose to the rank of Associate Professor. She traveled north to Northwestern University Feinberg School of Medicine in 2001, where she now practices neuropathology and leads the Neuropathology Core of the Northwestern University Cognitive Neurology and Alzheimer Disease Center. She rose to the rank of professor in 2005, when she also took over as Medical Director of Neuropathology upon Dr. Mauro Dal Canto's retirement. She developed an ACGME-accredited Neuropathology Fellowship training program at Northwestern University Feinberg School of Medicine in 2008. Of her over 170 published or in press articles, only 15 are not related to neurodegenerative disorders. She was the first investigator to show that FTLD-U, now FTLD-TDP, is the single most common FTD. She was chosen to be on the 2006-2007 NIA Biospecimen Task Force, which developed the NIA policy on Biospecimen Guidelines for banking and distribution. She was chair of the Neuropathology Core Leaders Steering Committee in 2006 and 2007. She was a participant in the NINDS- and AFTD-sponsored FTD Neuropathology Diagnosis Workshops in 2008 and 2010. She was a member of the work-group that developed the revised NIA-AA guidelines for the pathologic diagnosis of Alzheimer disease. She has been on the Ad Hoc NIH Review Committees for ADRC and ADCC competitive renewals in 2003, 2004, 2008, 2009, and 2014. She was a member of the International Advisory Committees for the 7th, 8th, and 9th International Conferences on Frontotemporal Dementias in 2010, 2012, and 2014. She was a member of the review panel for the NIMH, NICHD, and NINDS Brain and Tissue Repository Contract applications in April 2013, a member of the review committee for the competitive renewal of the NIH/NIA U19 Dominantly Inherited Alzheimer Network grant in October 2013, and a member of the NIH/NIA Special Emphasis Panel for the review of ADNI-3 ZAG1 ZIJ-6 (M3) in February 2016. She was named the Paul E. Steiner Research Professor of Pathology in 2012, renewed in 2015. In 2014 she was recognized by Thomson Reuters as being one of six Northwestern Feinberg School of Medicine physicians having highly cited papers (top 1% most cited) for 2002-2012. Dr. Bigio has served on the Program Committee, Awards Committee, and Professional Affairs Committee of the American Association of Neuropathologists, and since 2014 Dr. Bigio has been an Executive Council Member-At-Large for the AANP.

ENDOWED LECTURESHIP

MATTHEW T. MOORE LECTURE

In 1970, Dr. Matthew T. Moore made a contribution to the AANP to establish the Moore Award, which is given annually to recognize the "Best Paper on Clinico-Pathological Correlation Presented at the Annual Meeting." In 1987, Rechelle Fishman, a former patient of Dr. Moore, bequeathed $75,000 to the Moore Award Fund. Dr. Moore requested that this bequest be used to establish a "Rachelle Fishman-Matthew Moore Distinguished Lectureship" (later shortened to just the "*Moore Lectureship*"), which is "to be given by a distinguished lecturer, on a subject which represents the leading edge of advanced research in neuropathological subjects of contemporary interest. The lecture is to take place on the day of the Presidential Address." In 1988, it was decided that this Lectureship would replace the "Distinguished Lectureship" that had been sponsored each year by the Association. The Moore Lecturer is selected annually by the President in conjunction with the Nominating Committee and the Chair of the Program Committee.
We are pleased to have Ted M. Dawson join our list of distinguished speakers.

Year	Lecturer	Title
1990	Robert H. Horvitz	The Genetic Control of GABAergic and Serotonergic Neuronal Differentiation and of Programmed and Pathological Cell Death in a Nematode Nervous System
1991	Charles Janeway	Induction, Mediation and Continuation of Immune Responses
1991	Ramzi S. Contran	Cytokine-Endothelial Interactions in inflammation, Immunity and Vascular Injury
1992	D. Carleton Gajdusek	The genetic Control of Spontaneous Generation of Infectious Amyloids: Kuru-CJD-GSS-Scrapie-BSE
1995	Leroy Hood	Deciphering the Human Genome: Implciations for Medicine of the 21st Century
1996	Martin Raff	Programmed Cell Death--Mechanisms and Social Controls
1998	James Eberwine	Single Cell Molecular Neuropathology
1999	Richard T. Johnson	Viral Pathogenesis, an Overview
2001	Dennis Choi	Ischemia-Induced Perturbations in Neuronal Ionic Homeostasis
2002	J. William Langston,	MPTP: Its impact on Parkinson's Disease Research
2003	Carolyn C. Meltzer	Future of PET in the Study of Neurological Disease
2004	Henry L. Paulson	Toward Understanding the Pathogenesis of Repeat Expansion Diseases
2005	Peter St. George Hyslop	Molecular Genetics and Biology of Alzheimer Disease Generate Clues for Therapeutics
2006	Keith L. Ligon	Stem and Progenitor Cell Insights into Gliomas: Novel Origins, Markers and Targets
2008	William Mobley	Trafficking Trophic Signals to Prevent Neurodegeneration
2009	Donald W. Cleveland	From Charcot to Lou Gehrig: Mechanisms and Treatment of ALS
2011	Mark Gilbert	RTOG: Clinical Trials and the Increasing Role of Neuropathology
2012	Kevin P. Campbell	Mechanistic and Molecular Insights into the Pathogenesis of Glycosylation – Deficient Muscular Dystrophy
2013	Bradley Hyman	How does Alzheimer's Disease know Neuroanatomy?
2014	David N. Louis	WHO's Next? Guidelines for the Next WHO Classification of Brain Tumors
2015	Eric C. Holland	Brain Tumors in Mouse and Man
2016	Ted M. Dawson	Unlocking the Secrets of Parkinson's

MATTHEW T. MOORE LECTURE

Unlocking the Secrets of Parkinson's

Time: 4:30 pm – 5:30 pm

Date: Saturday, June 18, 2016

Ted M. Dawson, MD, PhD, *John Hopkins Medicine, Baltimore, MD*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Cite new information on the underlying causes and mechanisms of Parkinson's disease.
2. Discuss research findings related to the molecular mechanisms of neurodegeneration in Parkinson's disease.
3. Incorporate new knowledge regarding Parkinson's disease into improving everyday clinical practice and teaching of neuropathology.

II. Abstract & Relevant References

Parkinson's disease (PD) is due, in part, to the progressive loss of dopamine neurons in the substantia nigra pars compacta, which leads to bradykinesia, rigidity, rest tremor and postural instability. Degeneration of other neuronal populations and/or neuronal dysfunction due to the accumulation and aggregation of α-synuclein, the major protein constituent of Lewy Bodies and Lewy Neurites leads other clinical features including autonomic dysfunction, anxiety, depression, abnormalities of sleep, cognitive impairment, among others. Fresh insights into the pathogenesis of PD have come from understanding the genetic underpinnings of PD. Mutations in parkin, PINK1 and DJ-1 cause autosomal recessive PD. Defects in mitochondrial quality control contribute substantially to the demise of DA neurons due to parkin, PINK1 or DJ-1 inactivation. Mutations in α-synuclein, leucine-rich repeat kinase 2 (LRRK2) and eukaryotic translation initiation factor 4 gamma-1 (EIF4G1) cause autosomal dominant PD through defects in protein proteostasis. Understanding the changes in mitochondrial quality control and protein proteostasis may provide clues to disease pathways that result in Parkinson's disease and offer disease modifying therapies for this common age-related progressive neurodegenerative disorder.

References:

1. Shin, J.-H., H.S. Ko, H.C. Kang, Y. Lee, Y.-I. Lee, O. Pletinkova, J.C. Troncoso, V.L. Dawson and T.M. Dawson. "PARIS (ZNF746) Repression of PGC-1α Contributes to Neurodegeneration in Parkinson's Disease." Cell, 144:689-702 (2011) (Featured Article).
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3. Martin, I., J.W. Kim, B.D Lee, H.C. Kang, J.-C. Xu., H. Jia, J. Stankowski, M.-S. Kim, J. Zhong, M. Kumar, S. Andrabi, A Pandey, T.M. Dawson*, V.L. Dawson*. "Ribosomal protein s15 phosphorylation mediates LRRK2 neurodegeneration in Parkinson's disease" Cell, 157:472-485 (2014). PMID:24725412
4. Stevens, D.A., Y. Lee, H.C. Kang, B.D. Lee, Y.I. Lee, A. Bower, H. Jiang, S.A. Andrabi, V.L. Dawson, J.-H. Shin and T.M. Dawson. "Parkin Loss Leads to PARIS-Dependent Declines in Mitochondrial Mass and Respiration, " Proc. Natl. Acad. Sci., U.S.A., 113:11696-701 2015. PMID: 26324925

III. Faculty Biography

Dr. Dawson is the Leonard and Madlyn Abramson Professor in Neurodegenerative Diseases and Director of the Institute for Cell Engineering at the Johns Hopkins University School of Medicine. Dr. Dawson's honors include the Derek Denny-Brown Young Neurological Scholar Award, the Paul Beeson Physician Faculty Scholar Award, and the Santiago Grisolia Medal and a Javits Neuroscience Investigator Award. He was elected to the Association of American Physicians and he is a Fellow of the American Association for the Advancement of Science. He elucidated the molecular mechanisms by which NO kills neurons through activation of poly [ADP-ribose] (PAR) polymerase (PARP) and release of apoptosis inducing factor (AIF) via PAR polymer and discovered Parthanatos. Dr. Dawson has been at the forefront of research into the biology and pathobiology of mutant proteins linked to familial Parkinson's disease. These studies are providing novel opportunities for therapies aimed at preventing the degenerative process of PD and other neurodegenerative disorders.

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Meritorious Awards

Friday, June 17, 2016
11:15 am – 11:30 am
Honoring Dennis W. Dickson, MD
Presented by: Melissa E. Murray, PhD

Saturday, June 18, 2016
11:15 am – 11:30 am
Honoring Barbara J. Crain, MD, PhD
Presented by: Michael N. Hart, MD

MERITORIOUS AWARDS

Awards for Meritorious Contributions to Neuropathology

The *Award for Meritorious Contributions to Neuropathology* recognizes a member who has made significant contributions to the advancement of knowledge in neuropathology and provided service to the American Association of Neuropathologists. Each recipient of the award is nominated by the President, in conjunction with the Nominating Committee and with the approval of the Executive Council. The qualities of outstanding scientific achievement and service are embodied in this year's recipients, **Dr. Dennis W. Dickson** and **Dr. Barbara J. Crain**. They join the rich roster of distinguished former award recipients.

Year	Recipient
1959	Armando Ferraro
	Arthur Weil
1960	Joseph H. Globus
	George B. Hassin
1968	Abner Wolf
	Paul I. Yakovlev
	Harry M. Zimmerman
1970	Webb E. Haymaker
1971	James W. Kernohan
1972	George A. Jervis
1979	Raymond D. Adams
	David Cowen
	Matthew T. Moore
1981	Richard Lindenberg
1983	Orville T. Bailey
1984	Margaret Murray
1985	Kenneth M. Earle
	Nathan Malamud
	Leon Roizin
1986	Martin G. Netsky
1987	*No Award Presented*
1988	Edward P. Richardson, Jr.
	F. Stephen Vogel
1989	Lucien J. Rubinstein
	Robert D. Terry
1991	Lysia K. S. Forno
1992	John Moossy
	Gabriele M. ZuRhein
1993	Peter W. Lampert
	Elias E. Manuelidis
1994	Murray B. Bornstein
	Samuel P. Hicks
	Lowell W. Lapham
1995	Amico Bignami
	Asao Hirano
1997	Henryk M. Wisniewski
1998	Richard L. Davis
	Wolfgang Zeman
1999	Lucy B. Rorke
2000	William R. Markesbery
2001	John J. Kepes
	Henry de Forest Webster
2002	Dikran S. Horoupian
	Fusahiro Ikuta
	Kurt A. Jellinger
2003	Bernardino F. Ghetti
2004	Michael N. Hart
2005	E. Tessa Hedley-Whyte
	Suzanne S. Mirra
2006	Joseph E. Parisi
	Jeannette J. Townsend
2007	James M. Powers
	Cedric S. Raine
2008	Kinuko Suzuki
	Margaret G. Norman
2009	Peter C. Burger
	Pierluigi Gambetti
	Nicholas K. Gonatas
2010	Stephen J. DeArmond
	Samuel K. Ludwin
2011	William W. Schlaepfer
	Leroy R. Sharer
2012	Bernd W. Scheithauer
	Donald L. Price
2013	Reid Heffner
	Dawna Armstrong
2014	Floyd Gilles
	Françoise Gray
2015	John Q. Trojanowski
	Bette K. Kleinschmidt-DeMasters
2016	Dennis W. Dickson
	Barbara J. Crain

MERITORIOUS AWARDS

American Association of Neuropathologists Awards for Meritorious Services to Neuropathology 2016

For formal expositions of the winners' contributions to the field, please read the Meritorious Award Features in the 2016 Meeting Application.

Biography: Dennis W. Dickson, MD

The primary research focus of Dennis W. Dickson, M.D., is the neuropathologic characterization of brains from prospective and longitudinal research studies sponsored by the National Institute on Aging.

His studies, which differ in patient characteristics, include elderly community volunteers and recruits from population-based sampling. Fixed and frozen brain samples are obtained at autopsy and used for diagnostic evaluations and research with neurohistology, immunohistochemistry, electron microscopy and image analysis, and immunoassays. In addition to providing a final neuropathology diagnosis for brains in the brain bank, which provides closure to the family and feedback to the physicians involved in antemortem care of the patient, these studies aim to understand the molecular pathology of neurodegenerative disorders that will lead to better diagnosis, treatment and eventually prevention of these devastating disorders.

Dr. Dickson's focus areas include genetic studies, Non-Alzheimer's degenerative diseases, disorders in tau pathology, and ALS and frontotemporal degeneration with TDP-43 pathology. He is a distinguished neuropathologist, with professional highlights such as the Potamkin Prize for Research in Pick's, Alzheimer's and Related Diseases (American Academy of Neurology, 2011) and the Award for Medical Research (Metropolitan Life, 2001).

Biography: Barbara J. Crain, MD, PhD

Dr. Crain is a neuropathologist with expertise in neurodegenerative and vascular diseases. She is an Associate Professor Department of Pathology, Division of Neuropathology, and Director of the Autopsy Service at John Hopkins Medicine.

Dr. Crain is the liaison of the PDRC Neuropathology Core D with the Autopsy Service, provides neuropathological evaluations for cases of PD, LBD, and controls, and she is also responsible for night and weekend call for PDRC autopsies.

In addition, Dr. Crain contributes to studies involving clinical-pathological correlations and in the training of young investigators. Her research interests concern the patterns and mechanisms of neuronal vulnerability in different disease states. Most of her current work is in the area of neurodegenerative disease and stroke.

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Diagnostic Slide Session

Saturday, June 18, 2016

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-1

Submitted by:
Angela Wu, MD[1], Karen S. SantaCruz, MD[2], Leslie Morrison, MD[3] and Steven A. Moore, MD, PhD[1]

1. The University of Iowa, Department of Pathology, 200 Hawkins Drive, Iowa City, IA 52242
2. University of New Mexico, Department of Pathology, BMSB 3rd Floor, Room 313, MSC 08 4640, Albuquerque, New Mexico 87131
3. University of New Mexico, Departments of Neurology and Pediatrics, 2211 Lomas Blvd NE, Albuquerque, NM 87131

Clinical History:
A 9-year-old boy has a past medical history significant for cerebral palsy, inturning right foot, and a left clubfoot that underwent surgery at 3 years of age. He was crawling before the surgery, was able to walk with a walker afterwards, and ultimately walk independently. His parents report a 6-month history of increasing weakness that is both proximal and distal on examination. He has difficulty rising from the floor and uses a Gower-type maneuver by pulling up on a chair. He shows a steppage gait that is slightly wide based. Stretch reflexes are absent. His serum creatine kinase (CK) is 2800 IU/L. Electromyography (EMG) shows complex repetitive discharges in the gastrocnemius. There is no family history of neuromuscular problems.

A left quadriceps muscle biopsy is performed.

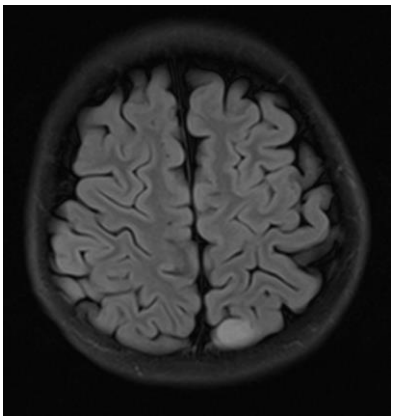
Material submitted:
H&E stained cryosection of muscle

Points for discussion:
1. Approach to diagnostic testing
2. Differential diagnosis

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-2

Submitted by:
Katherine E. Schwetye, MD, PhD and Dr. Robert E. Schmidt, M.D., Ph.D., Department of Pathology and Immunology, Campus Box 8118 - Washington University School of Medicine, 660 S. Euclid Ave., St. Louis,

Clinical history:

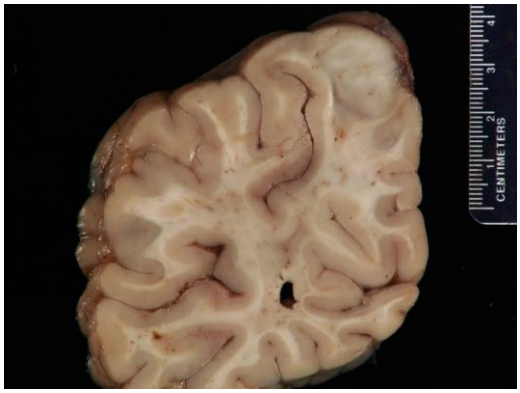


Seven year-old boy with a history of epilepsy. Developmentally, he was delayed in multiple academic areas as well as fine and gross motor skills. EEG at age 4 demonstrated focal slowing over the left posterior electrodes. Brain MRI at age 4 demonstrated a T2 / FLAIR abnormality over the left posterior parietal lobe, a left parietal arachnoid cyst, and a 5 mm inferior cervical tonsillar herniation (Chiari I malformation). The patient had been admitted to the hospital for status epilepticus twice in the last 4 years, and for meningococcal meningitis 3 years earlier.

In August 2014, the patient complained of his usual prodrome which progressed to a generalized tonic-clonic seizure, bradycardia, and cardiac arrest. Despite aggressive resuscitation, the patient's prognosis remained poor due to ongoing seizure activity, an aspiration event, fever up to 104° F, and development of disseminated intravascular coagulation complicated by bleeding from dislodged femoral arterial catheters. His family elected to redirect care. Death was pronounced approximately 18 hours after seizure onset. His parents requested autopsy.

Autopsy findings:

The general autopsy showed bilateral acute bronchopneumonia, consistent with aspiration, and pulmonary and groin hemorrhage, consistent with a history of coagulopathy.



On neuropathologic examination, coronal sections of the cerebral hemispheres showed a firm, well-circumscribed, gray-tan focus extending from the leptomeningeal surface and displacing/infiltrating the underlying cortical ribbon measuring approximately 1.9 cm in diameter in the superior left posterior parieto-occipital cortex . A superficial cystic expansion of leptomeninges consistent with an arachnoidal cyst was immediately adjacent to the firm, well-circumscribed focus. Also identified were multiple, bilateral hemorrhagic watershed infarcts at the gray-white matter junction and in the bilateral basal ganglia.

Materials submitted:

H&E slide (1) of lesion depicted in gross photographs

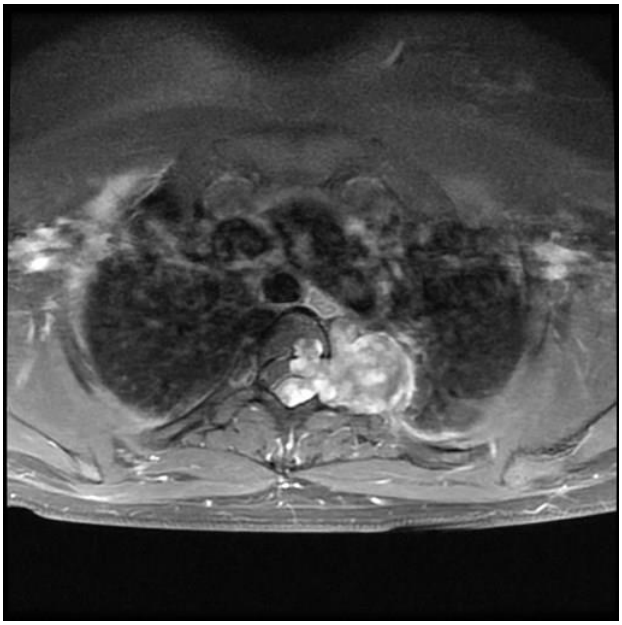
Points for discussion:

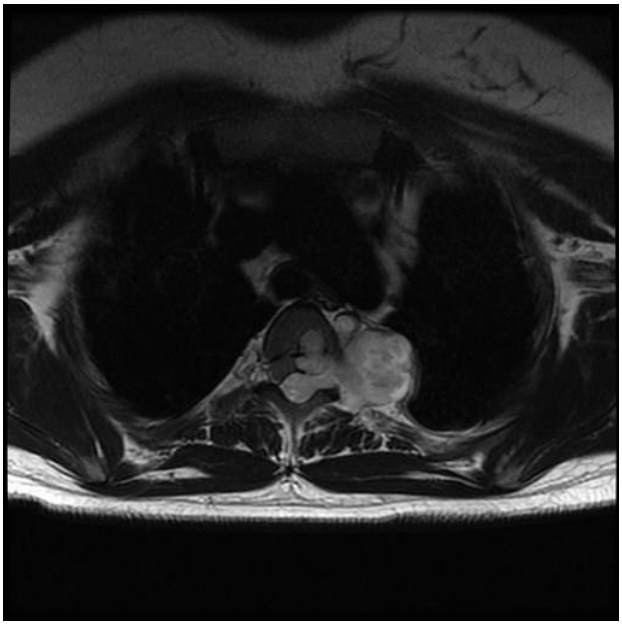
1. Differential diagnosis of T2-FLAIR abnormality, given a history of epilepsy
2. The role of neuropathological examination in deaths related to epilepsy

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-3

Submitted by:
Elaine S. Keung, MD, MPH and Patrick Malafronte, MD.
Walter Reed National Military Medical Center
Department of Pathology and Laboratory Medicine
8900 Wisconsin Avenue
Bethesda, MD 20889-5600

Clinical History:
Patient is a 23 year old previously health female seen in ophthalmology for bilateral scleritis with new symptoms of right year chondritis. She was referred to Rheumatology for a workup and was incidentally found to have a large posterior mediastinal mass on imaging. MRI revealed a 5cm mass centered on the left neural foramen at the level of T3-T4 causing moderate spinal canal stenosis in the intraspinal component. The radiologic differential diagnosis was a neuroblastic tumor or nerve sheath tumor. The patient had an unremarkable neurologic physical exam. A core biopsy of the lesion and a subsequent resection was performed. Initial MRI images of spinal cord included: Non-contrast Axial T2 (left) and Post-contrast Axial T1 fat saturated (right)





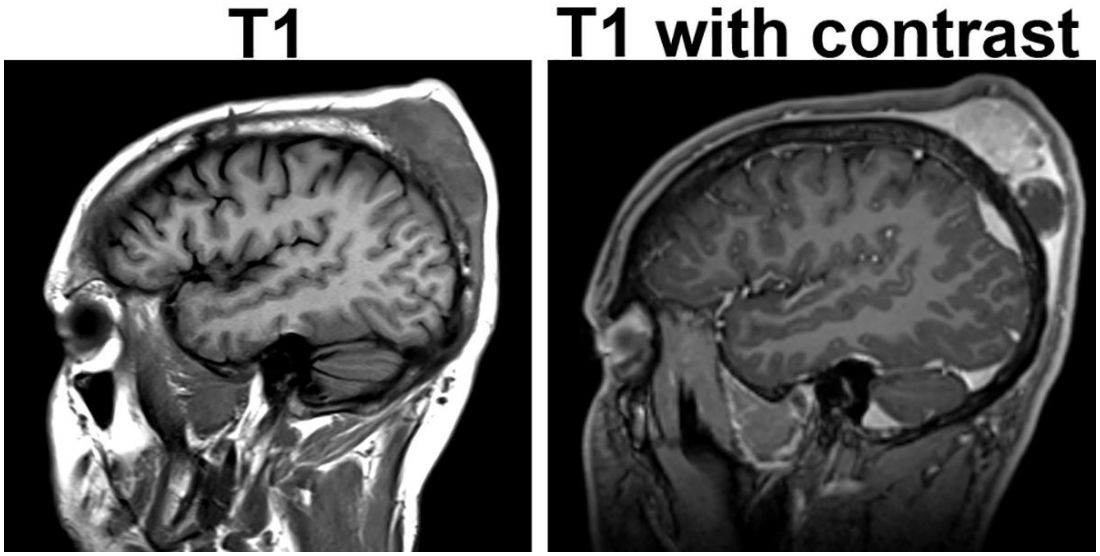
Material submitted:
1. H&E stained section of resection (virtual slide)

Points for discussion:
1. Differential diagnosis
2. Prognosis

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-4

Submitted by:
Craig Horbinski, Benjamin Liu, Christina Appin, and Qinwen Mao
Northwestern University, Tarry 2-705, 300 East Superior Street, Chicago IL 60611

Clinical History:
The patient was a 24-year-old man, with no significant PMH, who noticed a small mass on his head that grew rapidly over the next several weeks. He did not seek medical care until one month after he first noticed the mass, when he had a generalized tonic-clonic seizure. An MRI demonstrated a 7.7 x 5.4 x 1.8 cm subgaleal soft tissue mass in the posterior superior aspect (see separate MRI images). There was also an intracranial component of the mass that measured 2.1 x 0.7 cm. The tumor was resected.



Intraoperatively, the mass was rather firm, invading bone and dura.
The lesion received in surgical pathology was a 5.3 x 3.4 x 1.6 cm yellow and white-tan lobulated, rubbery mass. Dura was attached.

Material submitted:
1 H&E-stained slide

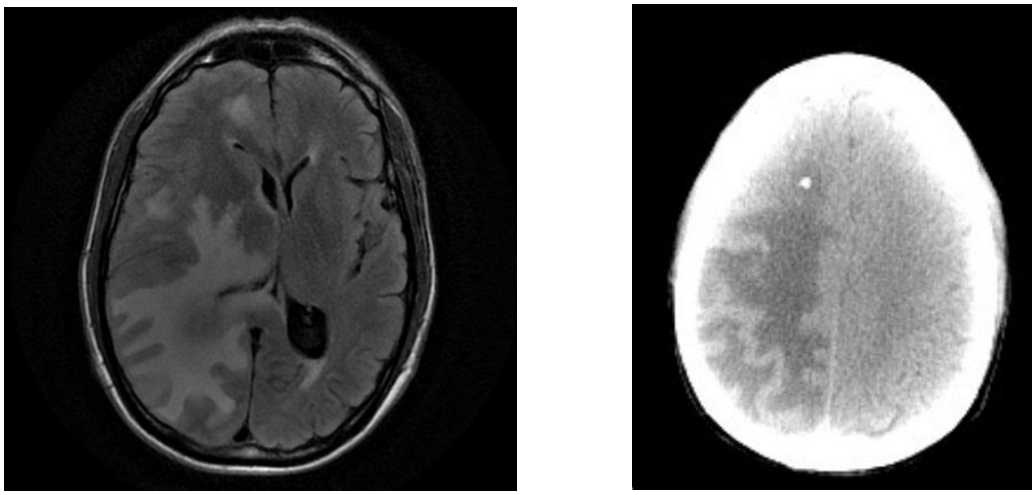
Points for discussion:
1. Differential diagnosis and additional stains
2. Final diagnosis and optimal therapy

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-5

Submitted by:
Derek H Oakley[1], Bruce S Tronic[2], Ivana Vodopivec[1], CA Perugino[1], Nagopal Venna[1], John H Stone[1] and E Tessa Hedley-Whyte[1].

[1] Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114
[2] Lahey Clinic, 41 Mall Road, Burlington, MA 01805

Clinical History:
This middle aged man was admitted after he fell to his knees while getting out of bed when his legs gave way. His past medical history included hypertension, uveitis, bilateral macular degeneration status post interferon treatment, and chronic progressive kidney disease (stage 4, status post 2 biopsies with results unavailable on this admission). Over the previous year he had had progressive memory loss, malaise, and intermittent confusion and vision loss. A CT scan, 4 months earlier, had shown multiple punctate areas of calcification and hemorrhage with surrounding vasogenic edema in the bilateral frontal and right parietal white matter.
CSF: myelin basic protein was 10.6; JC virus, flow cytometry and VDRL were within normal limits. CSF IgG index was slightly elevated. Repeat MRI 2 months prior to presentation showed "progression of complex T2 hyperintensity" associated with focal infarction in right parietal white matter". "Complete immunologic and vasculitic workup had been negative". He had never smoked. He had travelled extensively in Europe.
CT on admission showed edema involving white matter in right frontoparietal region with mass effect and a 12 mm midline shift. The clinical differential diagnoses included infectious, TB, syphilis, viral, and toxoplasmosis, sarcoid, vasculitis, neoplastic and demyelination (PML). The right-sided subcortical brain lesion was biopsied twice over the next two weeks with similar histological findings. The section comes from the second brain biopsy.



MRI: T2 sequence (left) and CT (right)

Material submitted: One H&E stained slide, virtual

Points for discussion:
1. Diagnosis
2. Pathogenesis and prognosis

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-6

Submitted by:
Amber Nolan, MD PhD and Marta Margeta, MD PhD, Department of Pathology, 505 Parnassus Ave, University of California San Francisco, San Francisco, CA 94143

Clinical History:
The patient is a 42-year-old man with a history of HIV infection (CD4 counts in 800-900 range on anti-retroviral therapy), bipolar disorder, and prior episodes of atrial fibrillation, who developed a severe progressive sensorimotor axonal polyneuropathy. The first symptoms (gluteal muscle cramps) appeared after he started a time release form of lithium therapy, but did not improve after discontinuing this medication. Over the next 4-5 months, the patient developed weakness and atrophy of the leg muscles and a loss of sensation with burning in hands and feet. Physical exam was significant for frequent spasms of the masseters, severe atrophy of the leg muscles with rare fasciculations, and strength measurements as follows: deltoids, biceps, triceps, wrist extensors, wrist flexors, and finger extensors all 5/5; finger flexors 4/4; abductor pollicis brevis 4+/4-; abductor digiti minimi 4+/5; first dorsal interosseous 4/5; iliopsoas 5/5; hip abductors 5/5; hip adductors 5/5; quadriceps 5/5; hamstrings 4/4; and very little movement in muscle groups distal to the knees. Pain sensation was impaired in a stocking distribution, ascending halfway up the shin. Vibration was intact. Several EMG/NCS studies demonstrated a sensorimotor polyneuropathy with axonal > demyelinating features. Additional workup was notable for a normal SPEP and free light chain ratio. A sural nerve biopsy was performed.

Material submitted: H&E-stained slides from the nerve biopsy.

Points for discussion:
1. Diagnosis.
2. Differential diagnosis and ancillary testing.

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-7

Submitted by:
David A. Solomon, MD, PhD and Andrew Bollen, MD, DVM, Department of Pathology, University of California, San Francisco, 505 Parnassus Ave, Box 0102, Moffitt M-576, San Francisco, CA 94143.

Clinical History:
The patient is a 78 year old woman who presented with approximately 10 years of progressive lower extremity weakness causing difficulty with ambulation requiring her to use a cane or walker and eventually a wheelchair. She has also had progressive weakness in her arms more recently over the last couple years. She has been evaluated at multiple institutions throughout her disease course, and her serum CK level has never been elevated. She has had multiple electromyography and nerve conduction studies in the past that were reportedly without abnormalities. Acetylcholine receptor autoantibody studies were negative. She has not responded to trials of prednisone, mycophenolate, azathioprine, or pyridostigmine. Physical exam at current presentation revealed normal muscle tone and bulk in all extremities. However, she had diminished strength in her bilateral hip flexors (3/5), hip abductors (4/5), hamstrings (4/5), anterior tibialis (4/5), and extensor halluces longus (4/5). She had decreased vibratory, pin pick, and light touch sensation bilaterally in the lower extremities up to her shins. She demonstrated a kyphotic posture and antalgic gait. Repeat electromyography and nerve conduction studies demonstrated myopathic motor units without evidence of muscle membrane instability in multiple muscle groups consistent with a myopathic process. A biopsy of the biceps muscle was performed.

Material submitted:
H&E, Gomori trichrome, NADH, ATPase at pH 9.2, fast myosin, and slow myosin stained frozen sections from biceps muscle biopsy. Also toluidine blue stained sections from a portion of the biopsy that was glutaraldehyde-fixed and Epon embedded for ultrastructural analysis.

Points for discussion:
1. Diagnosis
2. Pathogenesis

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-8A

Submitted by:
Angelica Oviedo, M.D., IWK Health Centre, Department of Pathology

Clinical History:
13 year old female presented with a 2-3 months history of headache, initially left supra-orbital, then holocephalic. Occasional horizontal diplopia and perception of lower extremity weakness. Some nausea and vomiting. MRI showed left intra-ventricular enhancing cystic and solid tumor with significant surrounding vasogenic edema. Mass effect on left thalamus with slight mid-line shift.

Material submitted:
H and E section of tumor.

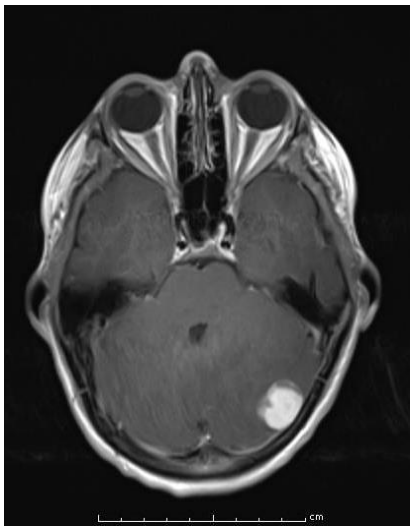
Points for discussion:
1. Diagnosis

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-8B

Submitted by:
Tejus Bale, M.D, PhD; Harry Kozakewich, M.D.; Sanda Alexandrescu, M.D Department of Pathology, Boston Children's Hospital

Clinical History:
This 12-year-old boy presented with slight headaches of approximately one month duration. Magnetic resonance imaging (MRI) demonstrated a 2.2 centimeter mass in the left cerebellar region (see Neuroimaging). His past medical history was notable for adrenal neuroblastoma diagnosed at the age of 7, and treated with chemotherapy, surgical resection, radiotherapy and stem cell transplant. He responded well to therapy and there has been no evidence of recurrent disease.

Neuroimaging: Axial T1 post-contrast MRI: 2.2 cm lobulated, contrast-enhancing, dural mass without a tail-sign, contrast enhancing.



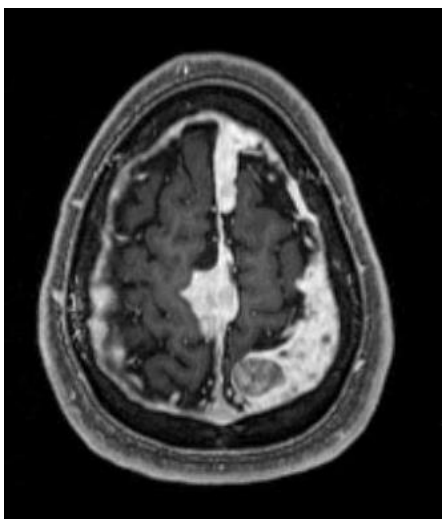
Material Submitted:
One virtual H&E slide

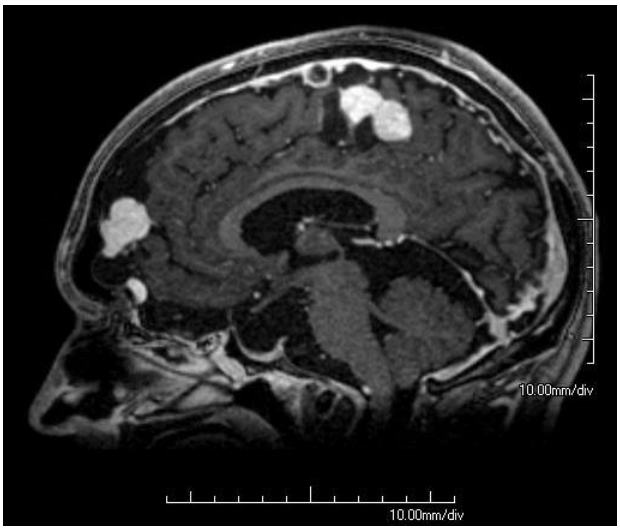
Points for discussion:
1. Differential diagnosis
2. Ancillary studies
3. Selection of molecular tests

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-9

Submitted by:
MacLean P. Nasrallah, MD PhD[1]; Mariarita Santi, MD PhD[2]; Maria Martinez-Lage, MD[1]
[1]Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania
[2]Department of Pathology and Laboratory Medicine, Children's Hospital of Philadelphia

Clinical History:
A 19-year-old male with history of narcolepsy, but otherwise healthy with normal development and cognition, presented in April 2015 with one month of daily headache and a single unprovoked transient confusional episode consistent with a seizure. During the episode, the patient experienced right upper extremity incoordination, orolingual automatisms and aphasia. Physical examination was notable only for macrocephaly. MRI of the brain revealed multiple heterogeneously enhancing dural-based masses and dural nodularity with mild parenchymal volume loss, thinning and remodeling of the calvarium, remodeling of the skull base, and sagging appearance of brainstem.





Cerebrospinal fluid analysis was normal except for elevated protein content. Electroencephalography (EEG) showed left temporal focal slowing with sharp transients. Extensive serologic testing was within normal limits, notable for normal ANA, ANCA, RF, RPR, Quantiferon Gold, FSH, LH, prolactin, TSH, SPEP, antigliadin antibody, and IgG4, as well as negative HIV. A biopsy of the left parietal dural-based nodule was performed, but did not yield a definitive diagnosis. The patient was treated with levetiracetam and corticosteroid therapy and discharged home with planned outpatient follow up. Approximately four weeks later, he presented with recurrence of severe retro-orbital headache and emesis. A second biopsy, this time of a left frontal dural-based nodule was performed.

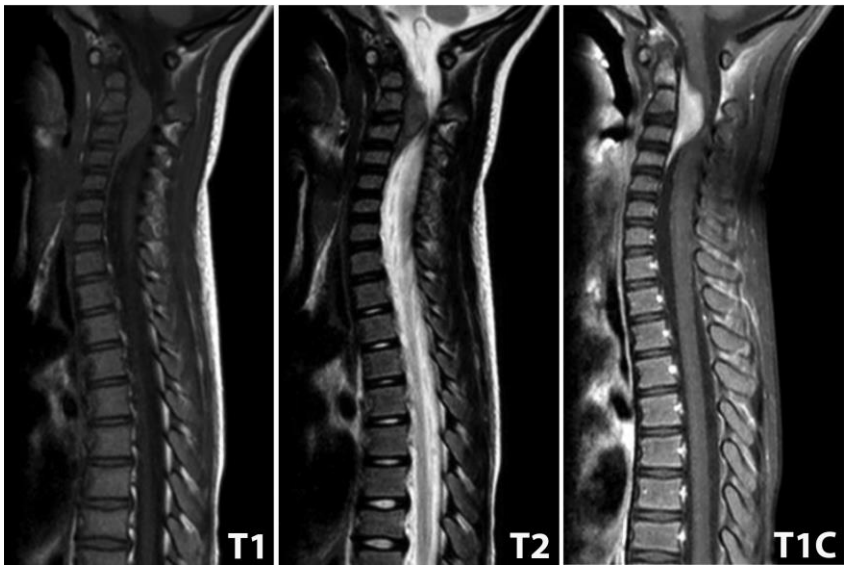
Material submitted:
H&E-stained section of left frontal dural-based nodule

Points for discussion:
1. Differential diagnosis and ancillary studies
2. Prognosis

57th ANNUAL DIAGNOSTIC SLIDE SESSION 2016
CASE 2016-10

Submitted by:
Bette K. Kleinschmidt-DeMasters, MD
University of Colorado Anschutz Medical Campus, Department of Pathology, 12605 East 16th Avenue, Room 3017 - Aurora, CO 80045 P.O. Box 6510

Clinical History:
The patient is a 5-year-old girl with Down syndrome, obstructive sleep apnea, and an AV canal defect present at birth (now repaired). She had complaints of headaches and progressively worsening neck pain over 2 or 3 months. She then began to have severe arm pains that lead to imaging, which demonstrated an avidly enhancing, extradural soft tissue mass centered within the left anterolateral aspect of the C2-C3 spinal canal, extending through and remodeling the left C2-C3 neural foramen.



Primary consideration included a nerve sheath tumor, such as a schwannoma or neurofibroma, or meningioma, though it would be highly unusual in a patient of this age.
A cervical osteoplastic laminectomy and microsurgical radical subtotal resection of tumor was performed. Somatosensory and motor evoked potentials were diminished on the left side at the outside of the case, but they gradually improved, as the case proceeded. The tumor was densely adherent to dura, and not at all adherent to the spinal cord. The left cervical nerve roots 2, 3, and 4 could easily be separated from the tumor and were left largely intact.
Preliminary frozen section diagnosis was consistent with a fibrous meningioma.

Material submitted:
One virtual H&E slide

Points for discussion:
1. Diagnosis

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Presidential Symposium

Sunday, June 19, 2016

Learning Objectives:

1. *Discuss the overall neuropathologic assessment of ALS.*
2. *Recall appropriate staining and sectioning of tissue for examination of an ALS assessment.*
3. *Summarize the model of seeding and propagation of SOD1 misfolding in ALS.*
4. *Explain the components and features of TDP-43 proteinopathies.*

JNEN ADDRESS

What Every Neuropathologist Needs to Know About the JNEN

Time: 8:05 am – 8:35 am

Raymond A. Sobel, MD, *Editor-in-Chief, Journal of Neuropathology and Experimental Neurology*

The *Journal of Neuropathology & Experimental Neurology* is the official journal of the American Association of Neuropathologists, Inc. (AANP). The Journal publishes original articles on neuropathology and experimental neuroscience, book reviews, letters, and Association news. It is written by and for neuropathologists, neurologists, neurosurgeons, pathologists, psychiatrists, and basic neuroscientists from around the world. Publication has been continuous since 1942.

Please note that this session is not offered for CME Credit. The CME Portion of the Presidential Symposium will begin after this discussion.

PRESIDENTIAL SYMPOSIUM

Neuropathological Assessment of ALS

Time: 8:50 am – 9:40 am

Ian R. Mackenzie, MD FRCPC, *Professor of Neuropathology, University of British Columbia & Vancouver Coastal Health, Vancouver, Canada*

I. Learning Objectives:

At the end of this activity, learners should be able to:

1. List the range of molecular pathologies that may be associated with clinical ALS.
2. Describe specific pathological features that correlate with underlying genetic defects.
3. Recognize the overlap between ALS and other neurodegenerative conditions, particularly FTD.
4. Develop a systematic approach to the neuropathological evaluation of ALS.

II. Abstract

Amyotrophic lateral sclerosis (ALS) is an age-related neurodegenerative condition, characterized by the progressive loss of upper and lower motor neurons, which usually results in death due to muscle weakness within a few years. In addition to dysfunction of the pyramidal motor system, it is increasingly recognized that ALS is a multisystem disorder that may involve a wide range of neuroanatomical structures and which overlaps clinically with other movement disorders, dementia syndromes and psychiatric conditions. The past decade has seen remarkable advances in our understanding of the molecular basis of ALS, including the discovery of several new disease causing genetic mutations and disease associated pathological proteins. Most cases of sporadic and familial ALS are characterized by cellular inclusions composed of abnormal fragments of the transactive response DNA binding protein with M_r 43 kD (TDP-43). In addition to TDP-43 pathology, the most common genetic cause of ALS, abnormal repeat expansion in the *C9ORF72* gene, has a unique pathological signature that also includes accumulation of the dipeptide repeat proteins generated through the unconventional translation of the expanded repeat. In contrast, familial ALS due to mutations in the copper/zinc superoxide dismutase gene (*SOD1*) is associated with intracellular accumulation of misfolded SOD1 protein and mutations in the fused in sarcoma gene (*FUS*) cause ALS due to cytoplasmic mis-localization and accumulation of FUS. Detailed neuropathological studies of ALS autopsy cases are needed to better define clinical-genetic-pathological correlations and to shed light on the underlying pathogenic mechanisms which is crucial in the development of targeted therapies.

References:

1. Strong MJ, *et al*. Amyotrophic lateral sclerosis, primary lateral sclerosis and spinal muscular atrophy. In: *Neurodegeneration: The molecular pathology of dementia and movement disorders.,* (Dickson DW and Weller RO, eds.), pp. 418-433.. Blackwell Publishing Ltd., Chichester, UK.
2. Neumann M, *et al* . Ubiquitinated TDP-43 in frontotemporal lobar degeneration and amyotrophic lateral sclerosis. Science 2006; 314: 130-133.
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4. Mackenzie IR and Rademakers R. The role of TDP-43 in amyotrophic lateral sclerosis and frontotemporal dementia. Curr Opin Neurol 2008; 21: 693-700.
5. Mackenzie IRA, *et al* . TDP-43 and FUS in amyotrophic lateral sclerosis and frontotemporal dementia. Lancet Neurol 2010; 9: 995-1007.
6. Mackenzie IR, *et al* . Pathological heterogeneity in amyotrophic lateral sclerosis with FUS mutations: two distinct patterns correlating with disease severity and mutation. Acta Neuropathol 2011; 122: 87-98.

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8. Stewart H, *et al* . Clinical and pathological features of amyotrophic lateral sclerosis caused by mutation in the *C9ORF72* gene on chromosome 9p. Acta Neuropathol 2012; 123: 409-417.
9. Mackenzie IRA, *et al* . The neuropathology associated with repeat expansions in the *C9ORF72* gene. Acta Neuropathol 2014; 127: 347-357.
10. Grad LI, *et al*. Intercellular propagated misfolding of wild-type Cu-Zn superoxide dismutase: Implications for amyotrophic lateral sclerosis. PNAS 2014; 111: 3620-3625.

III. Faculty Biography:

Ian R. A. Mackenzie is Professor of Neuropathology at the University of British Columbia and Head of the Division of Neuropathology at Vancouver General Hospital. His research focuses on the neuropathology and genetics of neurodegenerative disease with special interest in the molecular basis of FTD and ALS. He established and is lead investigator of the FTD research program at the University of British Columbia. Major accomplishments include co-PI on studies that identified *progranulin* as the gene that causes the most common form of FTD (*Nature*, 2006), collaborator on research that identified TDP-43 as the pathogenic protein in most cases of FTD and ALS (*Science*, 2006) and PI of recent studies identifying FUS as the pathological protein in most cases of tau/TDP-negative FTD. Most recently, he was co-PI on studies that identified mutations in *C9ORF72* as the most common genetic cause of both ALS and of FTD (*Neuron*, 2011). He has a led an international consortium of neuropathologists which developed a molecular classification system for FTD. He has published more than 180 peer-reviewed research papers and 10 book chapters and was included on the Thomson Reuters's list of "Highly Cited Researchers" and "The World's Most Influential Scientific Minds" in both 2014 and 2015. He is an editorial board member of several international neuroscience journals, is the Canadian representative to the International Society of Neuropathology, the recent past President of the Canadian Association of Neuropathology and the Vice President of the newly formed International Society for Frontotemporal Dementias.

PRESIDENTIAL SYMPOSIUM

Seeding and Propagation of SOD1 Misfolding in Amyotrophic Lateral Sclerosis

Time: 10:15 am – 11:00 am

Neil R. Cashman MD, *Department of Medicine (Neurology), Djavad Mowafaghian Centre for Brain Health, University of British Columbia, Vancouver, BC, CANADA*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Describe the key features of prion disorders.
2. Identify candidate proteins that participate in the prion-like neurodegenerative diseases Alzheimer's and Parkinson's disease, and amyotrophic lateral sclerosis.
3. Describe how SOD1 and TDP43 pathologically interact in ALS.

II. Abstract & Relevant References

Approximately 10% of ALS cases are familial, with ~20% of these due to mutations in the gene encoding Cu/Zn superoxide dismutase (SOD1), a ubiquitous free-radical defense enzyme. A consequence of SOD1 mutation and/or oxidation is a propensity of the protein to misfold and aggregate. We sought to molecularly dissect the effects of intracellular obligate misfolded SOD1 mutant proteins on natively structured wild-type SOD1 (1). Expression of the enzymatically inactive, natural familial ALS SOD1 mutations G127X and G85R in human cell lines induced misfolding of wild-type natively-structured SOD1, as indicated by: 1) acquisition of immunoreactivity with SOD1 misfolding-specific monoclonal antibodies; 2) markedly enhanced protease sensitivity suggestive of structural loosening; and 3) non native disulfide-linked oligomer and multimer formation. Expression of G127X and G85R in mouse cell lines did not induce misfolding of murine wild-type SOD1, and a species restriction element for human wild-type SOD1 conversion was mapped to a region of sequence divergence in loop II and beta-strand 3 of the SOD1 beta-barrel (residues 24-36), then further refined surprisingly to a single tryptophan residue at codon 32 in human SOD1 (1). We now find that small molecules interacting with Trp32 can inhibit SOD1 propagated misfolding. Cytosolic mislocalization of FUS and TDP43, two proteins implicated in familial and sporadic ALS, was associated with human wild-type SOD1 misfolding (2). Culture medium from cells transiently transfected with wild-type or mutant SOD1 (3), or TDP43/FUS mutations (4), induced misfolding of endogenous SOD1 when incubated with naive cell cultures, and this process was stably propagated in serial passage. Nonspecific uptake of misfolded SOD1 from the supernatant was excluded by siRNA knockdown of SOD1 in the fresh recipient cells, indicating a requirement for endogenously expressed SOD1 as a substrate (3,4). The agent responsible for induction of misfolding was determined to be a relatively massive particle pelleted by ultracentrifugation, consistent with transmission by exosomes or protein aggregates (3). Transmission of SOD1 misfolding in vitro was abrogated by extracellular pan- and misfolding-specific SOD1 antibodies (3,4). On quantitative immunoprecipitation, misfolded SOD1 was found to constitute ~4% of total SOD1 in spinal cord from SOD1- and C9ORF72-FALS, as well as sporadic ALS (3). G37R Tg mice treated with misfolding-specific SOD1 antibodies displayed prolonged survival of ~11 days ($p < 0.001$). In conclusion, SOD1 misfolding can propagate within and between cells, and can be triggered by pathologies induced by other ALS-implicated genes. ALS joins company with Alzheimer's, Parkinson's, and other neurodegenerative diseases as a "prion-like" disorder, opening new therapeutic avenues for this dreadful disorder (3,4).

***References*:**

1. Grad LI, Guest WC, Yanai A *et al* *PNAS* 2011; 108, 16398-403.
2. Pokrishevsky E, Grad LI, Yousefi M et al *PLoS-One* 2012; 7, e35050.
3. Grad LI, Yerbury JJ, Turner BJ, *et al PNAS* 2014; 111, 3620-5.
4. Pokrishevsky E, Grad LI, Cashman NR. Scientific Reports, 2016

III. Faculty Biography:

Dr. Neil Cashman is a neurologist-neuroscientist working in neurodegeneration and neuroimmunology. His special areas of work are the motor neuron diseases, particularly amyotrophic lateral sclerosis, and the amyloid encephalopathies, including prion illnesses and Alzheimer's disease. He is Professor of Medicine at the University of British Columbia, where he holds the Canada Research Chair in Neurodegeneration and Protein Misfolding Diseases. He is Founder and Chief Scientific Officer of ProMIS Neurosciences in Toronto. Special honors include the Jonas Salk Prize (2000), his Tier 1 Canada Research Chair in at the UBC (2005-2018), election to the Canadian Academy of Health Sciences (2008), and Genome BC award for Scientific Excellence (2012).

PRESIDENTIAL SYMPOSIUM

Next-Generation Neuropathology: The Molecular Biology of TDP-43 Proteinopathies

Time: 11:00 am – 11:45 am

Edward B. Lee, M.D., Ph.D., *Assistant Professor, Department of Pathology and Laboratory Medicine, University of Pennsylvania*

I. Learning Objectives

At the end of this activity learners should be able to:

1. Describe and understand the role of hnRNP proteins in the regulation of RNA.
2. Determine the similarities and differences between experimental mouse models of TDP-43 proteinopathies and human disease.
3. Describe some of the changes in RNA processing that are associated with TDP-43 dysfunction in amyotrophic lateral sclerosis and frontotemporal degeneration.
4. Conceptualize future molecular analyses of specific cell types within human brain tissue.

II. Abstract & Relevant References

Amyotrophic lateral sclerosis (ALS) and frontotemporal degeneration (FTD) are two fatal neurodegenerative diseases which share a common molecular neuropathology, the loss of nuclear TAR DNA binding protein 43 (TDP-43) due to sequestration of TDP-43 protein within cytoplasmic inclusions. TDP-43 protein is a heterogeneous nuclear ribonucleoprotein which binds RNA and affects RNA splicing, stability and trafficking. Both the loss of nuclear TDP-43 and the formation of cytoplasmic TDP-43 aggregates are hypothesized to contribute to neurotoxicity. A brief review of TDP-43 transgenic mouse models will be presented in order to determine how well they recapitulate the pathologic features of ALS and FTD. Given some key differences between transgenic mouse models and human disease, we sought to determine the changes in nuclear RNA metabolism associated with the loss of nuclear TDP-43 protein using human tissue. However, the spatial resolution afforded by microscopic methods is often lost in standard biochemical or molecular analyses. To address this problem, we have developed a novel method of fractionating pathologic human brain tissue to isolate neuronal nuclei with or without TDP-43 protein for RNA sequencing. Our bioinformatics analyses will be presented which reveals that the loss of TDP-43 in human neurons is associated with profound transcriptomic alterations, including alterations in auto- and cross-regulation of hnRNP proteins. These studies demonstrate the utility of using advanced molecular methods to analyze human post-mortem brain tissue in order to better understand the underlying molecular changes associated with disease, all the while revealing novel basic insights into the regulation of gene expression.

References:

1. Ling SC et al., Converging mechanisms in ALS and FTD: disrupted RNA and protein homeostasis. Neuron 79(3): 416-38, 2013.
2. Walker AK et al., Functional recovery in new mouse model of ALS/FTLD after clearance of pathologic cytoplasmic TDP-43. Acta Neuropathologica 130(5): 643-60, 2015.
3. Amlie-Wolf A et al., Transcriptomic changes due to cytoplasmic TDP-43 expression reveal dysregulation of histone transcripts and nuclear chromatin. PLoS One 10(10): e0141836, 2015
4. Lee EB et al., Gains or losses: molecular mechanisms of TDP43-mediated neurodegeneration. Nat Rev Neurosci 13(1); 38-50, 2011.

5. Igaz LM et al., Dysregulation of the ALS-associated gene TDP-43 leads to neuronal death and degeneration in mice. JCI 121(2): 726, 38, 2011.

III. Faculty Biography:

Edward B. Lee, M.D., Ph.D. is an Assistant Professor in the Division of Neuropathology, Department of Pathology and Laboratory Medicine in the Perelman School of Medicine at the University of Pennsylvania. He graduated Phi Beta Kappa and with honors from Stanford University in 1997 followed by M.D. and Ph.D. degrees from the University of Pennsylvania in 2005 where he studied the production and deposition of amyloid beta peptide in experimental Alzheimer's disease models. After clinical training in Anatomic Pathology and Neuropathology at the Hospital of the University of Pennsylvania, Edward was appointed Assistant Professor in 2011 and is currently principle investigator of the Translational Neuropathology Research Laboratory. The Translational Neuropathology Research Laboratory seeks to understand the basic molecular causes of age-related neurodegenerative diseases, in particular amyotrophic lateral sclerosis, frontotemporal degeneration and Alzheimer's disease. Edward is also a practicing physician at the Hospital of the University of Pennsylvania, and a co-leader of the Penn Neurodegenerative Disease Brain Bank as part of the Penn Alzheimer's Disease Core Center and the Penn Udall Center for Parkinson's Disease Research. He has obtained multiple awards, including a Clinical Scientist Development Award from the Doris Duke Charitable Foundation, multiple NIH grants, the Experimental Pathologist in Training Award from ASIP, the Excellence-In-Science award from ASIP and the Robert Terry Award from AANP. He serves on the editorial board of JNEN and Acta Neuropathologica, and has served on multiple committees for AANP including the Program, Website, Award and Education Committees.

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