95TH ANNUAL MEETING

June 6-9, 2019

Grand Hyatt Atlanta

American Association of Neuropathologists

American Association of Neuropathologists 95TH ANNUAL MEETING

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

June 6 - 9, 2019

Grand Hyatt Atlanta

Atlanta, Georgia

This activity is provided by the American Association of Neuropathologists.

TABLE OF CONTENTS

The American Association of Neuropathologists
8156-E S. Wadsworth Blvd., Suite 197
Littleton, Colorado 80128
Phone: 720-372-0888; Fax: 303-568-0406
Email: aanp@aoeconsulting.com

Dear Colleagues:

For more than 90 years, the American Association of Neuropathologists (AANP) has been working to advance the science, teaching, and training of diseases of the nervous system and the field of neuropathology. To this end, it is my pleasure as the President of the AANP, to welcome you to the AANP's 95th Annual Meeting in Atlanta, Georgia. This year's conference will not only connect attendees with key leaders but will serve to provide the latest insights into revolutionary research and front-line science.

You can expect a riveting scientific experience over the course of the Annual Meeting, leading off with a one-day Special Course on Thursday dedicated to the "*Unintended Consequences: The Iatrogenic Neuropathology of Systemic Therapies."* Friday and Saturday will be full days of scientific platform and poster sessions, allowing you to learn and discuss topics across the breadth of our discipline. This presentation of new research will be complemented by the DeArmond, Korey and Parisi lectures. Saturday evening will also include the Diagnostic Slide Session and wrapping up the Annual Meeting on Sunday will be a half-day Presidential Symposium titled "*New Ways of Looking at the Brain – What Can Neuropathologists See"* which will include the Moore lecture.

Education is not the only aspect of the meeting, as attendees will have plenty of time to network with new colleagues and socialize with long-time friends, reaffirming relationships and expanding connections with neuropathologists around the world. Our annual meeting also provides the opportunity for trainees and others at the start of their careers to meet the leaders of the community as well as each other. Attendees will also have time to explore the exhibit space and discuss the high-quality products and services available to neuropathologists with the exhibitor representatives. I would like to thank the exhibitors for their presence and support of the AANP and urge each of you to personally thank the exhibitors for joining us at the 95th Annual Meeting, as their support is important to our association.

I look forward to seeing you all and sharing knowledge and insights, as we strive to promote discovery and advancement in our field. As my term as President winds down, it is my hope that the Annual Meeting is rewarding, memorable, and leaves you with elevated energy and new ideas to drive the profession forward. I look forward to seeing you in Atlanta for the AANP's 95th Annual Meeting.

Sincerely,

Matthew P. Frosch, MD, PhD
President
The American Association of Neuropathologists

Save the Date!

June 11-14, 2020

Hyatt Regency Monterey
Monterey, California

96TH ANNUAL MEETING

American Association of Neuropathologists

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

AANP OFFICE

8156-E S. Wadsworth Blvd., Suite 197, Littleton, CO 80128
Phone: 720-372-0888; Fax: 303-568-0406
Email: aanp@aoeconsulting.com

OFFICERS

Matthew Frosch, MD, PhD, *Harvard Medical School*, President
R. Ross Reichard, MD, *Mayo Clinic*, Vice President
Daniel J. Brat, MD, PhD, *Northwestern University Feinberg School of Medicine*, President Elect
Eileen H. Bigio, MD, *Northwestern University Feinberg School of Medicine*, Vice President Elect
Douglas Anthony, MD, PhD, *Brown University*, Vice President for Professional Affairs
Charles L. White III, MD, *University of Texas Southwestern*, Interim Secretary-Treasurer
Edward Lee, MD, PhD, *University of Pennsylvania*, Assistant Secretary-Treasurer

OTHER EXECUTIVE COUNCIL MEMBERS

Rebecca D. Folkerth, MD, *New York City Office of the Chief Medical Examiner*
John (Jack) Lee, MD, PhD, *NorthShore University HealthSystem*
Peter T. Nelson, MD, PhD, *University of Kentucky*
Suzanne Z. Powell, MD, *Houston Methodist Hospital*
Arie Perry, MD, *University of California San Francisco*
Elizabeth J. Cochran, MD, *Medical College of Wisconsin*

ARCHIVIST

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

OFFICIAL JOURNAL

Journal of Neuropathology and Experimental Neurology
John (Jack) Lee, MD, PhD, 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, *Mayo Clinic,* Moderator
Rebecca D. Folkerth, MD, *New York City Office of the Chief Medical Examiner,* Manager

COUNCILORS TO THE INTERNATIONAL SOCIETY OF NEUROPATHOLOGY

Alexander Judkins, MD, *Children's Hospital Los Angeles*
George Perry, PhD, *The University of Texas at San Antonio*
Arnulf H. Koeppen, MD, *Albany Stratton Veterans Affairs Medical Center*
E. Tessa Hedley-Whyte, MD, *Massachusetts General Hospital; Harvard Medical School*
Adekunle Adesina, MD, PhD, *Texas Children's Hospital*

AANP COMMITTEES

Awards Committee

Mirna Lechpammer, MD, PhD (Chair)
Malek Abedalthagafi, MD
Sanda Alexandrescu, MD
Ewa Borys, MD
Sonika Dahiya, MD
Cheng-Ying Ho, MD, PhD, FRCPC
Craig Horbinski, MD, PhD
Kyle Hurth, MD, PhD
Karra Jones, MD, PhD
James W. Mandell, MD, PhD
Carrie Ann Mohila, MD
David Nauen, MD, PhD
Hilary Nickols, MD, PhD
Edward Plowey, MD, PhD
Michael Punsoni, MD
Aditya Raghunathan, MD
Marie Rivera-Zengotita, MD
Matija Snuderl, MD
Joshua Sonnen, MD
David Solomon, MD, PhD

Education Committee

Edward B. Lee, MD, PhD (Chair)
Jennifer Baccon, MD, PhD
Rati Chkheidze, MD*
Sonika Dahiya, MD
Brent Harris, MD
Jesse Kresak, MD
Qinwen Mao, MD, PhD
J. Stephen Nix, MD
Angelica Oviedo, MD
Anat Stemmer-Rachamimov, MD
Cynthia Welsh, MD
Charles L. White III, MD
Qian Wu, MD
Gabrielle A. Yeaney, MD

Constitution Committee

Steven L. Carroll, MD, PhD (Chair)
Kevin Bieniek, PhD*
James Hackney, MD
William T. Harrison, MD*
Ryan Miller, MD, PhD

Membership Committee

Anne Buckley, MD, PhD (Chair)
Jared Ahrendsen, MD, PhD*
Ewa Borys, MD
John DeWitt, MD, PhD*
Xuemo (Sean) Fan, MD, PhD
Jane Uyehara-Lock
Jose Velazquez Vega, MD

Nominating Committee

Elizabeth J. Cochran, MD (Chair)
Arie Perry, MD
Suzanne Z. Powell, MD
Thomas J. Montine, MD, PhD

Neuropathology Fellowship Program Directors Committee (Sub-Committee of Professional Affairs)

Suzanne Z. Powell, MD (Chair)
Sanda Alexandrescu, MD
Matthew P. Anderson, MD, PhD
Sandra Camelo-Piragua, MD
Kenneth Fallon, MD
Mary Fowkes, MD, PhD
Matthew P. Frosch, MD, PhD
Marjorie Grafe, MD, PhD
Leslie Hamilton, MD
Robert Hammond, MD
Christine M. Hulette, MD
C. Dirk Keene, MD, PhD
Maria Beatriz S. Lopes, MD
Qinwen Mao, MD, PhD
Janna Neltner, MD
Joseph E. Parisi, MD
Arie Perry, MD
Edward Stopa, MD
Juan C. Troncoso, MD
Hannes Vogel, MD
Cynthia Welsh, MD
Charles L. White III, MD
Clayton Wiley, MD, PhD
Thomas Wisniewski, MD
Anthony T. Yachnis, MD
William H. Yong, MD

Professional Affairs Committee

Douglas Anthony, MD, PhD (Chair)
Leomar Y. Ballester, MD, PhD*
Meghan Driscoll, MD*
Alexander Feldman, MD*
Jennifer Libien, MD, PhD
Bradley Miller, MD, PhD
MacLean Nasrallah, MD, PhD
Amyn Rojiani, MD, PhD

Program Committee

Julia Kofler, MD (Chair)
Adekunle Adesina, MD, PhD
Jason Chiang, MD, PhD
Sean Ferris, MD, PhD*
Miguel Guzman, MD
Kimmo J. Hatanpaa, MD, PhD
Anne Hiniker, MD, PhD
Nancy C. Kois, MD, FCAP
Michael Lawlor, MD
Han Lee, MD
Michelle Madden Felicella, MD
Hsiang-Chih (Sean) Lu, MD, PhD*
Qinwen Mao, MD, PhD
Maria Martinez-Lage, MD
Brent Orr, MD, PhD
Richard Perrin, MD, PhD

Website Committee (Ad Hoc of Professional Affairs)

Michael Punsoni, MD (Chair)
Douglas Anthony, MD, PhD
Henry G. Brown, MD, PhD
John Crary, MD, PhD
Sonika Dahiya, MD
John Donahue, MD, PhD
Kar-Ming Fung, MD, PhD
Murat Gokden, MD
Luis F. Gonzalez-Cuyar, MD
Joshua Klonoski, MD, PhD*
Edward Lee, MD, PhD
Brian Moore, MD
Hilary Nickols, MD, PhD
J. Stephen Nix, MD*
Jingxin Qiu, MD, PhD
Charles L. White, III, MD

*Junior Member

CME INFORMATION

TARGET AUDIENCE

The educational design of the 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:

1. Discuss recent advances in the field of neuropathology that impact research and practice.
2. Outline new information on the underlying causes and mechanisms of neurologic disease.
3. Explain how to translate the latest developments in neuropathology into clinical practice.

DISCLAIMER

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in 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 DESIGNATION

The American Association of Neuropathologists designates this live educational activity for a maximum of 25.25 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

MAINTENANCE OF CERTIFICATION

The 95th Annual Meeting of the American Association of Neuropathologists will offer both Continuing Medical Education (CME) and American Board of Pathology (ABPath) Continuous Certification, formerly Maintenance of Certification (MOC), Part II: Lifelong Learning and Self-Assessment. Participation in the live activity and successful completion of the corresponding evaluation component for each eligible session enables participants to earn up to a maximum of 16.25 SAM credits.

CME INFORMATION (Continued)

CME AND SAM CREDIT

Instructions to Receive CME 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 or by using the following link http://eventmobi.com/aanp2019.

Instructions to Receive SAM Credit

Shortly after the 95th Annual Meeting, the evaluation component for SAM credit will launch at www.neuropath-education.org. Participants will need to use their Dayspring website log-in to gain access to each evaluation component and must have attended the live session held at the 2019 Annual Meeting in Atlanta, GA. Each SAM costs $25.00 unless you previously purchased the SAMs bundle.

To purchase the SAMs bundle visit this link: www.neuropath.org/sams-bundle. Please note there is a one to two-week delay in unlimited access being set up on your Dayspring account.

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 accredited for *AMA PRA Category 1 Credit*™ at this year's Annual Meeting. The chart also outlines the SAM credit available for each session.

Activity	CME Credit Hours	SAM Credit Hours
Special Course	6.75	6.75
Scientific Sessions	8.00	0
Korey Lecture	1.00	1.00
DeArmond Lecture	1.00	1.00
Parisi Lecture	1.00	1.00
Moore Lecture	1.00	1.00
What Every Neuropathologist Needs to Know	1.00	0
Diagnostic Slide Session	3.00	3.00
Presidential Symposium	2.50	2.50
Total	**25.25**	**16.25**

CONTACT INFORMATION

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

DISCLOSURE INFORMATION

Disclosure of Commercial Support:
This activity is supported by an educational, in-kind donation of microscopes, provided by Nikon Instruments, Inc.

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 all relevant financial relationships with commercial interests 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.

Planners and Managers

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

Adekunle **Adesina**, Douglas **Anthony**, Jennifer **Baccon**, Eileen **Bigio**, Daniel **Brat**, Jason **Chiang**, Rati **Chkheidze**, Elizabeth **Cochran**, Sonika **Dahiya**, Sean **Ferris**, Rebecca **Folkerth**, Matthew **Frosch**, Caterina **Giannini**, Miguel **Guzman**, Brent **Harris**, Kimmo **Hatanpaa**, Anne **Hiniker**, Julia **Kofler**, Nancy **Kois**, Jesse **Kresak**, Edward **Lee**, Hsiang-Chih (Sean) **Lu**, Michelle **Madden Felicella**, Qinwen **Mao**, Maria **Martinez-Lage**, Peter **Nelson**, Stephen **Nix**, Brent **Orr**, Angelica **Oviedo**, Richard **Perrin**, Arie **Perry**, Sarah **Porter**, Suzanne **Powell**, R. Ross **Reichard**, Anat **Stemmer-Rachamimov**, Cynthia **Welsh**, Charles **White**, Qian **Wu**, Gabrielle **Yeaney**

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.

Michael Lawlor	**Consultant/Independent Contractor:** Dynacure, Wave Life Sciences, Valerion Therapeutics **Grant/Research Support:** Audentes Therapeutics, Solid Biosciences, Ichorion Therapeutics **Other:** Scientific Advisory Board Member for Audentes Therapeutics, Solid Biosciences, and Ichorion Therapeutics
Han Lee	**Stock Shareholder (Spouse/Partner):** Gilead Sciences, Inc., Theravance
John (Jack) Lee	**Consultant/Independent Contractor:** Holds joint patents on a drug for treatment of Alzheimer's disease/senile dementia and anxiety disorders with others and Cornelli Consulting, Milan, Italy (No royalties associated – patent tied to research in early clinical stages)

DISCLOSURE INFORMATION (Continued)

Faculty, Authors, Content Developers

*The following faculty, authors, and content developers have **nothing to disclose:***

Homa **Adle-Biassette**, Osama **Al Dalahmah**, Roland **Auer**, Jean **Augustinack**, Pavan **Auluck**, Jennifer **Baccon**, Tejus **Bale**, Matthew **Ball**, Amir **Banihashemi**, Barbara **Bendlin**, Edward **Boyden**, Rati **Chkheidze**, Kwanghun **Chung**, Kyle **Conway**, John **Crary**, Matthew **Cykowski**, Dale **Davis**, Marc **Del Bigio**, Dennis **Dickson**, Jorg **Dietrich**, Michael **Drumm**, Brittany **Dugger**, Charles **Eberhart**, Phyllis **Faust**, Cole **Ferguson**, Rebecca **Folkerth**, Fernando **Frassetto**, Matthew **Frosch**, Catherine K. **Gestrich**, Nikhil **Ghayal**, Bernardino **Ghetti**, Jason **Gregory**, Juliane **Gust**, Cynthia **Hawkins**, Lili-Naz **Hazrati**, Christopher **Heaphy**, Richard **Hickman**, Anne **Hiniker**, Cheng-Ying **Ho**, Craig **Horbinski**, Karra **Jones**, Kwok Ling **Kam**, C. Dirk **Keene**, Joshua **Klonoski**, Julia **Kofler**, Caitlin **Latimer**, Laetitia **Lebrun**, Mirna **Lechpammer**, Edward **Lee**, Julieann **Lee**, Seth **Love**, Lindsey **Lowder**, Jian-Qiang **Lu**, Calixto-Hope **Lucas**, Qinwen **Mao**, Maria **Martinez-Lage**, Michael **Miller**, Kanish **Mirchia**, Steven **Moore**, Edward Kelly **Mrachek**, MacLean **Nasrallah**, Avindra **Nath**, David **Nauen**, Peter **Nelson**, Kathy L. **Newell**, James **Nicoll**, Stephen **Nix**, Amber **Nolan**, Jose **Otero**, Thomas **Pearce**, Daniel **Perl**, Richard **Perrin**, David **Priemer**, Peter **Pytel**, Biswarathan **Ramani**, Cayrol **Romain**, Matthew **Rose**, Anne **Shepler**, Emily **Sloan**, Izabella **Smolicz**, David **Solomon**, Thor **Stein**, Sriram **Venneti**, Angela **Viaene**, Hannes **Vogel**, Jean Paul **Vonsattel**, Jonathan **Vordzorgbe**, Clayton **Wiley**, Changhong **Xing**, Zezhong **Ye**

The following **faculty, authors, content developers** 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.

Alison Goate	**Consultant/Independent Contractor:** AbbVie, Biogen, Cognition Therapeutics, Eisai, GSK, Illumina **Grant/Research Support:** Eli Lilly; **Royalties:** Taconic, Athena Diagnostics **Honoraria:** AbbVie, Biogen, Eisai, GSK
Marta Margeta	**Consultant/Independent Contractor:** Audentes Therapeutics
Beth Stevens	**Consultant/Independent Contractor:** Annexon Biosciences, Abelian New Co **Honoraria:** Abellian New Co **Stock Shareholder:** Abelian New Co, Annexon Biosciences
Michael Lawlor	**Consultant/Independent Contractor:** Dynacure, Wave Life Sciences, Valerion Therapeutics **Grant/Research Support:** Audentes Therapeutics, Solid Biosciences, Ichorion Therapeutics **Other:** Scientific Advisory Board Member for Audentes Therapeutics, Solid Biosciences, and Ichorion Therapeutics

Content Reviewers

*The following content reviewers have **nothing to disclose:***

Rati **Chkheidze**, Sonika **Dahiya**, Cynthia **Welsh**

GENERAL INFORMATION

LOCATION

Grand Hyatt Atlanta
3300 Peachtree Rd NE
Atlanta, GA 30305

All meeting sessions will be held at the Grand Hyatt Atlanta

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 the **Grand Ballroom** and **Buckhead Ballroom** of the hotel on the lower lobby level.

All poster sessions will be held in the **Highland Ballroom** on the lobby level.

REGISTRATION DESK

Top of the Escalators	
Wednesday, June 5	4:00 pm – 8:00 pm
Thursday, June 6	7:00 am – 5:00 pm
Friday, June 7	7:00 am – 5:00 pm
Saturday, June 8	7:00 am – 5:00 pm
Sunday, June 9	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 the June 2019 issue of the *Journal of Neuropathology and Experimental Neurology (JNEN),* inclusive of Annual Meeting abstracts, ready for pick-up at the AANP Registration Desk, located in the **Prefunction** on the lower lobby level. 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 Thursday evening Annual Reception.

MICROSCOPE VIEWING ROOM

Multi-headed microscopes will be available in **Cascade** on the lower lobby level of the hotel.

Location: Downs	
Thursday, June 6	7:00 am – 7:30 pm
Friday, June 7	7:00 am – 7:30 pm
Saturday, June 8	7:00 am – 7:30 pm
Sunday, June 9	7:00 am – 10:30 am

GENERAL INFORMATION (Continued)

SPECIAL MEETINGS BY INVITATION

Day/Date	Meeting	Time/Location
Wednesday, June 5	**Neuropathology Fellowship Program Directors Committee Meeting**	4:30 pm – 6:30 pm **Veranda**, Garden Level
	Education Committee Meeting	6:30 pm – 9:30 pm **Library**, Lobby Level
Thursday, June 6	**Awards Committee Meeting #1**	5:30 pm – 6:00 pm **Library**, Lobby Level
	Executive Council Meeting	7:00 pm – 10:00 pm **Ivy**, Lobby Level
Friday, June 7	**Trainee Luncheon*** ***Open to all Trainees and Travel Award Winners**	11:45 am – 2:00 pm **Azalea**, Lobby Level
	Website Committee Meeting	12:15 pm – 1:30 pm **Ivy I**, Lobby Level
	Awards Committee Meeting #2	5:30 pm – 6:30 pm **Library**, Lobby Level
	Professional Affairs Committee Meeting	5:30 pm – 7:00 pm **Ivy II**, Lobby Level
Saturday, June 8	***JNEN* Editorial Board Meeting**	7:00 am – 8:00 am **Azalea**, Lobby Level
	Awards Committee Meeting #3	6:00 pm – 8:00 pm **Library**, Lobby Level
	Presidential Reception	6:00 pm – 8:00 pm **Azalea**, Lobby Level
Sunday, June 9	**DSS Founders Breakfast**	7:00 am – 8:00 am **Veranda,** Garden Level

ANNUAL RECEPTION

The annual reception will be held from 5:30 pm to 7:30 pm, Thursday, June 6 in the **East/West Terrace and Pool Deck** on the garden level of the Grand Hyatt. 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.

East/West Terrace and Pool Deck	
Thursday, June 6, 2019	5:30 pm – 7:30 pm

TRAINEE LUNCHEON

Trainees and Travel Award winners are invited to attend the 2019 Trainee Luncheon and Networking Event on Friday, June 7 in **Azalea** (lobby level), hosted by Dr. Suzanne Z. Powell. Lunch will be provided. The agenda is posted below.

2019 Trainee Luncheon Agenda

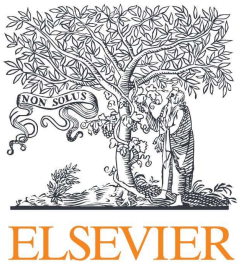
I. 11:45 am – 12:15 pm: Welcome & Lunch
II. 12:15 pm – 12:45 pm: Travel Awards Recognition
III. 12:45 pm – 1:30 pm: Panel Discussion – *Neuropathology Job Market: Finding a Job*
    a. Panel Members: Leomar Ballester, Daniel Brat, Elizabeth Cochran, Qinwen Mao, William McDonald
IV. 1:30 pm – 2:00 pm: Mingle with Executive Council

EXHIBITORS & SPONSORS

Thank you to our 2019 exhibitors and sponsors! Please visit the exhibit booths in the Prefunction.

Location: Prefunction (Lower Lobby Level)	
Thursday, June 6	7:00 am – 5:30 pm
Friday, June 7	7:00 am – 5:30 pm
Saturday, June 8	7:00 am – 5:30 pm

EXHIBITORS

	Elsevier is a world-leading provider of information solutions that enhance the performance of science, health, and technology professionals, empowering them to make better decisions, and deliver better care.
University of Pittsburgh Medical Center's Molecular and Genomic Pathology Laboratory is an innovative clinical lab with the mission to provide the most advanced support for personalized patient care, with focus on complex genetic tests in the areas of solid tumors, hematologic malignancies, and genetics. Our proprietary test, GlioSeq, is a targeted next-generation sequencing-based test designed to assist in the diagnosis, prognostication, and treatment of adult and pediatric CNS tumors, including low- and high-grade gliomas, ependymomas, meningiomas, and medulloblastomas. The GlioSeq test can accept small sample sizes and provides clinically actionable information with a fast turnaround time.	UPMC LIFE CHANGING MEDICINE
OXFORD UNIVERSITY PRESS	Oxford University Press is the proud publisher of the *Journal of Neuropathology & Experimental Neurology (JNEN)*. OUP also publishes some of the most renowned and respected medicine books and journals in the world. Visit our stand for promotional items and more information about your AANP member benefits to publishing in *JNEN*. **Note:** Copies of the June Edition of the *JNEN* have been provided by Oxford University Press.
Nikon Instruments Inc. is the US microscopy arm of Nikon Healthcare, a world leader in the development and manufacture of optical and digital imaging technology for biomedical applications. Leveraging our expertise in optics, image acquisition, and image analysis, Nikon Instruments is able to offer a wide range of solutions for clinical applications from digital slide scanners to remote viewing systems. For more information, visit https://www.microscope.healthcare.nikon.com/ or contact us at 1-800-52-NIKON.	Nikon®

MAYO CLINIC LABORATORIES	Mayo Clinic Laboratories partners with health care organizations around the globe to help answer the most complex questions facing patients. With the most sophisticated test menu in the world, laboratory diagnostic testing and pathology services from Mayo Clinic span every medical subspecialty. We are committed to putting the needs of all patients first by focusing on providing clinically relevant answers, not just test results.
Autism BrainNet is a collaborative network for the acquisition and distribution of postmortem brain tissue to facilitate autism research. By providing this precious resource for research, Autism BrainNet aims to improve the understanding of the underlying neurobiological causes of autism and related neurodevelopmental disorders. Our mission, in partnership with the medical community and families, is to communicate the need for donated brain and other tissue and develop a sensitive, transparent and effective strategy for acquiring and distributing the highest quality tissue for research worldwide. Autism BrainNet is supported by the Simons Foundation Autism Research Initiative (SFARI). Learn more at: autismbrainnet.org	autism BRAIN NET

SPONSORS

abbvie	AbbVie is a global, research-based biopharmaceutical company which combines the focus of a leading-edge biotech with the expertise and structure of a long-established pharmaceutical leader. AbbVie is committed to using unique approaches to innovation to develop and market advanced therapies that address some of the world's most complex and serious diseases. Sponsorship: Meeting Application
The Oskar Fischer Prize is aimed at engaging the world's brightest minds to find the missing piece of the puzzle that explains Alzheimer's. The University of Texas at San Antonio (UTSA) College of Sciences issues the challenge for revolutionary thinking from any discipline to synthesize information from a comprehensive literature review. The Oskar Fischer Prize will award the best ideas that unravel the mysteries of neurodegeneration. The grand prize is $2,000,000; two second-place prizes are $500,000 each; and four third-place prizes are $250,000 each. The call for proposals to this challenge will open soon. Visit oskarfischerproject.com for information and updates. Sponsorship: Tote Bag Insert	The Oskar Fischer Prize Hosted by The University of Texas at San Antonio

NGS PANEL TESTING FOR BRAIN TUMORS

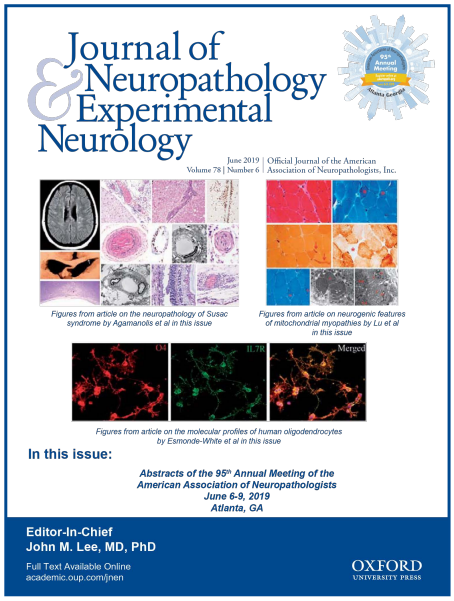
GlioSeq®

- ► Adult & Pediatric CNS Tumors
- ► Small Sample Size
- ► Fast Turnaround Time

- ✓ Strategically designed to sequence clinically relevant genes for mutations, copy number changes, and gene fusions, including *BRAF, NTRK1–3, FGFR3, YAP1, RELA,* and *EGFRvIII*
- ✓ Performed on small stereotactic brain biopsies and resected FFPE tumor specimens
- ✓ Fast turnaround time (7–10 days)
- ✓ Aids in the diagnosis of adult and pediatric CNS tumors, including glioma, medulloblastoma, meningioma, and ependymoma

For more information: visit our booth,
go to GlioSeq.com,
scan this QR code,
or email OrderGlioSeq@upmc.edu

Journal of Neuropathology & Experimental Neurology



Journal of Neuropathology & Experimental Neurology is the official journal of the American Association of Neuropathologists, Inc. (AANP). The journal publishes peer-reviewed studies on neuropathology and experimental neuroscience, book reviews, letters, and Association news, covering a broad spectrum of fields in basic neuroscience with an emphasis on human neurological diseases. It is written by and for neuropathologists, neurologists, neurosurgeons, pathologists, psychiatrists, and basic neuroscientists from around the world.

Why Publish in *JNEN*?

- Reduced Open Access fees for AANP members
- No page charges for active AANP members
- Special features that highlight AANP members e.g. autobiographies
- Free color
- Rapid first decision and online publication

Explore a new virtual issue featuring leading *JNEN* research on the topic of Central Nervous System Tumors.

Freely available here: bit.ly/**CNSTumors**

American Association of Neuropathologists

OXFORD UNIVERSITY PRESS

Improve Your Workflow with Remote Live Viewing

Reduce collaboration time and increase confidence with Nikon Pathology Solutions

- Share live images with multiple facilities and specialists.
- No additional equipment requirements or ongoing charges.
- Improve patient outcomes by eliminating specimen transportation.
- Assess with greater image accuracy and speed.

ECLIPSE Ci-L

DIGITAL SIGHT
DIGITAL CAMERA SYSTEM

The Clear Choice in Clinical Microscopy

For more information, or to schedule a demonstration, go to
www.microscope.healthcare.nikon.com/ci or call 1-800-52-NIKON

nikon-instruments-inc. nikoninstrumentsinc nikoninst nikoninstruments
Nikon Instruments Inc. ▪ www.microscope.healthcare.nikon.com ▪ nikoninstruments@nikon.net

UPDATES OF THE WHO CLASSIFICATION OF BRAIN AND PITUITARY TUMORS

SEPT. 19-20, 2019

USCAP INTERACTIVE CENTER
PALM SPRINGS, CALIFORNIA

JOIN AANP AND USCAP IN PALM SPRINGS, CA THIS SEPTEMBER

For the first time, the 2016 WHO classification of central nervous system (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. These new updates will facilitate clinical, experimental and epidemiological studies that will lead to improvements in the lives of patients with brain tumors. General pathologists, in particular, must become familiar with changes in diagnostic criteria and utilize them in their practice improvement strategies. The WHO classification of pituitary adenomas was revised in 2017 and includes (1) a recommendation for the assessment of pituitary transcription factors with focus on adenohypophysial-cell lineage and (2) replacement of "atypical adenoma" with "high risk adenoma" based on tumor proliferation markers and other clinical parameters (such as invasion) to predict aggressiveness. This course will illustrate and reinforce these important updates.

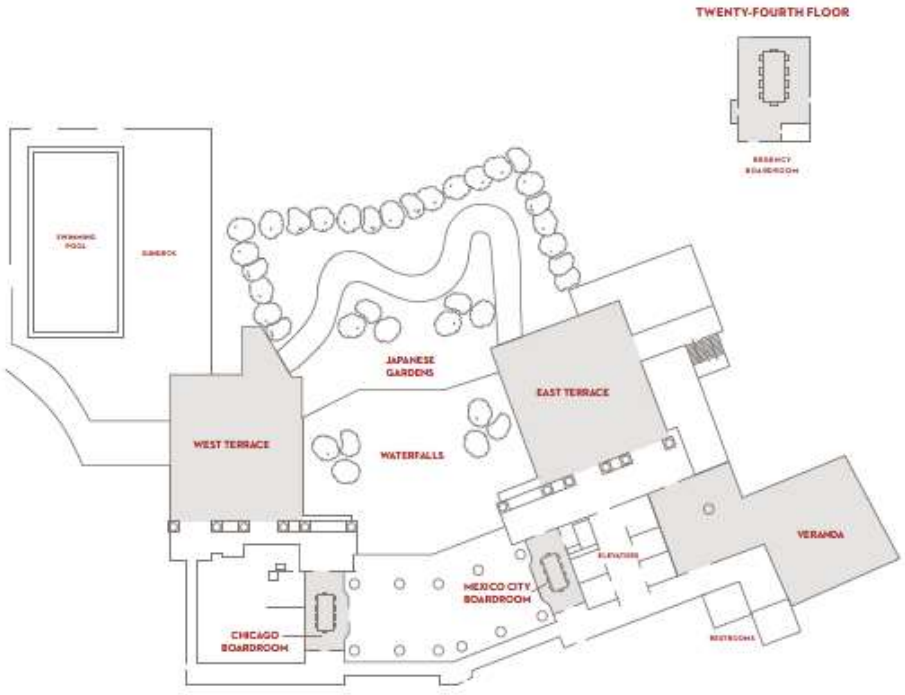
REGISTER TODAY AT
uscap.org/AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

The Powers - Sanchez USCAP Interactive Center

THE GRAND HYATT FLOOR PLANS

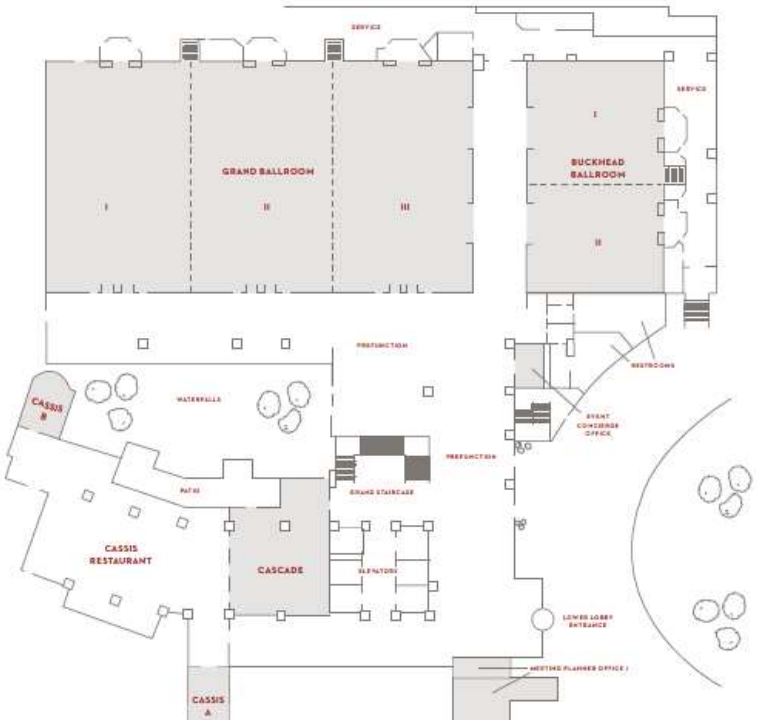
Garden Level–Third Floor



THE GRAND HYATT FLOOR PLANS

Lobby Level

Lower Lobby Level



2019 MEETING AT A GLANCE

2019 SPECIAL COURSE

Unintended Consequences: The Iatrogenic Neuropathology of Systemic Therapies

Directors: R. Ross Reichard, MD and Maria Martinez-Lage, MD

Thursday, June 6, 2019	
Time:	**Grand Ballroom**
7:00 am – 8:00 am	**CONTINENTAL BREAKFAST** Prefunction
8:00 am – 8:15 am	*Welcome and CME Pre-Test*
8:15 am – 9:05 am	*CAR-T Cell Therapy Associated Neurotoxicities* Jörg Dietrich, MD, PhD, MBA, MMSc, FAAN Massachusetts General Hospital, Boston, MA
9:05 am – 9:30 am	*Cases: Neurotoxicity Associated with CAR T Cell Immunotherapy* Juliane Gust, MD, PhD University of Washington, Seattle Children's Hospital, Seattle, WA
9:30 am – 10:20 am	*Methotrexate and Other Cancer Chemotherapy Effects on the Brain and Peripheral Nervous System* Hannes Vogel, MD Stanford University, Palo Alto, CA
10:20 am – 10:50 am	**REFRESHMENT BREAK** Prefunction
10:50 am – 11:40 am	*Immune Response within the Central Nervous System to Systemic Therapies* Avindra Nath, MD National Institute of Neurological Disorders and Stroke, Bethesda, MD
11:40 am – 12:30 pm	*The Neuropathology of Immune-Related Adverse Events in Checkpoint Inhibitor Therapy* Maria Martinez-Lage, MD Massachusetts General Hospital, Boston, MA
12:30 pm – 1:45 pm	**LUNCH ON OWN**
1:45 pm – 2:35 pm	*The Neuropathology of Amyloid-β Immunotherapy for Alzheimer's Disease: Implications for Pathogenesis and Clinical Trials* James Nicoll, BSc, MBChB, MD, FRCPath University of Southampton, Southampton, United Kingdom
2:35 pm – 3:25 pm	*Gut Microbiome and Alzheimer's Disease* Barbara B. Bendlin, PhD University of Wisconsin, Madison, WI
3:25 pm – 3:55 pm	**REFRESHMENT BREAK** Prefunction
3:55 pm – 4:45 pm	*The Pathology of Systemic Therapy-Related Neuromuscular Disease* Karra Jones, MD, PhD The University of Iowa, Iowa City, IA
4:45 pm – 5:00 pm	*Closing Remarks and CME Post-Test*
5:30 pm – 7:30 pm	**ANNUAL RECEPTION** *All Attendees Welcome* East and West Terrace

2019 MEETING AT A GLANCE

2019 ABSTRACTS AND NAMED LECTURES, DAY 1

Director: Matthew P. Frosch, MD, PhD

<table>
<tr><th colspan="3">Friday, June 7, 2019</th><th rowspan="2">Highland Ballroom</th></tr>
<tr><td>7:00 am – 8:00 am</td><td colspan="2">CONTINENTAL BREAKFAST
Prefunction</td></tr>
<tr><td></td><td>Grand Ballroom</td><td>Buckhead Ballroom</td><td rowspan="14">Posters #33-117
Friday, June 7
8:00 am – 5:00 pm</td></tr>
<tr><td>8:00 am – 10:00 am</td><td>PLATFORM 1
Neurodegenerative: FTLD/Lewy Body/Other
Abstracts #1-8</td><td>PLATFORM 2
Muscle/Nerve
Abstracts #9-16</td></tr>
<tr><td>10:00 am – 10:30 am</td><td colspan="2">REFRESHMENT BREAK
Prefunction</td></tr>
<tr><td></td><td colspan="2">Grand Ballroom</td></tr>
<tr><td>10:30 am – 11:30 am</td><td colspan="2">PARISI LECTURE
Microglia Function and Dysfunction in Neurologic Disease

Beth Stevens, PhD
Boston Children's Hospital, Harvard Medical School, Boston, MA</td></tr>
<tr><td>11:30 am – 11:45 am</td><td colspan="2">MERITORIOUS AWARD
Honoring Eileen Bigio, MD
Presented by Qinwen Mao, MD, PhD</td></tr>
<tr><td>11:45 am – 12:45 pm</td><td colspan="2">BUSINESS MEETING I
All Members Welcome</td></tr>
<tr><td>12:45 pm – 2:00 pm</td><td colspan="2">LUNCH ON OWN</td></tr>
<tr><td></td><td>Grand Ballroom</td><td>Buckhead Ballroom</td></tr>
<tr><td>2:00 pm – 4:00 pm</td><td>PLATFORM 3
Glial Tumors
Abstracts #17-24</td><td>PLATFORM 4
Developmental/Pediatrics/ Infectious
Abstracts #25-32</td></tr>
<tr><td>4:00 pm – 4:45 pm</td><td colspan="2">POSTER VIEWING & REFRESHMENT BREAK
Prefunction</td></tr>
<tr><td></td><td colspan="2">Grand Ballroom</td></tr>
<tr><td>4:45 pm – 5:45 pm</td><td colspan="2">DEARMOND LECTURE
Rare and Common Genetic Variation Implicate Microglial Function in Alzheimer’s Disease Risk

Alison Goate, D.Phil
Icahn School of Medicine at Mount Sinai, New York, NY</td></tr>
</table>

2019 MEETING AT A GLANCE

2019 ABSTRACTS AND NAMED LECTURES, DAY 2

Director: Matthew P. Frosch, MD, PhD

<table>
<tr><th colspan="3">Saturday, June 8, 2019</th><th rowspan="2">Highland Ballroom</th></tr>
<tr><td>7:00 am – 8:00 am</td><td colspan="2">CONTINENTAL BREAKFAST
Prefunction</td></tr>
<tr><td></td><td>Grand Ballroom</td><td>Buckhead Ballroom</td><td rowspan="16">Posters #150-234
Saturday, June 8
8:00 am – 5:00 pm</td></tr>
<tr><td>8:00 am – 10:00 am</td><td>PLATFORM 5
Neurodegenerative: Alzheimer
Abstracts #118-125</td><td>PLATFORM 6
New Methods and Technologies
Abstracts #126-133</td></tr>
<tr><td>10:00 am – 10:30 am</td><td colspan="2">REFRESHMENT BREAK
Prefunction</td></tr>
<tr><td></td><td colspan="2">Grand Ballroom</td></tr>
<tr><td>10:30 am – 11:30 am</td><td colspan="2">KOREY LECTURE
Approaching the Challenge of Determining Mechanism Through Neuropathology
Jean Paul Vonsattel, MD
Columbia University, New York, NY</td></tr>
<tr><td>11:30 am – 11:45 am</td><td colspan="2">MERITORIOUS AWARD
Honoring Raymond Sobel, MD
Presented by Jeffrey Golden, MD</td></tr>
<tr><td>11:45 am – 12:45 pm</td><td colspan="2">BUSINESS MEETING II
All Members Welcome</td></tr>
<tr><td>12:45 pm – 2:00 pm</td><td colspan="2">LUNCH ON OWN</td></tr>
<tr><td></td><td>Grand Ballroom</td><td>Buckhead Ballroom</td></tr>
<tr><td>2:00 pm – 4:00 pm</td><td>PLATFORM 7
Glioneuronal and Non-Glial Tumors
Abstracts #134-141</td><td>PLATFORM 8
Trauma and Forensics
Abstracts #142-149</td></tr>
<tr><td>4:00 pm – 4:45 pm</td><td colspan="2">POSTER VIEWING & REFRESHMENT BREAK
Prefunction</td></tr>
<tr><td></td><td colspan="2">Grand Ballroom</td></tr>
<tr><td>4:45 pm – 5:15 pm</td><td colspan="2">What Every Neuropathologist Needs to Know:
Muscle
Steven Moore, MD, PhD
The University of Iowa, Iowa City, IA</td></tr>
<tr><td>5:15 pm – 5:45 pm</td><td colspan="2">What Every Neuropathologist Needs to Know:
Nerve
Peter Pytel, MD
The University of Chicago, Chicago, IL</td></tr>
<tr><td></td><td colspan="2">Grand Ballroom</td></tr>
<tr><td>8:00 pm – 11:00 pm</td><td colspan="2">DIAGNOSTIC SLIDE SESSION
11 Cases for Discussion
(Caterina Giannini, MD, PhD, Moderator and Rebecca D. Folkerth, MD, Manager)</td></tr>
</table>

2019 MEETING AT A GLANCE

2019 PRESIDENTIAL SYMPOSIUM

New Ways to Look at the Brain - What Can Neuropathologists See?

Director: Matthew P. Frosch, MD, PhD

Sunday, June 9, 2019	
Time:	**Grand Ballroom**
7:00 am – 8:00 am	**CONTINENTAL BREAKFAST** Prefunction
8:00 am – 8:05 am	*Welcome and CME Pre-Test* Matthew P. Frosch, MD, PhD Massachusetts General Hospital, Boston, MA
8:05 am – 8:45 am	*Neuropathology for the Future: Knowing Where to Look and New Ways to Look* Matthew P. Frosch, MD, PhD Massachusetts General Hospital, Boston, MA
8:45 am – 9:35 am	**MOORE LECTURE** *Rapid and Holistic 3D Imaging of Large-scale Tissues* Kwanghun Chung, PhD Massachusetts Institute of Technology, Cambridge, MA
9:35 am – 10:05 am	**AANP AWARDS PRESENTATIONS**
10:05 am – 10:20 am	**REFRESHMENT BREAK** Prefunction
10:20 am – 11:10 am	*Expansion Microscopy* Edward Boyden, PhD Massachusetts Institute of Technology, Cambridge, MA
11:10 am – 12:00 pm	*Histologic Validation of High-Resolution Ex Vivo Neuroimaging* Jean Augustinack, PhD Massachusetts General Hospital, Boston, MA
12:00 pm – 12:30 pm	**INSTALLATION OF NEW OFFICERS AND ADJOURNMENT**

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Special Course

Thursday, June 6, 2019

Learning Objectives:

1. *Discuss the adverse effects of systemic therapies on the central and peripheral nervous systems and neuromuscular system.*
2. *Identify ways to mitigate the adverse effects of systemic therapies.*
3. *Cite 2-3 examples of new research providing information on underlying mechanisms of neurological diseases.*

SPECIAL COURSE

CAR-T cell therapy associated neurotoxicities

Time: 8:15 am – 9:05 am

Jörg Dietrich, MD, PhD, MMSc, FAAN, *Massachusetts General Hospital, Boston, MA*

I. Learning Objectives

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

1. Describe common types and patterns of neurotoxicities encountered in patients treated with CAR-T cells for systemic malignancies.
2. Define potential mechanisms of CAR-T cell related neurotoxicities.
3. Explain management considerations of patients with CAR-T cell associated neurotoxicities.

II. Abstract & Relevant References

Novel immunotherapies, such as CAR-T cell therapies, are associated with unique patterns of neurotoxic syndromes not previously encountered with traditional cancer therapies. An increase in knowledge about the clinical presentation, underlying mechanisms and potential biomarkers of neurotoxicity is a critical step to improve patient management and overall outcomes. This session will provide an overview of challenging neurotoxic symptoms encountered in patients treated with CAR-T cells, discuss unique laboratory and neuroimaging findings and review management considerations of affected patients.

References

1. Karschnia P et al. Clinical presentation, management, and potential biomarkers of neurotoxicity after adoptive immunotherapy with CAR T-cells. *Blood,* Feb 26, 2019 (epub ahead of print)
2. June CH and Sadelain M. Chimeric antigen receptor therapy. *N Engl J Med.* 2018;379(1): 64-73
3. Santomasso BD et al. Clinical and biological correlates of neurotoxicity associated with CAR T-cell therapy in patients with B-cell acute lymphoblastic leukemia. *Cancer Discov*. 2018;8(8): 958-971
4. Neelapu SS et al. Chimeric antigen receptor T-cell therapy - assessment and management of toxicities. *Nat Rev Clin Oncol*. 2018;15(1): 47-62
5. Gust J et al. Endothelial activation and blood-brain barrier disruption in neurotoxicity after adoptive immunotherapy with CD19 CAR-T cells. *Cancer Discov*. 2017;7(12): 1404-1419.

III. Faculty Biography

Jörg Dietrich, MD, PhD, MMSc, FAAN, is the Director of the *Cancer & Neurotoxicity Clinic and Brain Repair Research Program* at the Massachusetts General Hospital (MGH) Cancer Center, Attending Physician at MGH, and Assistant Professor of Neurology at Harvard Medical School. His clinical interests are management of patients with benign and malignant brain tumors and neurologic complications of cancer therapy, including toxicity from conventional radiation and chemotherapy and novel immunotherapies. His research activities include clinical, translational and basic research in the fields of brain tumor biology, biomarkers of cancer, neurotoxicity from cancer therapies and brain repair mechanisms. Dr. Dietrich is the author of over 150 publications, including original research articles, review papers, book chapters and other scientific contributions. His work has been supported by the National Institute of Health (NIH), the American Cancer Society (ACS), the American Academy of Neurology (AAN) and other foundations.

SPECIAL COURSE

Neurotoxicity associated with CAR T cell immunotherapy

Time: 9:05 am – 9:30 am

Juliane Gust, MD, PhD, *University of Washington, Seattle Children's Hospital, Seattle, WA*

I. Learning Objectives

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

1. Correlate acute imaging abnormalities with pathology findings in CAR T cell associated neurotoxicity.
2. Categorize typical manifestations of immunotherapy-associated neurotoxicity.
3. Explain the role of different components of the blood-brain-barrier with proposed mechanisms of neurotoxicity.

II. Abstract & Relevant References

Neurotoxicity is seen in about 30-40% of patients undergoing CD19-directed CAR T cell cancer immunotherapy. This neurotoxicity is beginning to be understood as part of the emergent entity of immune effector cell associated neurotoxicity syndrome (ICANS). A rare complication is fatal cerebral edema. This presentation will show histopathologic findings from several autopsy cases of CAR T cell patients who succumbed to neurotoxicity, as well as chronic pathology in patients who survived neurotoxicity but died later from cancer-related complications.

References:

1. Gust, J., Hay, K.A., Hanafi, L.-A., Li, D., Myerson, D., Gonzalez-Cuyar, L.F., Yeung, C., Liles, W.C., Wurfel, M., Lopez, J.A., et al. (2017). Endothelial Activation and Blood-Brain Barrier Disruption in Neurotoxicity after Adoptive Immunotherapy with CD19 CAR-T Cells. Cancer Discov. 7, 1404–1419.
2. Gust, J., Taraseviciute, A., and Turtle, C.J. (2018). Neurotoxicity Associated with CD19-Targeted CAR-T Cell Therapies. CNS Drugs 32, 1091–1101.
3. June, C.H., O'Connor, R.S., Kawalekar, O.U., Ghassemi, S., and Milone, M.C. (2018). CAR T cell immunotherapy for human cancer. Science 359, 1361–1365.
4. Lee, D.W., Santomasso, B.D., Locke, F.L., Ghobadi, A., Turtle, C.J., Brudno, J.N., Maus, M.V., Park, J.H., Mead, E., Pavletic, S., et al. (2019). ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biol. Blood Marrow Transplant. J. Am. Soc. Blood Marrow Transplant. 25, 625–638.
5. Santomasso, B.D., Park, J.H., Salloum, D., Riviere, I., Flynn, J., Mead, E., Halton, E., Wang, X., Senechal, B., Purdon, T., et al. (2018). Clinical and Biological Correlates of Neurotoxicity Associated with CAR T-cell Therapy in Patients with B-cell Acute Lymphoblastic Leukemia. Cancer Discov. 8, 958–971.
6. Torre, M., Solomon, I.H., Sutherland, C.L., Nikiforow, S., DeAngelo, D.J., Stone, R.M., Vaitkevicius, H., Galinsky, I.A., Padera, R.F., Trede, N., et al. (2018). Neuropathology of a Case with Fatal CAR T-Cell-Associated Cerebral Edema. J. Neuropathol. Exp. Neurol.
7. Gust, J., Finney, O.C., Li, D., Brakke, H.M., Hicks, R.M., Futrell, R.B., Gamble, D.N., Rawlings-Rhea, S.D., Khalatbari, H.K., Ishak, G.E., et al. (2019). Glial injury in neurotoxicity after pediatric CD19-directed CAR-T cell therapy. Ann. Neurol.

III. Faculty Biography

Dr. Gust is a pediatric neurologist at Seattle Children's/University of Washington who is interested in the effects of systemic inflammation and cancer on the developing brain. During residency training at the University of Washington, she saw many cases of neurologic toxicity in patients undergoing treatment on early CAR T cell clinical trials and began work to define and understand this emergent syndrome. She has received the Child Neurology Career Development Program K12 award to continue research on the basic mechanisms and clinical manifestations of immunotherapy-associated neurotoxicity.

SPECIAL COURSE

Methotrexate and Other Cancer Chemotherapy Effects on the Brain and Peripheral Nervous System

Time: 9:30 am – 10:20 am

Hannes Vogel, MD, *Stanford University, Palo Alto, CA*

I. Learning Objectives

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

1. Recall the key historical advances in characterizing cancer therapy-induced leukoencephalopathies, and the important epidemiological aspects of current cancer chemotherapy upon brain function.
2. Summarize the etiological factors in producing cognitive deficiencies ("chemo brain") and key neuropathological changes following methotrexate and other chemotherapeutic treatments, including the combined effect of radiation therapy.
3. List the dose and duration-limiting chemotherapies that are toxic to the peripheral nervous system and their pathological effects.

II. Abstract & Relevant References

Characterizing the neuropathology of cancer chemo- and radiation therapy has paralleled the advent of drugs and modes of therapy in the modern era of cancer treatment. Disseminated necrotizing leukoencephalopathy (DNL) was first described as a severe, progressive, and usually fatal form of disease in children with metastatic acute lymphoblastic leukemia treated with high-dose methotrexate (MTX) and whole brain irradiation. Similar examples were later reported both in adults and in other tumor types, especially tumors which continue to require otherwise less frequently used whole brain irradiation. Pathologically, multifocal isolated or confluent foci of noninflammatory demyelination or white matter necrosis is seen. Radiation itself carries a risk of injury, especially to endothelial cells and oligodendrocytes, but the rate of leukoencephalopathy is enhanced 3-fold when chemotherapy is added.

Another significant consequence of cancer chemotherapy in addition to a reversible form of acute injury is a syndrome of cognitive decline, learning and memory difficulties, and mental slowing termed "chemotherapy brain". The syndrome affects over three quarters of people treated for cancer. Currently, 15.5 million cancer survivors live in the US alone, and this number is projected to increase to 20.3 million by 2026. Neural precursor cell dysfunction and white matter dysfunction are thought to contribute to this debilitating syndrome, which is particularly associated with chemotherapeutic regimens that include agents such as MTX as well as other anti-metabolite drugs. Recent studies provide evidence that chemotherapy-related white matter pathology and cognitive impairment are caused by primary changes in glial cell (microglia and astrocyte) circuitry, in which persistent depletion of oligodendrocyte precursor cells (OPCs) is a hallmark feature of the disease. OPCs are particularly sensitive to chemotherapeutic agents. Treatment reduces OPC proliferation and increases OPC differentiation, leading to long-term depletion of mature white matter oligodendrocytes, a reduction in myelin sheath thickness and behavioral deficits, all demonstrable in a mouse model. The effect was mediated by resident microglia: pharmacologic depletion of microglia corrected the MTX-induced reductions in oligodendrocyte density and myelin sheath thickness, as well as the associated cognitive and behavioral deficits. A histological mimic occurs in the pons without exposure to chemotherapy but in apparent association with immunosuppression.

Chemotherapy-induced peripheral neuropathies are a rapidly emerging form of toxicity whereby the doses and duration of therapies is strictly limited by resulting neuropathies. Most are subacute or chronic, length-dependent distal symmetrical, mostly sensory neuropathies. Implicated drugs include microtubular agents (vinca alkaloids, taxanes), ion channel agents (ex. cisplatin), proteasome inhibitors (bortezomib), and mitotoxins. Combinations between commonly used agents such as paclitaxel and bevacizumab may predispose to peripheral neuropathies. The nerve pathology in most cases is that of an axonal neuropathy with few distinguishing features between these chemotherapy neurotoxins.

References:

1. Anders, KH, et al. (1993). Multifocal necrotizing leukoencephalopathy with pontine predilection in immunosuppressed patients: a clinicopathologic review of 16 cases. Hum Pathol; 24: 897–904. PMID: 8375859
2. Bilbao, JM, and Schmidt. (2015). "Toxic neuropathies" In: Biopsy Diagnosis of Peripheral Neuropathy. 355-367
3. Dietrich, J, et al. (2006). CNS progenitor cells and oligodendrocytes are targets of chemotherapeutic agents in vitro and in vivo. J. Biol. 5, 22. PMID: 17125495
4. Ebi J, Sato H, Nakajima M, Shishido F. Incidence of leukoencephalopathy after whole-brain radiation therapy for brain metastases. Int J Radiat Oncol Biol Phys. 2013 Apr 1;85(5):1212-7. PMID: 23102839
5. Ellenberg, L, et al. (2009). Neurocognitive status in long-term survivors of childhood CNS malignancies: a report from the Childhood Cancer Survivor Study. Neuropsychology 23, 705–717. PMID: 19899829
6. Gibson, E, and Monje, M. (2012). Effect of cancer therapy on neural stem cells: implications for cognitive function. Curr. Opin. Oncol. 24, 672–678. PMID: 22913969
7. Gibson, EM, et al. (2019). Methotrexate chemotherapy induces persistent tri-glial dysregulation that underlies chemotherapy-related cognitive impairment. Cell 176, 43–55. PMID 30528430
8. Matsuoka, A, et al. (2016). Bevacizumab Exacerbates Paclitaxel-Induced Neuropathy: A Retrospective Cohort Study. PLoS One. 11(12):e0168707. doi: 10.1371/journal.pone.0168707. eCollection 2016. PMID: 27992556
9. Rubinstein, LJ, et al. (1975). Disseminated necrotizing leukoencephalopathy: a complication of treated central nervous system leukemia and lymphoma. Cancer. 35:291-305 PMID1053934
10. Wefel, JS, and Schagen, SB. (2012). Chemotherapy-related cognitive dysfunction. Curr Neurol Neurosci Rep. 12:267-275 PMID22453825

III. Faculty Biography

Hannes Vogel is Professor of Pathology and Pediatrics at Stanford University where he has served as Director of Neuropathology since 2002. His background in medical training also includes board certification in Pediatrics. Dr. Vogel completed a residency in Anatomic Pathology at Beth Israel Hospital in Boston, followed by a neuropathology fellowship at Stanford University under Dikran Horoupian. He returned to Baylor College of Medicine in Houston, TX where he became the Director of Neuropathology at Texas Children's Hospital before returning to Stanford. His principle interests include mitochondrial diseases, muscle and nerve pathology, brain tumors and the toxic effects of therapy, and forensic neuropathology.

SPECIAL COURSE

Immune Response within the CNS to Systemic Therapies

Time: 10:50 am – 11:40 am

Avindra Nath, MD, *National Institute of Neurological Disorders and Stroke, Bethesda, MD*

I. Learning Objectives

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

1. Identify systemic therapies that cause T cell encephalitis.
2. Describe neuropathology of immune reconstitution inflammatory syndrome (IRIS).
3. Outline pathophysiological mechanisms that cause IRIS.

II. Abstract & Relevant References

T cell encephalitis can occur from a number of systemic therapies. It has been best studied in the context of antiretroviral therapy in HIV infected patients. Here, it may occur despite adequate control of the virus in the periphery and in the absence of opportunistic infections. The clinical syndrome may vary from an acute to a chronic encephalitis. Pathological findings include multifocal infiltration of predominantly CD8 T cells, neurodegeneration and glial cell activation. Demyelination is unusual although further characterization of the pathological findings is needed. Activated T cells cause non-specific neurotoxicity by releasing granzyme B which activates PAR receptors on neurons and causes cytokine release from glial cells. This provides several novel therapeutic targets that might be broadly applicable to T cell medicated encephalitis.

References:

1. Lee PR, Johnson TP, Gnanapavan S, Giovannoni G, Wang T, Steiner JP, Medynets M, Vaal MJ, Gartner V, Nath A. Protease-activated receptor-1 activation by granzyme B causes neurotoxicity that is augmented by interleukin-1β. *J Neuroinflammation*. 2017 Jun 27;14(1):131
2. Johnson TP, Patel, K, Johnson K, Maric D, Calabresi, P, Hasbun R, Nath A. Induction of IL-17 and non-classical T-cell activation by HIV-Tat protein. *Proc Natl Acad Sci*, 2013,110(33):13588-93.
3. Bowen L, Nath A, Smith B. CNS immune reconstitution inflammatory syndrome. Chapter 13, *Handbook of Clinical Neurology* Vol 152 (3rd series). Pages 167-176. The Neurology of HIV infection. B.J. Brew Editor. Elsevier 2018
4. Johnson T, Nath A. Immune reconstitution inflammatory syndrome and the central nervous system. *Current Opinion Neurology* 2011; 24:284-290.
5. Post JD, Thurnher, MM, Clifford DB, Nath A, Gonzalez RG, Gupta, RK, Post KK. CNS-IRIS in the setting of HIV infection Part II: Overview and discussion of neuro-IRIS with and without other pathogens. *Am J Neuroradiology* July 12, 2012
6. Johnson T, Nath A. New insights into CNS-immune reconstitution inflammatory syndrome. *Current Opinion in HIV AIDS*. 2014 Nov;9(6):572-8.
7. Li T, McArthur JC, Clifford D, Major EO, Nath A. Immune reconstitution inflammatory syndrome in natalizumab-associated PML. *Neurology* 2011 Sep 13;77(11):1061-7. Editorial (pages 1033-34) and Podcast. Correspondence: *Neurology* 2012 Jan 3;78(1):73

III. Faculty Biography

Dr. Nath is the Clinical Director and the Chief of the Section of Infections of the Nervous System at the National Institute of Neurological Disorders and Stroke (NINDS) at NIH, positions he has held since 2011. Prior to this he was Professor of Neurology and Director of the Division of Neuroimmunology and Neurological Infections at Johns Hopkins University. He received his medical training from Christian Medical College in India and did a residency in Neurology and a fellowship in Neuroimmunology at the University of Texas Health Sciences in Houston where he trained in both clinical and bench research. This was during the beginning of the AIDS pandemic when he was one of the first to report neurological complications of HIV infection and characterize the immune dysfunction in these patients. He then did another research fellowship at NINDS where he studied the mechanisms of establishment of HIV reservoirs in the brain. Since then his clinical and laboratory research has focused on the neuropathogenesis of HIV infection and the development of novel therapeutic strategies. His laboratory is credited for demonstrating a critical role of HIV-Tat protein in HIV-mediated neuro-glial dysfunction and astrocytes as a long-term reservoir of HIV infection. He was one of the first to describe immune reconstitution inflammatory syndrome in the brain of HIV-infected patients and to study its pathophysiology. In recent years, his laboratory has been studying the role of endogenous retroviruses in neurodegenerative diseases. He is the past president and recipient of the Pioneer award from the International Society of Neurovirology. He is an elected member of the Association of American Physicians and the editor of a book on Clinical Neurovirology.

SPECIAL COURSE

The Neuropathology of Immune-related Adverse Events in Checkpoint Inhibitor Therapy

Time: 11:40 pm – 12:30 pm

Maria Martinez-Lage, MD, *Massachusetts General Hospital, Boston, MA*

I. Learning Objectives

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

1. Describe the general mechanism of action of checkpoint inhibitor therapy and immune-related adverse events.
2. Name the most common neurological immune-related adverse events associated with checkpoint inhibitor therapy.
3. Summarize the neuropathological findings found in neurological immune-related adverse effects associated with checkpoint inhibitors.

II. Abstract & Relevant References

Since the initial FDA approval of ipilimumab for metastatic melanoma in 2011, the field of cancer immunotherapy has exponentially advanced to include several approved drugs now considered standard of care for a variety of oncologic indications. Checkpoint inhibitors interfere with natural immune modulating pathways such as CTLA4 (ipilimumab) and PD1/PDL1 (pembrolizumab, nivolumab, atezolizumab, and others), through which individual cells negatively regulate the activity of T-cells. This interference "releases the break" set on the immune system by tumor cells, allowing for immune-mediated tumor degradation. Subsequently, however, immune-related adverse events (irAEs) arise as complications, since the effect of these drugs is not limited to the tumor niche. A "secondary autoimmunity" arises in some patients, directed preferentially towards a number of organ systems. As more and more patients receive these therapies, the less common adverse events, including neurological irAEs, are becoming more frequent. Neuropathologists will benefit from becoming familiar with these potential complications that resemble autoimmune disorders and vary in severity from the mild ones that improve with therapy interruption, to those that are life threatening.

References:

1. Cuzzubbo S, et al. Neurological adverse events associated with immune checkpoint inhibitors: Review of the literature. Eur J Cancer. 2017 Mar;73:1-8. PMID: 28064139
2. Fellner A, et al. Neurologic complications of immune checkpoint inhibitors. J Neurooncol. 2018 May;137(3):601-609. PMID: 29332184
3. Kao JC, et al. Neurological Complications Associated With Anti-Programmed Death 1 (PD-1) Antibodies. JAMA Neurol. 2017 Oct 1;74(10):1216-1222. PMID: 28873125
4. Knauss S, et al. PD1 pathway in immune-mediated myopathies: Pathogenesis of dysfunctional T cells revisited. Neurol Neuroimmunol Neuroinflamm. 2019 Apr 10;6(3):e558. PMID: 31044146
5. Yshii LM, et al. Inflammatory CNS disease caused by immune checkpoint inhibitors: status and perspectives. Nat Rev Neurol. 2017 Dec;13(12):755-763 PMID: 29104289

III. Faculty Biography

Maria Martinez-Lage, MD, is an assistant professor of pathology at Harvard Medical School, and a board-certified neuropathologist and head and neck/endocrine pathologist at Massachusetts General Hospital. After completing residency training in neurology in Barcelona, Spain, she decided to pursue a career in pathology and completed anatomic pathology and neuropathology training, followed by a fellowship in selective surgical pathology at the University of Pennsylvania, where she stayed as faculty. She has participated in neuropathology education at diverse national venues such as the ASCP and the USCAP annual meetings and has served as a member of several AANP committees. Her research interests include the morphological and molecular diagnosis of brain tumors, as well as their immunological microenvironment, the neurotoxicity of systemic and local therapies, and other disorders of the nervous system, with an emphasis on translational and clinical applications.

SPECIAL COURSE

The Neuropathology of Amyloid-β Immunotherapy for Alzheimer's Disease: Implications for Pathogenesis and Clinical Trials

Time: 1:45 pm – 2:35 pm

James Nicoll, BSc, MBChB, MD, FRCPath, *Clinical Neurosciences, Clinical & Experimental Sciences, University of Southampton; Cellular Pathology, University Hospital Southampton, Southampton, UK*

I. Learning Objectives

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

1. Explain the rationale for trying amyloid-β immunotherapy for Alzheimer's disease.
2. Assess the contribution of post mortem neuropathology to recent clinical trials of amyloid-β immunotherapy for Alzheimer's disease.
3. Appraise the evidence that progressive tau pathology explains the failure of clinical trials of amyloid-β immunotherapy for established Alzheimer's disease.

II. Abstract & Relevant References

The amyloid cascade hypothesis for Alzheimer's disease (AD) puts accumulation of amyloid-β (Aβ) as a key initiating factor in the pathogenesis. We have performed a long term neuropathology follow up of patients in the first trial of Aβ immunotherapy for AD. The main findings include removal of plaques, with an active vaccine effect that can last for as long as 14 years. There were additional alterations in vascular pathology, inflammation and tau pathology, providing information related to disease pathogenesis. These studies have helped to guide subsequent clinical trials of Aβ immunotherapy providing information on: (i) side effects encountered ("amyloid-related imaging abnormalities"); (ii) providing a possible explanation why most of these trials have not shown slowing of cognitive decline despite plaque removal, potentially due to persisting spread of tau pathology through the brain; (iii) as nearly a quarter of the subjects did not have AD as the cause of their dementia, highlighting the need for biomarkers for more accurate diagnosis during life; and (iv) encouraging intervention earlier in the disease process. In terms of pathogenesis, a sequence of Aβ accumulation followed by an inflammatory reaction which promotes tau accumulation and neurodegeneration explains much of the evidence. It is proposed that different therapeutic targets are required for different stages of the disease process: Aβ for primary prevention, inflammation for secondary prevention and tau for established disease. Despite recent advances in imaging technology, these studies highlight the value of post mortem neuropathology in trials of therapy for neurodegenerative conditions.

References:

1. Persistent neuropathological effects 14 years following amyloid-β immunisation in Alzheimer's disease JAR Nicoll, GR Buckland, C Harrison, A Page, S Harris, S Love, JW Neal, C Holmes, D Boche (in press).
2. Effect of active Aβ immunotherapy on neurons in human Alzheimer's disease. (2015) Paquet C, Amin J, Mouton-Liger F, Nasser M, Love S, Gray F, Pickering RM, Nicoll JA, Holmes C, Hugon J, Boche D. J Pathol. 235(5):721-30.
3. Aβ immunotherapy for Alzheimer's disease: effects on apoE and cerebral vasculopathy. (2014) Sakai K, Boche D, Carare R, Johnston D, Holmes C, Love S, Nicoll JA. Acta Neuropathol. 128:777-89.
4. Inflammatory components in human Alzheimer's disease and after active amyloid-β42 immunization. (2013) Zotova E, Bharambe V, Cheaveau M, Morgan W, Holmes C, Harris S, Neal JW, Love S, Nicoll JA, Boche D. Brain. 136, 2677-96.
5. Neuropathology after active Abeta42 immunotherapy: implications for Alzheimer's disease pathogenesis. Boche D, Denham N, Holmes C, Nicoll JA. (2010) Acta Neuropathol. 120: 369-384.

6. Reduction of aggregated Tau in neuronal processes but not in the cell bodies after Abeta42 immunisation in Alzheimer's disease. Boche D, Donald J, Love S, Harris S, Neal JW, Holmes C, Nicoll JA. (2010) Acta Neuropathol. 120: 13-20.
7. Long term effects of Aβ42 immunization in Alzheimer's disease: follow-up of a randomised, placebo-controlled phase I trial. Holmes C, Boche D, Wilkinson D, Yadegarfar G, Hopkins V, Bayer A, Jones RW, Bullock R, Love S, Neal JW, Zotova E, Nicoll JA (2008) Lancet 372, 216-23.
8. Neuropathology of human Alzheimer's disease after immunization with amyloid-β peptide: a case report. Nicoll JA, Wilkinson D, Holmes C, Steart P, Markham H, Weller RO (2003) Nature Medicine 9, 448-52.

III. Faculty Biography

Having graduated in Medicine from the University of Bristol, James Nicoll trained in Pathology in Oxford and Cardiff and returned to Bristol to undertake specialist training in Neuropathology. He then held a clinical academic post in Neuropathology at the Institute of Neurological Sciences/University of Glasgow. While in Glasgow he developed interests in the parallels between the response of the brain to acute injury, for example due to trauma or stroke, and Alzheimer's disease; specifically that they share common cellular reactions, upregulation of similar proteins and possibly share genetic influences. Prof Nicoll has been Professor of Neuropathology and Honorary Consultant Neuropathologist in Southampton since 2001. He shares responsibility for providing the clinical diagnostic neuropathology service to the Wessex Region (a population of approximately 4 million). In Southampton Prof Nicoll has continued his research interests in neuroinflammation, neurodegeneration and cerebrovascular disease. His work closely links diagnostic neuropathology and neuroscience research. He and his colleagues were the first in the world to describe and characterise the effects on the brain of immunisation against Aβ, being used as potential therapy in Alzheimer's disease.

SPECIAL COURSE

Gut Microbiome and Alzheimer's Disease

Time: 2:35 pm – 3:25 pm

Barbara B. Bendlin, PhD, *University of Wisconsin, Madison, WI*

I. Learning Objectives

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

1. Describe the experimental methods used to study gut microbiome.
2. Evaluate the evidence linking microbes to Alzheimer's disease.
3. Summarize the potentially modifiable mechanisms by which gut microbiota may impact neurodegenerative disease.

II. Abstract & Relevant References

Studies considering a microbial etiology of Alzheimer's disease have a controversial history, but emerging evidence points toward a potential role of microbes, including gut microbiota, in the development or exacerbation of Alzheimer's disease pathology. This presentation will provide a primer on microbes that have been studied in relation to Alzheimer's disease, introduce the tools used to study gut microbiota, provide an overview of recent studies that link gut microbiome to Alzheimer's disease, and finally, consider whether the evidence is strong enough to support exploration of new strategies for prevention and treatment of Alzheimer's disease.

References:

1. Readhead et al. Multiscale Analysis of Independent Alzheimer's Cohorts Finds Disruption of Molecular, Genetic, and Clinical Networks by Human Herpesvirus. Neuron. 2018 Jul 11;99(1):64-82.e7. doi: 10.1016/j.neuron.2018.05.023.
2. Dominy et al. Porphyromonas gingivalis in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors. Science Advances 23 Jan 2019: Vol. 5, no. 1, eaau3333, doi: 10.1126/sciadv.aau3333.
3. Harach et al. Reduction of Abeta amyloid pathology in APPPS1 transgenic mice in the absence of gut microbiota. Sci. Rep. 2017;7:41802. doi: 10.1038/srep41802.
4. Minter et al. Antibiotic-induced perturbations in microbial diversity during post-natal development alters amyloid pathology in an aged APPSWE/PS1ΔE9 murine model of Alzheimer's disease. Sci Rep. 2017 Sep 5;7(1):10411. doi: 10.1038/s41598-017-11047-w
5. Kumar et al. Amyloid-β peptide protects against microbial infection in mouse and worm models of Alzheimer's disease. Sci Transl Med. 2016 May 25;8(340):340ra72. doi: 10.1126/scitranslmed.aaf1059. doi: 10.1126/scitranslmed.aaf1059
6. Vogt et al. Gut microbiome alterations in Alzheimer's disease. Sci Rep. 2017 Oct 19;7(1):13537. doi: 10.1038/s41598-017-13601-y. doi: 10.1038/s41598-017-13601-y
7. Fülling et al. Gut Microbe to Brain Signaling: What Happens in Vagus… Neuron. 2019 Mar 20;101(6):998-1002. doi: 10.1016/j.neuron.2019.02.008.
8. Williams. Gnotobiotics. Proc Natl Acad Sci U S A. 2014 Feb 4; 111(5): 1661. 2014 Feb 4. doi: 10.1073/pnas.1324049111

III. Faculty Biography

Dr. Bendlin received her doctorate from the University of Arizona, and she is currently Associate Professor of Medicine at the University of Wisconsin-Madison, and Principal Investigator at the Wisconsin Alzheimer's Disease Research Center. Dr. Bendlin's research group is studying factors that may impact trajectories of brain aging and dementia risk, including type 2 diabetes, sleep, exercise, diet, gut microbiome, and socioeconomic disadvantage. She leads several NIH-funded studies, including the Alzheimer's Disease Connectome Project.

SPECIAL COURSE

The Pathology of Systemic Therapy-Related Neuromuscular Disease

Time: 3:55 pm – 4:45 pm

Karra Jones, MD, PhD, *The University of Iowa, Iowa City, IA*

I. Learning Objectives

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

1. Recognize common histopathologic patterns of systemic therapy-related neuromuscular disease.
2. Recall common neuromuscular diseases included in the differential diagnosis of toxic myopathies.
3. Plan an appropriate diagnostic approach for evaluation of toxic myopathies.
4. Summarize known and proposed mechanisms underlying systemic therapy-related neuromuscular disease.

II. Abstract & Relevant References

During the diagnostic workup of muscle biopsies, systemic therapy-related disease can be overlooked, particularly when the appropriate clinical history is not provided. Significant overlap in the histopathology of toxic myopathies and inherited myopathies, muscular dystrophies, or inflammatory/immune-mediated diseases contributes to this challenge. While some medications are widely known to cause iatrogenic muscle disease, others are less common and may not even be suspected by the treating clinicians. Yet, identification of the offending agent is of utmost importance because removal of the medication is always the first step in therapy and in some cases can result in a complete cure without additional treatment. In this lecture we will look at the histopathology of therapy-related neuromuscular disease using a pattern-based classification system and discuss pertinent differential diagnoses, how to plan a diagnostic approach using key muscle biopsy evaluation modalities and review the known or proposed mechanisms driving systemic therapy-related neuromuscular disease.

References:

1. Casado E, Gratacos J, Tolosa C, Martinez JM, Ojanguren I, Ariza A, Real J, Sanjuan A, Larrosa M. Antimalarial myopathy: an underdiagnosed complication? Prospective longitudinal study of 199 patients. Ann Rheum Dis. 2006 Mar;65(3):385-90.
2. Fernandez C, Figarella-Branger D, Alla P, Harle JR, Pellissier JF. Colchicine myopathy: a vacuolar myopathy with selective type I muscle fiber involvement. Acta Neuropathol. 2002; 103:100-106.
3. Lane R. Toxic and drug-induced myopathies. Chapter 23, pages 539-552. In Muscle Biopsy: A Practical Approach, 4th edition. Dubowitz, Sewry, and Oldfors. Elsevier Saunders, Philadelphia, 2013.
4. Mammen AL. Statin-associated autoimmune myopathy. N Engl J Med. 2016 Feb;374(7):664-9.
5. Pasnoor M, Barohn RJ, Dimachkie MM. Toxic myopathies. Neurol Clin. 2014 Aug;32(3):647-70.
6. Shepherd S, Batra A, Lerner DP. Review of critical illness myopathy and neuropathy. Neurohospitalist. 2017 Jan;7(1):41-48.

III. Faculty Biography

Karra Jones is a neuropathologist at the University of Iowa with a specific focus on neuromuscular diseases. She completed her MD/PhD training at the University of Kansas School of Medicine where she examined peripheral nerve innervation of muscle spindles in the setting of diabetic neuropathy in the Department of Anatomy and Cell Biology. She then completed anatomic pathology residency and neuropathology fellowship at the University of California, San Diego where she subsequently worked as a Clinical Instructor in diagnostic neuropathology, led the neuromuscular pathology service, and assisted in biorepository and biomarker laboratory efforts. Dr. Jones moved back to the Midwest in 2016 to join the neuropathology group at the University of Iowa Carver College of Medicine as a Clinical Assistant Professor where she practices clinical neurosurgical and neuromuscular pathology and autopsy and forensic-related neuropathology and loves teaching trainees of all levels. Her research is increasingly focused on neuromuscular diseases with interest in inherited muscular dystrophies, and she continues to collaborate on glioma and biomarker-related research projects. Dr. Jones is also a member of the College of American Pathologists Neuropathology Committee.

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Overview: Scientific Sessions

Friday, June 7, 2019 &
Saturday, June 8, 2019

All abstracts of the papers presented in this program are published in the June 2019 issue of the *Journal of Neuropathology and Experimental Neurology.*

FRIDAY PLATFORMS 1 & 2

	Platform Session 1: ***Neurodegenerative: FTLD/Lewy Body/Other*** **Grand Ballroom** **Moderators: Anne Hiniker, MD, PhD; Richard Perrin, MD, PhD**	**Platform Session 2:** ***Muscle/Nerve*** **Buckhead Ballroom** **Moderators: Marta Margeta, MD, PhD; Michael Lawlor, MD, PhD**
8:00 am – 8:15 am	**1** **Corticobasal degeneration with pallidonigroluysial atrophy and TDP-43 pathology: a distinct clinicopathologic variant** Nikhil Ghayal, Shunsuke Koga, Keith Josephs, J. Ahlskog, Zbigniew Wszolek, Dennis Dickson	**9** **A Keratinocyte-Derived Mechanism of Nicotinamide Riboside to Prevent and Reverse Diabetic Neuropathy** Cheng-Ying Ho, Krish Chandrasekaran, James Russell
8:15 am – 8:30 am	**2** **Intermediate C9orf72 Repeats in Corticobasal Degeneration** Christopher Cali, Maribel Patino, Jessica Phan, PSP Genetics Consortium, Bernardino Ghetti, Vivianna Van Deerlin, Virginia Lee, John Trojanowski, Kin Mok, Helen Ling, Dennis Dickson, Gerard Schellenberg, Edward Lee	**10** **Muscle Biopsy Evaluation to Interpret Genetic Variants of Unknown Significance: An Institutional Experience** Karra Jones, Steven Moore
8:30 am – 8:45 am	**3** **Dementia in ALS: the role of the cerebellum.** Lindsey Lowder, Seneshaw Asress, Eric Dammer, Juan Carlos Vizcarra, Duc Duong, Abigail Goodman, Pritha Bagchi, Marla Gearing, David Gutman, Nicholas Seyfried, Jonathan Glass	**11** **Gene Therapy Trial in X-Linked Myotubular Myopathy (XLMTM): Update on Preliminary Safety, Efficacy and Pathology with AT132** Michael Lawlor, Benedikt Schoser, Caroline Sewry, Marta Margeta, James Dowling, Carsten Bonnemann, Nancy Kuntz, Wolfgang Muller-Felber, Mo Noursalehi, Salvador Rico, Laurent Servais, Perry Shieh, Barbara Smith, Suyash Prasad
8:45 am – 9:00 am	**4** **Limbic-predominant Age-related TDP-43 Encephalopathy (LATE): Consensus Working Group Report** Peter Nelson, Dennis Dickson, John Trojanowski, Julie Schneider	**12** **Intra-mitochondrial lipofuscin accumulation with spherical dense body formation in mitochondrial myopathy** Jian-Qiang Lu, Thomas Hawke, Chuanzhu Yan, Mark Tarnopolsky
9:00 am – 9:15 am	**5** **Neuropathology of Parkinsonism in a Brain Bank for Neurodegenerative Disorders** Dennis Dickson	**13** **Adding Pompe disease to the list of autophagic vacuolar myopathies with sarcolemmal features** Peter Pytel, Karra Jones, Steve Moore
9:15 am – 9:30 am	**6** **Glial Heterogeneity in Huntington's Disease Through the Lens of Single Cell Nuclear RNA Sequencing** Osama Al Dalahmah, James Goldman	**14** **Neuromuscular pathology in Sjogren's syndrome: clinicopathologic features and associations with salivary gland inflammation** Kyle Conway, Sandra Camelo-Piragua
9:30 am – 9:45 am	**7** **Contextualizing the pathology in the essential tremor cerebellum: A patholog-omic approach in a spectrum of neurodegenerative diseases** Phyllis Faust, Chloë Kerridge, Debotri Chatterjee, Regina Martuscello, Sheng-Han Kuo, Peter Sims, Elan Louis	**15** **Dipeptide repeat and phospho-TDP pathology in the skeletal muscle of ALS patients with C9ORF72 repeat expansion** Matthew Cykowski, Dennis Dickson, Suzanne Powell, Joan Appel, Anithachristy Arumanayagam, Andreana Rivera, Stanley Appel
9:45 am – 10:00 am	**8** **FAM76B modulates microglia activation and neuroinflammation in neurodegenerative diseases** Qinwen Mao, Dongyang Wang, Xiaojing Zheng, Sandra Weintraub, William Muller, Marek-Marsel Mesulam, Eileen Bigio, Haibin Xia	**16** **Categorizing Peripheral Neuropathy Utilizing Machine Learning** Nkechi Okonkwo, Cheng-Ying Ho

FRIDAY PLATFORMS 3 & 4

	Platform Session 3 ***Glial Tumors*** **Grand Ballroom** **Moderators: Mirna Lechpammer, MD, PhD; David Solomon, MD, PhD**	**Platform Session 4** ***Developmental/Pediatrics/ Infectious*** **Buckhead Ballroom** **Moderators: Marc Del Bigio, MD, PhD; Jennifer Baccon, MD, PhD**
2:00 pm – 2:15 pm	**17** **Total Copy Number Variation and Clinical Outcome in Adult Astrocytoma Subtypes** Kanish Mirchia, Adwait Sathe, Jamie Walker, Mariano Viapiano, Kimmo Hatanpaa, Chao Xing, Timothy Richardson	**25** **The Neuropathology of MIRAGE Syndrome** Angela Viaene, Brian Harding
2:15 pm – 2:30 pm	**18** **De-convolving the Spatial and Molecular Landscapes of Infiltrating Glioma using Single Cell Nuclear RNA Sequencing** Osama Al Dalahmah, Athannasis Dovas, Erin Bush, Peter Sims, Jeffery Bruce, Vilas Menon, Peter Canoll	**26** **Neuropathological substrates of thanatophoric dysplasia** Homa Adle-Biassette, Aurèlie Beaufrère, Jeannette Nardelli, Suonavy Khung, Pierre Gressens, Annie Laquerrière
2:30 pm – 2:45 pm	**19** **Morphological And Molecular Characterization Of Intramedullary Astrocytomas.** Laetitia Lebrun, Barbara Meléndez Asensio, Oriane Blanchard, Nancy De Nève, Sarah De Clercq, Cedric Balsat, Matteo Riva, Olivier De Witte, Danielle Balériaux, Jacques Brotchi, Michael Bruneau, Christine Decaestecker, Nicky D'Haene, Isabelle Salmon	**27** **The Neuropathologic Spectrum of Krabbe Disease** Julia Kofler, Peter Pytel, Marc Del Bigio, Rafael Medina-Flores, Anne Rugari, Maria Escolar
2:45 pm – 3:00 pm	**20** **Not All p53-mutant Astrocytomas Are Created Equal** Thomas Pearce, Ronald Hamilton, Geoffrey Murdoch	**28** **Genetic mapping of diversity among developing brainstem motor neuron subtypes at single cell resolution** Matthew Rose, Alan Tenney, Daniel Creighton, Alon Gelber, Max Tischfield, Tommy Collins, Alicia Nugent, Phillip Ang, Sarah Izen, Matthew Bauer, Wentao Huang, Rahul Satija, Orit Rozenblatt-Rosen, Aviv Regev, Elizabeth Engle
3:00 pm – 3:15 pm	**21** **Predicted Frequency of False Positive FISH 1p/19q Co-deletion based on Chromosomal Microarray Analysis** Matthew Ball, Thomas Kollmeyer, Corinne Praska, Michelle McKenna, Caterina Giannini, Aditya Raghunathan, Mark Jentoft, Daniel Lachance, Benjamin Kipp, Robert Jenkins, Cristiane Ida	**29** **Ubiquitin Signaling in the Epigenetic Regulation of Neuronal Development** Cole Ferguson, Bonni Azad
3:15 pm – 3:30 pm	**22** **The Accuracy of Relying on Next Generation Sequencing (NGS) Alone to Diagnose Infiltrating Gliomas** Kwok Ling Kam, Christina Appin, Qinwen Mao, Sachie Ikegami, Marina Nikiforova, Somak Roy, Daniel Brat, Craig Horbinski	**30** **Graphite deposits are associated with distal catheter obstructions in ventriculoperitoneal shunts for hydrocephalus** Marc Del Bigio, Ravinder Sidhu, Colin Kazina, Demitre Serletis
3:30 pm – 3:45 pm	**23** **Targeted kinase inhibitor therapy for pediatric bithalamic diffuse gliomas with frequent EGFR exon 20 insertions** Gourish Mondal, Julieann Lee, Javier Villanueva-Meyer, Jessica Van Ziffle, Courtney Onodera, Patrick Devine, James Grenert, David Samuel, Rong Li, Laura Metrock, Lee-way Jin, Reuben Antony, Mouied Alashari, Samuel Cheshier, Nicholas Whipple, Carol Bruggers, Corey Raffel, Nalin Gupta, Cassie Kline, Alyssa Reddy, Anu Banerjee, Matthew Hall, Minesh Mehta, Ziad Khatib, Ossama Maher, Carole Brathwaite, Melike Pekmezci, Joanna Phillips, Andrew Bollen, Tarik Tihan, Arie Perry, David Solomon	**31** **Sepsis-Associated Axonal Injury (SAAXI)** Anne Shepler, Clayton Wiley, Geoffrey Murdoch, Julia Kofler
3:45 pm – 4:00 pm	**24** **Extensive brainstem infiltration is a common feature of end-stage cerebral glioblastomas** Michael Drumm, Karan Dixit, Sean Grimm, Priya Kumthekar, Rimas Lukas, Jeffrey Raizer, Kwok-Ling Kam, Alicia Steffens, Rodrigo Javier, Kathleen McCortney, Craig Horbinski	**32** **Neuropathological Alterations in Cases of Yellow Fever Submitted to Autopsy.** Fernando Frassetto, Amaro Nunes Duerte Neto, Sergio Rosemberg

FRIDAY POSTERS #33-#51

Friday, June 7, 2019		
Time:	**Poster #:**	**Highland Ballroom**
8:00 am – 5:00 pm	33	**An Institutional Experience with Low Level MGMT Promoter Methylation in Glioblastoma** Ernest Nelson, Stephen Bagley, Christopher Watt, Saima Rathore, Christos Davatzikos, MacLean Nasrallah
	34	**Fostering Antecedent T-cell Activation with 41BB Agonism Licenses Checkpoint Blockade in Murine Glioma** Karolina Woroniecka, Cosette Dechant, Kristen Rhodin, Pakawat Chongsathidkiet, Daniel Wilkinson, Xiuyu Cui, Peter Fecci
	35	**Clinically Determined Fusions in Gliomas: An Institutional Experience with a Fusion Transcript Panel** MacLean Nasrallah, Stephen Bagley, Arati Desai, Robyn Sussman, Jennifer Morrissette
	36	**Immunohistochemical Surrogates vs. Next Generation Sequencing for Molecular Alterations in Gliomas** Elena Daoud, Kimmo Hatanpaa, Rati Chkheidze, Paul Yell, Jack Raisanen, Chunyu Cai
	37	**Two Cases with Anaplastic Astroblastoma Histology and MN1 Gene Alterations** Oluwaseun Ogunbona, Lindsey Lowder, Abigail Goodman, Pia Mendoza, Jose Velazquez Vega, Stewart Neill, Matthew Schniederjan
	38	**Histopathology Evaluation of Recurrent Glioma Patients Enrolled to Phase I Clinical Trial of Oncolytic Virus rQNestin34.5v.2** Isaac Solomon, Hirotaka Ito, Hiroshi Nakashima, Yu Zeng, Kristine Pelton, Fiona Watkinson, Kin-Hoe Chow, Nathan Matthewson, Geoffrey Young, David Reardon, Scott Rodig, Sandro Santagata, Mario Suva, Kai Wucherpfennig, Sean Lawler, E. Chiocca, Keith Ligon
	39	**Targeted copy number analysis outperforms histological grading in predicting patient survival for WHO grade II/III IDH-mutant astrocytomas** P.J. Cimino, Eric Holland
	40	**Comprehensive Characterization of NT5E/CD73 Expression Shows Expression in Gliomas and Meningiomas and Associations with Genotype and Outcome** Shannon Coy, Mehdi Touat, Jaeho Hwang, Patrick Wen, Keith Ligon, Sandro Santagata
	41	**Brain tumor genomic profiling in Saudi Arabia: New insights into pediatric low-grade gliomas** Malak Abedalthagafi, Nahla Mobark, Musa AlHarbi, Lamees Al-Habeeb, Lori Ramkissoon, Shakti Ramkissoon
	42	**A Hybrid DNA/RNA-based Targeted Sequencing Platform Supports Routine Fusion Assessment in Tumors of the Central Nervous System** David Pisapia, Benjamin Liechty, Wei Song
	43	**Low-Grade Diffuse Glioma In The Elderly: A Novel Tumor Hiding In Plain Sight?** Abigail Goodman, Stewart Neill, Lindsey Lowder, Jeffery Olson, Jose Velazquez Vega, Matthew Schniederjan
	44	**IDH-wildtype Glioblastoma with Microcalcifications - Clinical and Genomic Characterization** Melissa Umphlett, Jane Houldsworth, Mary Fowkes, Nadejda Tsankova
	45	**Paraneoplastic Lymphocytic Ganglionitis Leading to Megacolon and Extended Survival in Glioblastoma** Jared Ahrendsen, Matthew Anderson
	46	**Oligodendroglioma with Neurocytic Differentiation: New perspectives on a known entity.** Janice Ahn, Elin Hughes, Thomas Cummings, Ann Buckley, Giselle Lopez
	47	**Creating Synthetic Glioma and Brain Tissue Histology** Marcello DiStasio, Meredith David
	48	**The FGFR3 p.K650T Mutation: Potential Surrogate Marker for the Identification of *FGFR3-TACC3*Fusion Glioma** Leomar Ballester, Soheil Zorofchian, Normal Leeds, Jason Huse, Gregory Fuller
	49	**Combined Immunohistochemistry for ATRX and p53 is Sensitive and Specific in Predicting 1p/19q Status in IDH-mutant Diffuse Gliomas** Kwok Link Kam, Craig Horbinski, Eileen Bigio, Xinyan Lu, Madina Sukhanova, Daniel Brat, Christina Appin
	50	**The Utility of SOX2 Immunohistochemistry in Differentiating Gliosarcoma from Histologic Mimics** Jared Woods, Jason Hornick, David Meredith
	51	**Glioblastoma Arising in Anaplastic Pleomorphic Xanthoastrocytoma in a Patient with TP53 Mutation and Family History of Li-Fraumeni Syndrome** Wen Zhong, Matthew Coco, Roger McLendon, Lenwood Smith, Hyder Arastu, Sarah Leonard, Philip Boyer

Posters are not offered for CME credit

FRIDAY POSTERS #52-#73

Friday, June 7, 2019		
Time:	**Poster #:**	**Highland Ballroom**
8:00 am – 5:00 pm	52	**A Case Report of Cerebellar GBM with H3 K27M Mutation** Yuan Shan, Sanjib Mukherjee, Ekokobe Fonkem, Danijela Levacic
	53	**BRAF V600E mutated, IDH wild type epithelioid glioblastomas in two young adult patients presented with extracranial or intradural metastases** Yang Liu, Evan Stein, Bernadine Donahue, Jim Huang, Jenny Libien, Jianying Zeng
	54	**Infratentorial Glioblastoma Metastasis to Bone** Jocelyn Ricard, Carolina Gil Tommee, Samuel Cramer, River Charles, An Le, W. Bell, Clark Chen, Margaret Flanagan
	55	**Next Generation Sequencing (NGS) Identifies Actionable Mutations in Glioblastoma Multiforme (GBM)** Mohammad Khan, Gaurav Khullar, Serguei Bannykh, David Engman, Eric Vail, Jean Lopategui, Xuemo (Sean) Fan
	56	**Primary glioblastoma with extracranial metastases: a case report and review of the literature** Yuan Rong, John Gao
	57	**IDH Mutant Glioblastoma Arising in Association with an Oligodendroglioma** Abigail Goodman, Stewart Neill, Lindsey Lowder, Pia Mendoza, Jose Velazquez Vega, Matthew Schniederjan
	58	**Histopathologic changes in a glioblastoma treated by MEK inhibition with Trametinib** Kyle Conway, Sandra Camelo-Piragua, Kathryn McFadden
	59	**H3 Mutations In Gliomas: A Case-to-Case Comparison Of H3 G35R Versus K28M Mutant Gliomas** Nicholas Coley, Martin Powers, Denise Malicki, Lawrence Hansen, Robert Hevner
	60	**Oligosarcoma, Case Report of a Rare Diagnosis with Rarer Presentation.** Vaibhav Chumbalkar, Jiang Qian
	61	**Spinal cord ependymoma with MYCN amplification** Amy Swanson, Robert Jenkins, Aditya Raghunathan, Caterina Giannini
	62	**Pediatric Myxopapillary Ependymomas: Clinico-Pathological Evaluation of 7 Cases** Kathryn Eschbacher, Amulya Nageswara Rao, Aditya Raghunathan
	63	**Anaplastic Ependymoma RELA Fusion-Positive with Extensive Neural Differentiation from Anaplastic Transformation of Clear Cell Ependymoma** Kenneth James, Samon Tavakoli, Alexander Papanastassiou, Andrea Gilbert
	64	**Anaplastic Glioneuronal Tumor with KIAA1549/BRAF Fusion** Zhenggang Xiong, Prithvi Narayan
	65	**Two Cases of Myxoid Glioneuronal Tumor of the Lateral Ventricle/Septum Pellucidum with *PDGFRA* p.K385L Mutation.** Erik Handberg, Marjorie Grafe, Christopher Corless, Lissa Baird, Ramon Barajas, Joshua Nickerson, Matthew Wood
	66	**Brainstem glioneuronal mass in a patient with Tetralogy of Fallot: is it a coincidence and is it a neoplasm?** Samasuk Thammachantha, Xinhai Zhang, William Yong
	67	**Polymorphous Low-Grade Neuroepithelial Tumor In A 70-Year-Old Man** Kathryn Scherpelz, Vera Paulson, Yajuan Liu, Caitlin Latimer, Patrick Cimino, Michael Dorschner, Luis Gonzalez-Cuyar
	68	**Dysembryoplastic Neuroepithelial Tumor in a 5-year old male.** Ma. Mercedes Victoria Tanchuling, Marie Christine F. Bernardo, Raymundo W. Lo
	69	**Cerebellar Liponeurocytoma: A Case Report with Cytogenetic Analysis** Bryan Morales-Vargas, Lindsey Lowder, Abigail Goodman, Stewart Neill, Stephen Hunter, Jeffrey Olson, Matthew Schniederjan
	70	**Activin Receptor-Like Kinase 1 Expression in Hippocampal Arterioles Decreases in Alzheimer's Disease and Amyloid Angiopathy** Thomas Bellio, Anderson Kelley, Stephanie Adams, Emily Aniskovich, Jan Blusztajn, Ivana Delalle
	71	**Examining ApoE Isoform-Specific Effects On Astrocytic Function By Use Of hiPSC-Derived Cortical Astrocytes** Talitha Kerrigan, Philip Regan, Lucy Crompton, Maeve Caldwell, Jon Lane, Andrew Randall, Seth Love
	72	**Alzheimer's disease neuropathologic change in a subject with trisomy 21 and a presenilin 2 mutation** Shannon Rose, Caitlin Latimer, Suman Jayadev, Thomas Bird, C. Keene
	73	**Neuropathology in Early-Onset Alzheimer Disease associated with the Ala431Glu mutation in the *Presenilin 1* gene** Jose Bonnin, Francine Epperson, Rose Marie Richardson, Holly Garringer, Bernardino Ghetti

Posters are not offered for CME credit

FRIDAY POSTERS #74-#95

Friday, June 7, 2019		
Time:	**Poster #:**	**Highland Ballroom**
8:00 am – 5:00 pm	74	**HIV-associated Neurocognitive Disorder and Alzheimer Pathology; a Clinicopathologic Pilot Study** Shino Magaki, Connie Do, Christopher Williams, Sergey Mareninov, Elyse Singer, Harry Vinters, William Yong
	75	**Neuropathological description of a case of familial Alzheimer's disease deriving from APP gene mutation V717L** Jorge Trejo-Lopez, Nilufer Taner, Benoit Giasson, Anthony Yachnis
	76	**Hyperspectral Stimulated Raman Scattering Imaging for Alzheimer's Disease** Kseniya Shin, Benjamin Figueroa, Christopher Keene, Gordana Juric-Sekhar, Dan Fu
	77	**Classification of Amyloid Beta Deposition Patterns: Comparison of Customized Deep Learning Approaches** Peter Chang, Turkay Kart, Daniel Chow, Edwin Monuki, Ziqi Tang, Michael Keiser, Brittany Dugger
	78	**Metabolomic Profile Alterations in the Rodent Brain Following DMSO Exposure in Infancy.** Zachary Rabow, Megan Showalter, Taryn Morningstar, Hilary Gonzales, Hailey Heil, Oliver Fiehn, Mirna Lechpammer
	79	**Autopsy Neuropathology of Neocerebellar Agenesis: Report of 2 Cases** Shana Straub, Rebecca Folkerth
	80	**Massive Congenital Midline Glioependymal Cyst with Associated CNS Maldevelopment** H. Brent Clark, Mark Luquette
	81	**Review of neuropathologic findings, mechanisms of neuronal migration and myelination in pediatric DiGeorge syndrome patients.** Dmitri Kapitonov, Christian Davidson, Mouied Alashari, Jessica Comstock, Cheryl Palmer
	82	**Neuropathologic Findings in *PIGT* Mutation** Steven Hemberger, Debopam Samanta, Raghu Ramakrishnaiah, Murat Gokden
	83	**Causes of Cardio-Respiratory Arrest in Infants and Toddlers with Retino-Dural Hemorrhage** Roland Auer, Francis Green
	84	**Non-Perfused Brain and Retino-Dural Hemorrhage in Infants and Toddlers** Roland Auer
	85	**CNS pathology as a cause of legal termination of pregnancy: a 5-year period retrospective study in a tertiary referral hospital (Barcelona, Spain)** Elena Martinez-Saez, Jessica Camacho, Sandra Buendía Bescos, Alexandra Navarro, Marta Garrido, Santiago Ramon y Cajal
	86	**Congenital classic moebius syndrome evaluated in adults shows abducens and facial motor nuclei lesions and abnormal tracts** Matthew Rose, Elizabeth Hutchinson, Junho Kim, Eunjung Lee, Irini Manoli, Carlo Pierpaoli, Elizabeth Engle
	87	**Multiple Periventricular Heterotopias: 2 unrelated cases of an unusual malformation complex** Brian Harding, M. Beatriz Lopes
	88	**Cortical Perivascular Satellitosis found in association with Polymorphous Low-grade Neuroepithelial Tumor of the Young** Vanessa Smith, Richard Hickman, Anne Buckley, James Goldman, Shih-Hsiu Wang
	89	**Perivascular CD8+ T-lymphocyte Infiltration and Astrocyte Damage in the Autism Brain** Marcello DiStasio, Ikue Nagakura, Monica Nadler, Matthew Anderson
	90	**Clustered Cytochrome-oxidase Negative Myofibers in Muscular Dystrophies: A Novel Finding** Romain Cayrol, Jenna Klotz, Hannes Vogel
	91	**Giant Cell Myositis in Association with Myasthenia Gravis: A Case Report** Melanie Lang-Orsini, Luisa Angel-Buitrago, Oscar Soto, Mithila Vullaganti, Knarik Arkun
	92	**Novel phenotype in *GFPT1* congenital myasthenic syndrome** Jane Persons, Karra Jones, Steven Moore
	93	**Major Histocompatibility Complex Class I Antigen Expression In Muscle Biopsies of Children With Congenital Myopathies** Lili Miles, Richard Finkel, Todd Maugans, Michael Miles
	94	**Muscle Biopsy With Calcium Oxalate Crystal Deposition In The Setting Of Renal And Cardiac Failure** Kathryn Scherpelz, Dennis Reichenbach, Kelly Smith, Luis Gonzalez-Cuyar, Caitlin Latimer
	95	**A Case of Becker Muscular Dystrophy in a 43-year-old Man Presenting Clinically as Polymyositis.** Ydamis Estrella, Stephen Martino[2], Ada Baisre

Posters are not offered for CME credit

FRIDAY POSTERS #96-#117

Friday, June 7, 2019		
Time:	**Poster #:**	**Highland Ballroom**
8:00 am – 5:00 pm	96	**Motor neuron pathology and ventral nerve root atrophy in sporadic inclusion body myositis (IBM)** Sahara Cathcart, Ericka Simpson, Suzanne Powell, Anithachristy Arumanayagam, Andreana Rivera, Stanley Appel, Matthew Cykowski
	97	**Cholesterol Reducing Agent Myopathy Including Immune-Mediated Necrotizing Myopathy: Spectrum of Histopathologic Features** Wen Zhong, Derek Schaap, Mike Singer, Kimberly Cerveny, Philip Boyer
	98	**Eosinophilic Myositis: A Rare Cause of Atraumatic Compartment Syndrome of the Forearm.** Galam Khan, Michael Boyajian, Lauren Roussel, Reena Bhatt, Edward Stopa
	99	**Diagnostic Yield and Clinical Utility of Nerve Biopsy in Evaluation of Neuropathy** Alexandru Olaru, Cheng-Ying Ho
	100	**Outer Nuclear Layer Retinal PrP^{Sc} Deposits in Sporadic Creutzfeldt-Jakob Disease Patients** Vanessa Goodwill, Christina Sigurdson, Jonathan Lin
	101	**Retinal Pathology in Chronic Traumatic Encephalopathy** Vanessa Goodwill, Christina Di Loreto, Christina Sigurdson, Victor Alvarez, Ann McKee, Jonathan Lin
	102	**A 10-year institutional review of sclerosing orbital lesions: broadening the differential diagnosis of "idiopathic sclerosing pseudotumor"** Brian Moore
	103	**Interpreting Discordant FISH and Microarray Monosomy 3 Results For Uveal Melanoma** Nicholas Coley, Simrin Sennik, John Thorson, Jonathan Lin
	104	**Lipoblast-like morphology in a uveal melanoma with delayed metastasis to the liver** Aimi Toyama, Faqian Li, W. Bell
	105	**Intraocular Ganglioneuroma In A Patient With NF1** Hannah Harmsen, Bret Mobley, Ty Abel
	106	**An Autopsy Case of Rhombencephalic Form Progressive Multifocal Leukoencephalopathy with an Extremely Low Copy Number of Pathogenic JCV DNA in CSF** Hajime Miyata, Satoshi Okawa, Dai Ichikawa, Hiroshi Fukaya, Hayato Kawakami, Kazuo Nakamichi, Masato Sageshima
	107	**Histopathologic Findings in a Case of Ehrlichia Encephalitis** Joseph Mininni, Heather Ames
	108	**Value of intraoperative Cerebro-Spinal fluid sampling in ventriculo-peritoneal shunting for non-infective cerebral pathology** Dewa Pakshage Chula Kanishka Ananda Lal, Deepal Attanayake
	109	**Chronic Hydrocephalus Following Mumps Encephalitis: Neuropathological Correlates** Cassie MacRae, Hemant Varma
	110	**Fatal Cerebral Abscess Secondary to Infection with Ochroconis Species In a Transplant Patient** Anna Mathew, Kyle Hurth
	111	**Congenital Zika Syndrome in Puerto Rico: Neuropathologic Findings and Review of Medical Literature** Jose Martinez-Correa, Juan Perez-Berenguer, Maria Correa-Rivas, Ines Garcia, Nicole Davila-Castrodad
	112	**Intra-Thrombus Polymer Coating Deposition in Patients Undergoing Endovascular Therapy for Acute Large Vessel Stroke** Rashi Mehta, Ansaar Rai, Jeffrey Vos, Orestes Solis, Rupal Mehta
	113	***In Situ* Hybridization Analysis of C3 Expression in Human Central Nervous System Disease** Daniel Marker, Geoffrey Murdoch, Clayton Wiley
	114	**Diffuse AVM resulting in spontaneous subarachnoid hemorrhage: an uncommon entity and challenging neuropathological diagnosis.** Heather Maioli, Marie Hensley, Kathryn Scherpelz, Desiree Marshall
	115	**Intracranial Hemorrhage resulting from AVM Rupture in a 7-Week-Old Female Infant: A Case Report** Xinhai Zhang, Leanna Huard, Harry Vinters
	116	**Tumefactive cerebral amyloid angiopathy mimicking central nervous system tumor: the pitfalls of neurosurgical biopsy in elderly patients** Yasuo Sugita, Takuya Furuta, Hiroko Muta, Koichi Ohshima, Joji Haratake, Yuji Okamoto, Seiya Kato, Akira Ookura
	117	**Juvenile Temporal Arteritis Masquerading as an Aneurysm Post-Trauma** Garrett Fitzpatrick, Jesse Kresak

Posters are not offered for CME credit

SATURDAY PLATFORMS 5 & 6

	Platform Session 5 ***Neurodegenerative: Alzheimer*** **Grand Ballroom** **Moderators: Qinwen Mao, MD, PhD; John Crary, MD, PhD**	**Platform Session 6** ***New Methods and Technologies*** **Buckhead Ballroom** **Moderators: Sriram Venneti, MD, PhD; Clayton Wiley, MD, PhD**
8:00 am – 8:15 am	**118** **Amyloid beta deposit identification by multiple expert trained machine learning models** Brittany Dugger, Ziqi Tang, Kangway Chuang, Justin Athey, Sakshi Das, Julia Kofler, Kirsty McAleese, Margaret Flannagan, Ewa Borys, Charles White, Nigel Cairns, Michael Keiser	**126** **Clinical Sequencing of Cell-free DNA from CSF is Superior to Cell pellet Genomic DNA** Tejus Bale, James Solomon, Khedoudja Nafa, Sumit Middha, Jacklyn Casanova, Justyna Sadowska, Anna Skakodub, Marc Rosenblum, Elena Pentsova, Alexandra Miller, Ingo Mellinghoff, Ahmet Zehir, Marc Ladanyi, Ryma Benayed, Maria Arcila
8:15 am – 8:30 am	**119** **Enhanced non-amyloidogenic amyloid precursor protein processing is a protective feature of brain aging** Jonathan Vordzorgbe, Soong Ho Kim, Kurt Farrell, Megan Iida, Jamie Walker, Tim Richardson, Charles White, John Crary	**127** **Label-free Histopathology of Human Brain Tissue with Multiphoton Imaging** Defu Chen, David Nauen, Xingde Li
8:30 am – 8:45 am	**120** **Somatic Mutations Accumulate in Neurons During Alzheimer's Disease** Michael Miller, Michael Lodato, August Huang, Junho Kim, Lariza Rento, Eduardo Maury, Eunjung Lee, Christopher Walsh	**128** **Single-nucleus RNA-seq in the human dorsolateral prefrontal cortex and subgenual anterior cingulate: implications for psychiatric disorders** Billy Kim, Paul Kim, Kory Johnson, Carolina Caban-Rivera, Ningping Feng, Qing Xu, Ajeet Mandal, Nirmala Akula, Francis McMahon, Barbara Lipska, Stefano Marenco, Pavan Auluck
8:45 am – 9:00 am	**121** **Resilience and resistance to AD pathology correlate with absence of pTDP-43 pathology and lower cortical pTau burden in a community-based cohort** Caitlin Latimer, Bridget Burke, Nicole Liachko, Heather Currey, Mitchell Kilgore, Laura Gibbons, Suman Jayadev, Paul Crane, Eric Larsen, Brian Kraemer, Thomas Grabowski, Thomas Bird, C. Keene	**129** **Diffusion Basis Spectrum Imaging (DBSI) To Assess Various Histologic Components in High-Grade Brain Tumors** Zezhong Ye, Joshua Lin, Jeffrey Viox, Sam Gary, Albert Kim, Sheng-Kwei Song, Joshua Rubin, Sonika Dahiya
9:00 am – 9:15 am	**122** **LR11/SorLA Expression is Modulated by APOE Genotype and Increased in Sporadic Alzheimer Disease** Richard Perrin, Meizi Jiang, Anne Fagan, Hideaki Bujo	**130** **Analysis of microscopic images via deep neural networks can predict outcome and IDH and 1p/19q codeletion status in gliomas** Muhammad Iftikhar, Saima Rathore, MacLean Nasrallah
9:15 am – 9:30 am	**123** **AmpliSeq transcriptome of laser captured neurons from Alzheimer brain: Comparison of single versus pooled 10 and 100 neurons** Wenjun Deng, Changhong Xing, Diego Mastroeni, MingMing Ning, Eng Lo, Paul Coleman	**131** **Machine Learning Pipeline to Differentiate Coexistent Tau Pathology in Cases of Mixed Alzheimer Disease and Progressive Supranuclear Palsy.** Rati Chkheidze, Anthony Vega, Satwik Rajaram, Charles White
9:30 am – 9:45 am	**124** **Biochemical Evidence Of Cerebral Hypoperfusion in Dementia: Associated With β-Secretase, Endothelin-1 And Arteriolosclerosis** Hannah Tayler, Robert MacLachlan, J Miners, Seth Love	**132** **Objective Image Analysis of Microglial and Astroglial Morphology in Rstudio** Jessica Blackburn, Evgin Goceri, Michele Alves, Catherine Czeisler, Jose Otero
9:45 am – 10:00 am	**125** **Patient H.M: A Preliminary Neuropathological Analysis** Bernardino Ghetti, Rose Marie Richardson, Matthew Frosch, David Amaral	**133** **Quantitative volumetric analysis using image reconstruction of post-mortem coronal slices** Mitchell Kilgore, Kody Zalewski, C. Keene, Christine Mac Donald, Caitlin Latimer

SATURDAY PLATFORMS 7 & 8

	Platform Session 7 ***Glioneuronal and Non-Glial Tumors*** **Grand Ballroom** **Moderators: Cynthia Hawkins, MD, PhD; Craig Horbinski, MD, PhD**	**Platform Session 8** ***Trauma and Forensics*** **Buckhead Ballroom** **Moderators: C. Dirk Keene, MD, PhD; Rebecca Folkerth, MD**
2:00 pm – 2:15 pm	**134** **Rosette-Forming Glioneuronal Tumor is Defined by FGFR1 Activating Alterations with Frequent Accompanying PI3K and MAPK Pathway Mutations** Calixto-Hope Lucas, Julieann Lee, Emily Sloan, Jeffrey Hofmann, Jessica Van Ziffle, Courtney Onodera, James Grenert, Boris Bastian, Cassie Kline, Anu Banerjee, Jennifer Clarke, Jennie Taylor, Nancy Ann Oberheim Bush, Robin Buerki, Nicholas Butowski, Susan Chang, Michael McDermott, Manish Aghi, Shawn Hervey-Jumper, Mitchel Berger, Corey Raffel, Nalin Gupta, Bette Kleinschmidt-DeMasters, Matthew Wood, Marjorie Grafe, Hua Guo, Peter Sun, Joseph Torkildson, Tabitha Cooney, Cynthia Fata, David Scharnhorst, David Samuel, Serguei Bannykh, Ziad Khatib, Ossama Maher, Gabriel Chamyan, Liset Pelaez, Carole Braithwaite, Lee-way Jin, Mirna Lechpammer, Donald Born, Hannes Vogel, Han Lee, Joanna Phillips, Melike Pekmezci, Andrew Bollen, Tarik Tihan, Arie Perry, David Solomon	**142** **Cortical somatostatin interneuron dysfunction after trauma.** Amber Nolan, Vikaas Sohal, Susanna Rosi
2:15 pm – 2:30 pm	**135** **The genomic landscape of spinal cord ependymoma** Biswarathan Ramani, Javier Villaneuva-Meyer, Christine Glastonbury, Ece Meram, Kyle Walsh, Jennie Taylor, Jessica VanZiffle, Courtney Onodera, James Grenert, Andrew Bollen, Arie Perry, Tarik Tihan, David Solomon, Melike Pekmezci	**143** **DNA Damage and Acquisition of a Senescence Associated Secretory Phenotype in Concussed Brains** Lili-Naz Hazrati, Nicole Schwab
2:30 pm – 2:45 pm	**136** **Telomere Alterations in NF1-associated Solid Tumors are Associated with Clinical Outcome** Fausto Rodriguez, Mindy Graham, Jacqueline Brosnan-Cashman, Christine Davis, M. Adelita Vizcaino, Doreen Palsgrove, Caterina Giannini, Melike Pekmezci, Sonika Dahiya, Murat Gokden, Michael Noë, Laura Wood, Christine Pratilas, Carol Morris, Allan Belzberg, Jaishri Blakeley, Christopher Heaphy	**144** **Evidence of interface astroglial scarring in the brains of military Service Members who have committed suicide** Daniel Perl, Regina Armstrong, C Rhodes
2:45 pm – 3:00 pm	**137** **Recurrent *KBTBD4* small in-frame insertions differentiate pineal parenchymal tumors of intermediate differentiation from pineoblastoma** Julieann Lee, Tali Mazor, Richard Lao, Eunice Wan, Alpha Diallo, Nicholas Hill, Naina Thangaraj, Katherine Wendelsdorf, David Samuel, Cassie Kline, Anuradha Banerjee, Kurtis Auguste, Corey Raffel, Nalin Gupta, Mitchel Berger, David Raleigh, Anny Shai, Joanna Phillips, Andrew Bollen, Tarik Tihan, Arie Perry, Joseph Costello, David Solomon	**145** **Chronic traumatic encephalopathy is associated with increased severity of frontal leptomeningeal cerebral amyloid angiopathy** Oliver Standring, Jacob Friedberg, Victor Alvarez, Bertrand Huber, Yorghos Tripodis, Alicia Chua, Ann McKee, Thor Stein
3:00 pm – 3:15 pm	**138** **The Biology Of Paediatric Central Nervous System Tumours At Post-Mortem** Izabella Smolicz, Amy Fairchild, Jessica Pickles, Thomas Stone, Jane Chalker, Jamie Gonzalez Zapata, Lisa Wilkhu, Shireena Yasin, Ashirwad Merve, Darren Hargrave, Neil Sebire, Thomas Jacques	**146** **Cryo-EM structures of tau filaments from chronic traumatic encephalopathy** Bernardino Ghetti, Benjamin Falcon, Jasenko Zivanov, Wenjuan Zhang, Alexey Murzin, Holly Garringer, Ruben Vidal, Anthony Crowther, Kathy Newell, Michel Goedert, Sjors Scheres
3:15 pm – 3:30 pm	**139** **Targeting Nodal/SMAD inhibits invasion and proliferation of retinoblastoma** Charles Eberhart, David White, Lynn Yoon, Jeff Mumm, Laura Asnaghi	**147** **Reappraisal of the Case of Dementia Pugilistica Discussed in *The New England Journal of Medicine*, April 22, 1999 (Case 12-1999)** Kathy L. Newell, Benjamin Falcon, Jasenko Zivanov, Wenjuan Zhang, Alexey G. Murzin, Holly J. Garringer, Ruben Vidal, R. Anthony Crowther, Bernardino Ghetti, Michel Goedert, Sjors H.W. Scheres
3:30 pm – 3:45 pm	**140** **Li-Fraumeni syndrome: a 20 year retrospective experience with a challenging clinical syndrome** Edward Kelly Mrachek, Lindsey Hoffman, Bette Kleinschmidt-DeMasters, Ahmed Gilani	**148** **Shaken Baby Brains Show No Acceleration-Deceleration Relative to Surrounding Fluid** Roland Auer
3:45 pm – 4:00 pm	**141** **Pseudosarcomatous changes and necrosis mimic anaplasia in otherwise Grade I meningiomas.** Tejus Bale, Sudarshana Roychoudhury, Jamal Benhamida, Liliana Villafania, Monika Wrzolek, John-Paul Bouffard, Kalyani Bapat, Todd Anderson, Marc Ladanyi, Marc Rosenblum	**149** **Dementia in the Forensic Setting: A Survey of Diagnoses Using a Condensed Protocol at a Resource-Limited Large Urban Medical Examiner's Office** David Priemer, Rebecca Folkerth

SATURDAY POSTERS #150-#167

Saturday, June 8, 2019		
Time:	**Poster #:**	**Highland Ballroom**
8:00 am – 5:00 pm	150	**Pathologic and radiologic features in a case of retinoblastoma with spinal epidural and bone marrow metastases** Kristyn Galbraith, Kavya Mirchia, Kalliopi Petropoulou, Abdelmohsen Hussien, Timothy Richardson
	151	**Ectopic Isolated Sporadic Sellar Retinoblastoma (RB): Quadrilateral RB without affected Retinae or Pineal (7 months post-Dx)** Alexander Feldman, Kathleen Schieffer, Matija Snuderl, Brent Orr, Christopher Pierson, Diana Osorio, Jonathan Finlay, Annie Drapeau, Jeffrey Leonard, Catherine Cottrell, Elaine Mardis, Daniel Boué
	152	**Review of medulloblastoma for the assessment of genetic profiles and histology: Multicentric Japanese study** Atsushi Sasaki, Junko Hirato, Takeshi Inoue, Yonehiro Kanemura, Yoshinori Kodama, Koichi Ichimura, Hiroaki Sakamoto, Ryo Nishikawa
	153	**Use Bayes theorem to analyze Array CGH and assist categorization of medulloblastoma subgroups** Peng Cheng Han, Cynthia Welsh, Daynna Wolff
	154	**Cerebrospinal versus hematogenous route for medulloblastoma leptomeningeal metastases** Ahmed Gilani, Bette Kleinschmidt-DeMasters
	155	**Medulloblastoma With Post-Therapy Maturation into Gangliocytoma: Case Report And Review Of Literature** Nfn Aakash, Matthew Mullarkey, Meenakshi Bhattacharjee, Manish Shah, Wafik Zaky, Gregory Fuller, David Sandberg, Leomar Ballester
	156	**Atypical teratoid/rhabdoid tumor in adults: the difficulty and importance of recognition and diagnosis in the older patient population** Patricia Pittman, William Harrison, Anne Buckley
	157	**Revisiting Brain Invasion as a Major Diagnostic Criteria for Atypical Meningioma** Rati Chkheidze, Kimmo Hatanpaa, Toral Patel, Jack Raisanen, Dennis Burns, Charles White III, Chunyu Cai
	158	**Multifocal atypical grade-II meningiomas in a pediatric patient with neurofibromatosis type 2** Suash Sharma, Ravindra Kolhe, Amyn Rojiani
	159	**Choroid Plexus carcinoma: Report of a rare case in an adult** Amir Banihashemi, Mary Fowkes
	160	**Papillary Tumor of Pineal Region, A Rare Mimic of Ependymoma** Erin Baumgartner, Danielle Fasciano, Winfield Fisher, James Hackney
	161	**Pineal germinoma presenting as an inflammatory/demyelinating disease** Darshan Trivedi, Suzanne Powell
	162	**Sclerosing Paraganglioma of the Cauda Equina** Eric Goold, Christian Davidson, Andrew Dailey, Tyler Smith
	163	**Variation of ACTH and Pituitary Transcription Factor Immunohistochemical Staining in Silent Corticotroph Adenomas** Angela Wu, Maria Beatriz Lopes
	164	**Invasive Non-functioning Thyrotroph Pituitary Macroadenoma** Jose Bonnin, Mercia Gondim, Stephen Kralik, Jonathan Ting, Troy Payner
	165	**Malignant Craniopharyngioma With Odontogenic Features. Case Report and Literature Review.** Monica Mezmezian, Gonzalo Fernandez Ugazio, Maria Paparella
	166	**Ebstein Barr Virus positive Diffuse Large B-cell Lymphoma in the CNS associated with Hemophagocytic Lymphohistiocytosis** Carolina Gil Tommee, Jocelyn Ricard, River Charles, Sophia Yohe, W Bell, Margaret Flanagan
	167	**Corticoid-Mitigated Lymphoma mimicking histiocytic lesions: A challenging diagnosis.** Shalla Akbar, Osama Elkadi, Wadad Mneimneh

Posters are not offered for CME credit

SATURDAY POSTERS #168-#186

Saturday, June 8, 2019		
Time:	**Poster #:**	**Highland Ballroom**
8:00 am – 5:00 pm	168	**ALK-Positive Histiocytosis with KIF5B-ALK Fusion in the Central Nervous System** Calixto-Hope Lucas, Ahmed Gilani, David Solomon, Xiayuan Liang, Ossama Maher, Gabriel Chamyan, Bette Kleinschmidt-DeMasters, Arie Perry
	169	**Secondary Cutaneous T-cell Lymphomas of the CNS: a Clinicopathologic Examination** David Meredith, Albert Kim, Lakshmi Nayak
	170	**Intravascular large B-cell lymphoma of the central nervous system, a masquerader on radiography and clinical presentation: case report.** Serge Kajaer Koujanian, John Provias, Sarah Al-Rawaf
	171	**GLUT1(Glucose transporter-1) is expressed on tumor cells in primary central nervous system lymphomas and correlates with survival** Yasuo Sugita, Takuya Furuta, Hiroko Muta, Koichi Oshima, Akiyoshi Kakita, Yukihiko Fujii, Takanori Nozawa
	172	**Rosai-Dorfman Disease Extending to the Brain: A Case Report** Aleksandar Krbanjevic, Henry Brown
	173	**Plasma Cell Leukemia Involving the Central Nervous System: An Uncommon Neurologic Manifestation of Multiple Myeloma** Joseph DelTondo, Alok Mohanty, Anna Balog, Edward Lynch, Kymberly Gyure, Jan Silverman
	174	**Primary intracranial sarcoma, DICER1-mutant: a pleomorphic sarcoma with myogenic or chondrogenic differentiation and eosinophilic globules** Julieann Lee, Javier Villaneuva-Meyer, Sean Ferris, Emily Sloan, Jeffrey Hofmann, Eyas Hattab, Brian Williams, Hua Guo, Joseph Torkildson, Adriana Florez, Mark Curtis, Caterina Giannini, Ankur Sangoi, Jessica Van Ziffle, Courtney Onodera, Patrick Devine, James Grenert, Soo-Jin Cho, Andrew Horvai, David Jones, Stefan Pfister, Christian Koelsche, Andreas von Deimling, Andrey Korshunov, Arie Perry, David Solomon
	175	**Primary Intracranial Sarcoma, *DICER1*-Mutant, with Meningioangiomatosis-Like Pattern at Presentation and Anaplastic Progression** Jeffrey Hofmann, Mark Curtis, Caterina Giannini, David Solomon
	176	**Intracranial myxoid mesenchymal neoplasms with *EWSR1* gene rearrangement: Report of two midline cases and review of the literature** Yanel De Los Santos, Marie Rivera-Zengotita, Jesse Kresak
	177	**Intracranial Angiomatoid Fibrous Histiocytoma** Marissa Spino, Nader Delavari, David Harter, George Jour, Matija Snuderl
	178	**Ewing Sarcoma of the Cervical Spine: An Unusual Neoplasm at an Unusual Location** Jessica LaVergne, Kandi Stallings-Archer, Laura Gonzalez-Krellwitz, Gregory Albert, Eylem Ocal, Murat Gokden
	179	**A rare case report of malignant peripheral nerve sheath tumor arising in schwannoma and literature review** Chao Li, Samir Kashyap, Piao Zhe, Mark Calayag
	180	**Intracranial Chondroblastoma-like Osteosarcoma Following Remote Radiation Therapy** Wen Zhong, Regis Hoppenot, Shawn Collins, Philip Boyer
	181	**Inflammatory Myofibroblastic Tumor of the Right Tentorium** Renee Stonebridge, John Donahue, Edward Stopa
	182	**Spinal Undifferentiated Round Cell Sarcomas with *CIC-DUX4* Fusion** José Velázquez Vega, Bryan Morales Vargas, Abigail Goodman, Lindsey Lowder, Stewart Neill, Arie Perry, David Solomon, Matthew Schniederjan
	183	**Intracranial Myxoid Neoplasm Morphologically Resembling Extraskeletal Myxoid Chondrosarcoma but without NR4A3 Rearrangement** Hsiang-Chih Lu, Jarod Roland, David Limbrick, Joseph Corbo
	184	**Effects of therapy: Denosumab in a patient with giant cell tumor of bone metastatic to the skull** Ahmed Gilani, Bette Kleinschmidt-DeMasters
	185	**Intravascular papillary endothelial hyperplasia (Masson's tumor) in the brain parenchyma of a pregnant female: A case report** Jake Maule, Janice Ahn, Giselle Lopez
	186	**A 24-year-old woman with primary intracranial synovial sarcoma** Amir Banihashemi, Elisa Nabel, Clare Bryce, Mary Fowkes

Posters are not offered for CME credit

SATURDAY POSTERS #187-#205

Saturday, June 8, 2019		
Time:	**Poster #:**	**Highland Ballroom**
8:00 am – 5:00 pm	187	**Psammomatoid ossifying fibroma collision with aneurysmal bone cyst tumor** Carolina Gil Tommee, Emilian Racila, Margaret Flanagan, W Bell
	188	**Recurrent Dural-Based Neuroendocrine Carcinoma with Chromothripsis And ARID1A/MLH1 Mutations** Nicholas Coley, Martin Powers, Denise Malicki, Lawrence Hansen, John Thorson, Robert Hevner
	189	**Hemorrhagic brain metastases: Think outside the melanoma!** Seema Shroff, Jie Ouyang, David Ward, Muchou Ma, Peter Pernicone
	190	**Metastatic Urothelial Carcinoma to the Central Nervous System** Danielle Fasciano, Erin Baumgartner, William Stetler, James Hackney
	191	**Metastatic sarcomatoid carcinoma to the brain: experiences in two cases** Karam Han, Dan Cai
	192	**Clinicopathologic Features and Assessment of *ADAM3A* Gene by FISH in Conjunctival Squamous Cell Carcinoma and its Precursors** M. Adelita Vizcaino, Abeer Tabbarah, Laura Asnaghi, Charles Eberhart, Fausto Rodriguez
	193	**Using an induced pluripotent stem cell model of frontotemporal dementia to identify altered metabolic profiles in patient-derived neurons** Tristan Winters, James Goldman, Peter Canoll, Markus Siegelin, Gunnar Hargus
	194	**Generation and Characterization of Novel Monoclonal Antibodies Targeting TDP-43 Across Human Tauopathies and α-Synucleinopathies** Jorge Trejo-Lopez, Zachary Sorrentino, Cara Riffe, Anthony Yachnis, Benoit Giasson
	195	**The predominant tauopathies in amyotrophic lateral sclerosis (ALS) are common pathologies associated with human aging** Alejandro Perez, Suzanne Powell, Anithachristy Arumanayagam, Andreana Rivera, Ericka Simpson, Stanley Appel, Matthew Cykowski
	196	**Frontotemporal Lobar Degeneration-TDP-43 and Hippocampal Sclerosis in an Alzheimer's Patient with Fornix Deep Brain Stimulators.** Bartholomew White, Liam Chen
	197	**Novel neuropathologic findings in the first American case of Frontotemporal Dementia associated with the T183A *PRNP* Mutation** David Priemer, Holly Garringer, Rose Richardson, Francine Epperson, Gianluigi Zanusso, Bernardino Ghetti
	198	**Cerebellar vascular brain injury presenting with clinical features of frontotemporal dementia** Troy Marxen, Erik Carlson, C. Keene, Thomas Bird, Kimiko Domoto-Reilly, Caitlin Latimer
	199	**Limbic TDP 43 proteinopathy, clinically mimicking Alzheimer disease** Tadayuki Takata, Suely Marie, Yuishin Izumi, Yuko Saito, Shigeo Murayama
	200	**Hippocampal Sclerosis in Chronic Traumatic Encephalopathy** Nathan Clement, Victor Alvarez, Bertrand Huber, Matthew Frosch, Ann McKee, Thor Stein
	201	**Dementia Pugilistica in a 77-Year-Old Former Boxing Champion** Kathy L. Newell, Rose M. Richardson, Bernardino Ghetti, Raymond A. Sobel, Lysia S. Forno* (*deceased)
	202	**Progressive Supranuclear Palsy with severe spinal cord involvement, presenting as Frontotemporal Lobar Degeneration and Motor Neuron Disease** Jose Bonnin, Eric Wasserman, Dimitrios Kapogiannis, Holly Garringer, Rose Richardson, Francine Epperson, Jordan Grafman, Bernardino Ghetti
	203	**Coexistence of Progressive Supranuclear Palsy with Pontocerebellar Atrophy and Myotonic Dystrophy Type 1: A Case Report** Shunsuke Koga, Eric Ahlskog, Michael Deture, Matthew Baker, Shanu Roemer, Takuya Konno, Rosa Rademakers, Owen Ross, Dennis Dickson
	204	**Identification of common variants influencing risk of primary age-related tauopathy** Kurt Farrell, Natalia Han, Megan Iida, Jamie Walker, Tim Richardson, Tushar Bhangale, Charles White, John Crary
	205	**Asymmetry Between Right and Left Hippocampal Pathology in Primary Age-Related Tauopathy (PART)** Yelena Fudym, Kurt Farrell, John Crary, Charles White, Jamie Walker, Timothy Richardson

Posters are not offered for CME credit

SATURDAY POSTERS #206-#225

Saturday, June 8, 2019		
Time:	**Poster #:**	**Highland Ballroom**
8:00 am – 5:00 pm	206	**Neurodegeneration in Advanced Age: A Comparison of Pathologies with Emphasis on Hippocampal Sclerosis, TDP-43, and Microvascular Disease.** William Harrison, John Ervin, Shih-Hsiu Wang
	207	**Frequency of neurodegenerative disease pathology in elderly subjects who die by suicide.** Christopher Hauch, Travis Danielsen, Jeffrey Barnard, Reade Quinton, Bret Evers, Dennis Burns, Jack Raisanen, Charles White
	208	**The Structural Basis for Leukoaraiosis is Decreased Microvessel Density in White Matter.** Paul Yell, Cherise Chin Fatt, Linda Hynan, Chan Foong, Ping Shang, Charles White
	209	**The Effectiveness of a Simplified Blocking Protocol for the Diagnosis of Neurodegenerative Diseases** Nathan Clement, John Dewitt, Matthew Frosch, Maria Martinez-Lage, Wesley Samore, E. Tessa Hedley-Whyte
	210	**A Neuropathologic Study of Machado-Joseph Disease (Spinocerebellar Ataxia Type 3) in a 62-Year-Old Man** Kathy L. Newell, Nelli S. Lakis, Bernardino Ghetti, Karla P. Figueroa, Stefan M. Pulst
	211	**A Case of Spinocerebellar Ataxia Type 3 with Degeneration of the Inferior Olivary Nucleus** Matthew McCord, Eileen Bigio, Jean Fischer, Farres Obeidin, William Muller, Daniel Brat, Qinwen Mao
	212	**Neuropathologic evaluation of spinocerebellar ataxia 14** Caitlin Latimer, Shannon Rose, Dong-hui Chen, Wendy Raskind, Thomas Bird, C. Keene
	213	**Fetal Allografts in Huntington's Disease: A neuropathologic review of four cases** Mitchell Kilgore, C. Keene, Suman Jayadev, Thomas Bird, Caitlin Latimer
	214	**Biochemical characterization of disease-associated prion protein in Q160X mutation and in other inherited prion protein cerebral amyloidoses** Gianluigi Zanusso, Michele Fiorini, Daniela Perra, Ruben Vidal, Holly Garringer, Michael Geschwind, Bernardino Ghetti
	215	**Biochemical characterization of pathological prion protein in genetic Creutzfeldt-Jakob Disease associated with the T183A PrP mutation** Gianluigi Zanusso, Michele Fiorini, Holly Garringer, Maurizio Pocchiari, David Priemer, Bernardino Ghetti
	216	**Prion disease associated with a novel 96bp insertional mutation in the octapeptide repeat region** Masaki Takao, Kazuhiro Honda, MIzuho Koide, Kimihito Arai, Ban Mihara, Tetsuyuki Kitamoto
	217	**Pediatric Idiopathic Basal Ganglia Calcification Associated with Chromosome 8p11.2-12 Deletion** Meaghan Morris, Liam Chen
	218	**Histopathologic presentation of two cases of GABAa-R autoimmune encephalitis** Josh Klonoski, Cheryl Palmer, Stacy Clardy, Miguel Paz Soldan, Eric Lancaster, Lisa Peterson
	219	**Neuropathologic Findings in a Patient with CAR T-Cell-Associated Inflammatory Cytokine Release Syndrome** Jonathan Lavezo, Christopher Mount, Michelle Monje, David Miklos, Hannes Vogel
	220	**Balo's Concentric Sclerosis: Autopsy of a Rare Demyelinating Process** Andrew Guajardo, Heather Jarrell
	221	**Adult-Onset Leukodystrophy in the Context of Immunosuppressive Therapy** Nalin Leelatian, Anita Huttner, Armine Darbinyan, Pallavi Gopal, Declan McGuone
	222	**Validation and Clinical Use of Whole Slide Digital Imaging at Stanford Neuropathology** Jonathan Lavezo, Donald Born, Seth Lummus, April Young, Thomas Montine, Hannes Vogel
	223	**The Quality of Frozen Sections for Neurosurgical Specimens Is Dependent on Freezing Technique** David Priemer, Alexander Vortmeyer
	224	**A new method to characterize hydrocephalus in hyperlipidemic LDLR$^{-/-}$APOB$^{100/100}$ transgenic mice** Rufei Lu, Sandra Gostynska, Jasimuddin Ahamed, Kwok Ling Kam, Kar-Ming Fung, Rohan Varshney
	225	**A highly sensitive sandwich ELISA to detect CSF progranulin, a potential biomarker for CNS disorders** Qinwen Mao, Yanqing Li, Xiaojing Zheng, Emily Rogalski, Haibin Xia, Eileen Bigio

Posters are not offered for CME credit

SATURDAY POSTERS #226-#234

Saturday, June 8, 2019		
Time:	**Poster #:**	**Highland Ballroom**
8:00 am – 5:00 pm	226	**Brain Autopsy Findings in Medical Examiner Cases with 'Seizure' In Cause of Death** J. Stephen Nix, Andrew Guajardo, Olga Pletnikova, Juan Troncoso, David Nauen
	227	**CNS Pathologic Abnormalities: A Retrospective Analysis of a 10-Year Autopsy Experience in an Academic Medical Center** Xinhai Zhang, Seyed Mohammad Haeri Hosseini, Negar Khanlou, Maria Inmaculada Cobos Sillero, William Yong, Harry Vinters
	228	**Sitting on a Goldmine: The Promise and Challenge of Academic and Forensic Neuropathology Collaboration** Melissa Blessing, Hannah Jarvis, Glenn Sandberg
	229	**UK Brain Banks Network Database – Recent Developments Enhance the Value of This Resource for Researchers and Brain Banks** Rich Cain, Laura Palmer, Seth Love
	230	**Autopsy Findings in New-onset Refractory Status Epilepticus** Courtney Healy, Rahul Chandra, James Valeriano, Kymberly Gyure
	231	**Neuropathology of chronically implanted, intracortical electrodes in a tetraplegic patient with robotic arm interface** Carol Miller, Linda Szymanski, Spencer Kellis, Charles Liu, Richard Andersen, Debra Commins, Brian Lee, Kymry Jones, Doug McCreery
	232	**Neuropathology Findings in Patients with History of Ventricular Assist Devices** Matthew Torre, Jeffrey Helgager, David Meredith, Robert Padera
	233	**Heroin inhalation leukoencephalopathy ("chasing the dragon"): an emerging entity to be recognized** Samantha Champion, Daniel Shepherd, David Louis, Maria Martinez-Lage
	234	**Pathological and Radiological Features of Traumatic Spinal Cord Injury** Omar Fayez, Kevin Johnson, Heather Simmons, Kevin Brunner, Dane Schalk, Arun Mensinkai, Hussein Abdullah, Nitin Seth, Farah Masood, John Sledge, Ervin Sedjic, Shanker Nesathurai

Posters are not offered for CME credit

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Endowed Lectureships

Friday, June 7, 2019

I. Parisi Lecture
II. DeArmond Lecture

Saturday, June 8, 2019

I. Saul R. Korey Lecture

Sunday, June 9, 2019

I. 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 Association, 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 **Beth Stevens** 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
2017	Sean J. Pittock	Autoimmune Gliopathies: A Journey of Discovery
2018	Philip L. De Jager	The Genomic Architecture of Aging-Related Neuropathologies: Spotlight on Microglia
2019	Beth Stevens	Microglia Function and Dysfunction in Neurologic Disease

PARISI LECTURE

Microglia Function and Dysfunction in Neurologic Disease

Time: 10:30 am – 11:30 am

Date: Friday, June 7, 2019

Beth Stevens, PhD, *Boston Children's Hospital, Harvard Medical School, Broad Institute, Member and HHMI Investigator*

I. Learning Objectives

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

1. Describe microglia development and its role in synapse elimination.
2. Explain how to model Alzheimer's risk pathways in vitro and in vivo.
3. Identify new biomarkers and approaches to target microglia in disease.

II. Abstract & Relevant References

Most of the risk genes associated with Alzheimer's disease (AD) is expressed in microglia. Given the complexity and diversity of microglia little is known about their contribution to AD pathogenesis. We showed that early synapse loss in AD, glaucoma, and other neurodegenerative diseases, is caused by an aberrant reactivation of pruning in vulnerable brain regions. Inhibiting the classical complement cascade, by deleting the genes for C1q, C3, or the microglia phagocytic receptor CR3, rescues synapse loss and some cognitive impairment, including learning and memory defects. Using single cell RNA sequencing and other emerging technologies we are examining microglia transcriptional changes in human AD brain and in AD mouse models to ask how they relate to neurons and astrocytes during periods of synapse loss. Knowledge of the functional states of microglia in normal aging and disease may lead to the identification of new biomarkers and therapeutic targets.

References:

1. Hong S, Beja-Glasser VF, Nfonoyim BM, Frouin A, Li S, Ramakrishnan S, Merry KM, Shi Q, Rosenthal A, Barres BA, Lemere CA, Selkoe DJ, Stevens B (2016). Complement and Microglia Mediate Early Synapse Loss in Alzheimer's Mouse Models. Science. May 6;352(6286):712-716. PMID: 27033548; PMC5094372
2. Hammond, TR, Dufort C, Dissing-Olesen L, Giera S, Young A, Wysoker A, Walker AJ, Gergits F, Segel M, Nemesh J, Marsh SE, Saunders A, Macosko E, Ginhoux F, Chen J, Franklin RJM, Piao, X, McCarroll, SA, and Stevens B. (2019) Single-Cell RNA Sequencing of Microglia throughout the Mouse Lifespan and in the Injured Brain Reveals Complex Cell-State Changes. Immunity. Jan 15;50(1): 253-271. ePub 2018 Nov 21. PMID: 30471926 PMC in process.
3. Hammond TR, Marsh SE, Stevens B. (2019) Immune Signaling in Neurodegeneration. Immunity. Apr 16;50(4):955-974. PMID: 30995509
4. Salter MW, Stevens B (2017) Microglia emerge as central players in brain disease; Nat Med Sept 8;23(9):1018-1027; PMID: 28886007; PMC N/A
5. Schafer DP, Lehrman EK, Kautzman AG, Koyama R, Mardinly AR, Yamaskaki R, Ransohoff RM, Greenberg ME, Barres BA, and Stevens B (2012). Microglia Sculpt Postnatal Neural Circuits in an Activity and Complement-Dependent Manner. Neuron. May 24;74(4);691-705. PMID: 22632727 PMC3528177

III. Faculty Biography

Beth Stevens is an Associate Professor at Harvard Medical School in the FM Kirby Neurobiology Center at Boston Children's Hospital, an Institute Member of the Broad Institute and Stanley Center for Neuropsychiatric Research, and a Howard Hughes Medical Institute Investigator.

Her research seeks to understand the mechanisms that regulate the disappearance of synapses by focusing on how immune-related molecules mediate this process. Her most recent work seeks to uncover the role that microglial cells, the immune cells of the central nervous system, and their connectivity play in neurodevelopmental and neuropsychiatric disorders. She and her team recently identified how microglia affect synaptic pruning, the critical developmental process of cutting back on synapses that occurs between early childhood and puberty. Problems with pruning is hypothesized to contribute to developmental disorders such as schizophrenia and autism. In addition, her work is providing novel insight into the mechanisms by which microglia contribute to synaptic and cognitive dysfunction in neurodegenerative diseases, including Alzheimer's that could lead to new therapies and biomarkers.

Stevens was named a MacArthur Fellow in 2015. She has also shared the National Alliance on Mental Illness (NAMI) Research Award with Steven McCarrolla and Michal Carroll in 2016 for their collaborative work on C4 and Schizophrenia

Stevens received her B.S. at Northeastern University. She carried out her graduate research at the National Institutes of Health and received her Ph.D. from University of Maryland, College Park. She completed her postdoctoral research at Stanford University with Ben Barres.

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 **Alison M. Goate** 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
2017	David C. Van Essen	Structure, Function, Connectivity, Development and Evolution of Human Cerebral Cortex
2018	Suzanne M. de la Monte	Dysregulated Metabolism in the Pathogenesis of Alzheimer's Disease: Type 3 Diabetes
2019	Alison M. Goate	Rare and Common Genetic Variation Implicate Microglial Function in Alzheimer's Disease Risk

DEARMOND LECTURE

Rare and Common Genetic Variation Implicate Microglial Function in Alzheimer's Disease Risk

Time: 4:45 pm – 5:45 pm

Date: Friday, June 7, 2019

Alison M. Goate, D.Phil, *Icahn School of Medicine at Mount Sinai, New York, NY*

I. Learning Objectives

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

1. List the methodologic approaches used to identify rare and common genetic risk factors.
2. Identify the major genetic risk factors for Alzheimer's disease.
3. Describe the importance of different neural cell types to disease.
4. Outline the hypothesized mechanisms underlying these genetic risk factors.

II. Abstract & Relevant References

Over the last thirty years genetics has provided important insights into the mechanisms underlying Alzheimer's disease (AD). Early studies used genetic linkage in families to identify highly penetrant mutations in APP, PSEN1 and PSEN2. These genes implicated Aß metabolism in AD risk. Since then the focus of genetics has been on the sporadic disease largely using genome-wide association studies in case control cohorts to identify both common and rare variation contributing to disease risk. By far the most important genetic risk factor for AD is APOE genotype. However, over thirty other loci have been implicated in disease. Network and pathway analyses have shown that these loci are enriched for genes expressed in microglia that are involved in lipid metabolism, endocytic trafficking/phagocytosis and innate immunity. Molecular studies in model systems are beginning to pinpoint the specific microglial functions that contribute to AD risk.

References:

1. Pimenova AA, Raj T, Goate AM. Untangling Genetic Risk for Alzheimer's Disease. Biol Psychiatry. 2018 Feb 15;83(4):300-310. doi: 10.1016/j.biopsych.2017.05.014. Epub 2017 May 22. Review.
2. Pimenova AA, Marcora E, Goate AM. A Tale of Two Genes: Microglial Apoe and Trem2.Immunity. 2017 Sep 19;47(3):398-400. doi: 10.1016/j.immuni.2017.08.015.
3. Guerreiro R, Wojtas A, Bras J, Carrasquillo M, Rogaeva E, Majounie E, Cruchaga C, Sassi C, Kauwe JS, Younkin S, Hazrati L, Collinge J, Pocock J, Lashley T, Williams J, Lambert JC, Amouyel P, GoateA, Rademakers R, Morgan K, Powell J, St George-Hyslop P, Singleton A, Hardy J; Alzheimer Genetic Analysis Group. TREM2 variants in Alzheimer's disease. N Engl J Med. 2013 Jan 10;368(2):117-27. doi: 10.1056/NEJMoa1211851. Epub 2012 Nov 14.
4. Huang KL, Marcora E, Pimenova AA, Di Narzo AF, Kapoor M, Jin SC, Harari O, Bertelsen S, Fairfax BP, Czajkowski J, Chouraki V, Grenier-Boley B, Bellenguez C, Deming Y, McKenzie A, Raj T, Renton AE, Budde J, Smith A, Fitzpatrick A, Bis JC, DeStefano A, Adams HHH, Ikram MA, van der Lee S, Del-Aguila JL, Fernandez MV, Ibañez L; International Genomics of Alzheimer's Project; Alzheimer's Disease Neuroimaging Initiative, Sims R, Escott-Price V, Mayeux R, Haines JL, Farrer LA, Pericak-Vance MA, Lambert JC, van Duijn C, Launer L, Seshadri S, Williams J, Amouyel P, Schellenberg GD, Zhang B, Borecki I, Kauwe JSK, Cruchaga C, Hao K, Goate AM. A common haplotype lowers PU.1 expression in myeloid cells and delays onset of Alzheimer's disease. Nat Neurosci. 2017 Aug;20(8):1052-1061. doi: 10.1038/nn.4587. Epub 2017 Jun 19.
5. Kunkle BW, Grenier-Boley B, Sims R, Bis JC, Damotte V, Naj AC, Boland A, Vronskaya M, van der Lee SJ, Amlie-Wolf A, Bellenguez C, Frizatti A, Chouraki V, Martin ER, Sleegers K, Badarinarayan N, Jakobsdottir J, Hamilton-Nelson KL, Moreno-Grau S, Olaso R, Raybould R, Chen Y, Kuzma AB, Hiltunen M, Morgan T, Ahmad

S, Vardarajan BN, Epelbaum J, Hoffmann P, Boada M, Beecham GW, Garnier JG, Harold D, Fitzpatrick AL, Valladares O, Moutet ML, Gerrish A, Smith AV, Qu L, Bacq D, Denning N, Jian X, Zhao Y, Del Zompo M, Fox NC, Choi SH, Mateo I, Hughes JT, Adams HH, Malamon J, Sanchez-Garcia F, Patel Y, Brody JA, Dombroski BA, Naranjo MCD, Daniilidou M, Eiriksdottir G, Mukherjee S, Wallon D, Uphill J, Aspelund T, Cantwell LB, Garzia F, Galimberti D, Hofer E, Butkiewicz M, Fin B, Scarpini E, Sarnowski C, Bush WS, Meslage S, Kornhuber J, White CC, Song Y, Barber RC, Engelborghs S, Sordon S, Voijnovic D, Adams PM, Vandenberghe R, Mayhaus M, Cupples LA, Albert MS, De Deyn PP, Gu W, Himali JJ, Beekly D, Squassina A, Hartmann AM, Orellana A, Blacker D, Rodriguez-Rodriguez E, Lovestone S, Garcia ME, Doody RS, Munoz-Fernadez C, Sussams R, Lin H, Fairchild TJ, Benito YA, Holmes C, Karamujić-Čomić H, Frosch MP, Thonberg H, Maier W, Roschupkin G, Ghetti B, Giedraitis V, Kawalia A, Li S, Huebinger RM, Kilander L, Moebus S, Hernández I, Kamboh MI, Brundin R, Turton J, Yang Q, Katz MJ, Concari L, Lord J, Beiser AS, Keene CD, Helisalmi S, Kloszewska I, Kukull WA, Koivisto AM, Lynch A, Tarraga L, Larson EB, Haapasalo A, Lawlor B, Mosley TH, Lipton RB, Solfrizzi V, Gill M, Longstreth WT Jr, Montine TJ, Frisardi V, Diez-Fairen M, Rivadeneira F, Petersen RC, Deramecourt V, Alvarez I, Salani F, Ciaramella A, Boerwinkle E, Reiman EM, Fievet N, Rotter JI, Reisch JS, Hanon O, Cupidi C, Andre Uitterlinden AG, Royall DR, Dufouil C, Maletta RG, de Rojas I, Sano M, Brice A, Cecchetti R, George-Hyslop PS, Ritchie K, Tsolaki M, Tsuang DW, Dubois B, Craig D, Wu CK, Soininen H, Avramidou D, Albin RL, Fratiglioni L, Germanou A, Apostolova LG, Keller L, Koutroumani M, Arnold SE, Panza F, Gkatzima O, Asthana S, Hannequin D, Whitehead P, Atwood CS, Caffarra P, Hampel H, Quintela I, Carracedo Á, Lannfelt L, Rubinsztein DC, Barnes LL, Pasquier F, Frölich L, Barral S, McGuinness B, Beach TG, Johnston JA, Becker JT, Passmore P, Bigio EH, Schott JM, Bird TD, Warren JD, Boeve BF, Lupton MK, Bowen JD, Proitsi P, Boxer A, Powell JF, Burke JR, Kauwe JSK, Burns JM, Mancuso M, Buxbaum JD, Bonuccelli U, Cairns NJ, McQuillin A, Cao C, Livingston G, Carlson CS, Bass NJ, Carlsson CM, Hardy J, Carney RM, Bras J, Carrasquillo MM, Guerreiro R, Allen M, Chui HC, Fisher E, Masullo C, Crocco EA, DeCarli C, Bisceglio G, Dick M, Ma L, Duara R, Graff-Radford NR, Evans DA, Hodges A, Faber KM, Scherer M, Fallon KB, Riemenschneider M, Fardo DW, Heun R, Farlow MR, Kölsch H, Ferris S, Leber M, Foroud TM, Heuser I, Galasko DR, Giegling I, Gearing M, Hüll M, Geschwind DH, Gilbert JR, Morris J, Green RC, Mayo K, Growdon JH, Feulner T, Hamilton RL, Harrell LE, Drichel D, Honig LS, Cushion TD, Huentelman MJ, Hollingworth P, Hulette CM, Hyman BT, Marshall R, Jarvik GP, Meggy A, Abner E, Menzies GE, Jin LW, Leonenko G, Real LM, Jun GR, Baldwin CT, Grozeva D, Karydas A, Russo G, Kaye JA, Kim R, Jessen F, Kowall NW, Vellas B, Kramer JH, Vardy E, LaFerla FM, Jöckel KH, Lah JJ, Dichgans M, Leverenz JB, Mann D, Levey AI, Pickering-Brown S, Lieberman AP, Klopp N, Lunetta KL, Wichmann HE, Lyketsos CG, Morgan K, Marson DC, Brown K, Martiniuk F, Medway C, Mash DC, Nöthen MM, Masliah E, Hooper NM, McCormick WC, Daniele A, McCurry SM, Bayer A, McDavid AN, Gallacher J, McKee AC, van den Bussche H, Mesulam M, Brayne C, Miller BL, Riedel-Heller S, Miller CA, Miller JW, Al-Chalabi A, Morris JC, Shaw CE, Myers AJ, Wiltfang J, O'Bryant S, Olichney JM, Alvarez V, Parisi JE, Singleton AB, Paulson HL, Collinge J, Perry WR, Mead S, Peskind E, Cribbs DH, Rossor M, Pierce A, Ryan NS, Poon WW, Nacmias B, Potter H, Sorbi S, Quinn JF, Sacchinelli E, Raj A, Spalletta G, Raskind M, Caltagirone C, Bossù P, Orfei MD, Reisberg B, Clarke R, Reitz C, Smith AD, Ringman JM, Warden D, Roberson ED, Wilcock G, Rogaeva E, Bruni AC, Rosen HJ, Gallo M, Rosenberg RN, Ben-Shlomo Y, Sager MA, Mecocci P, Saykin AJ, Pastor P, Cuccaro ML, Vance JM, Schneider JA, Schneider LS, Slifer S, Seeley WW, Smith AG, Sonnen JA, Spina S, Stern RA, Swerdlow RH, Tang M, Tanzi RE, Trojanowski JQ, Troncoso JC, Van Deerlin VM, Van Eldik LJ, Vinters HV, Vonsattel JP, Weintraub S, Welsh-Bohmer KA, Wilhelmsen KC, Williamson J, Wingo TS, Woltjer RL, Wright CB, Yu CE, Yu L, Saba Y; Alzheimer Disease Genetics Consortium (ADGC),; European Alzheimer's Disease Initiative (EADI),; Cohorts for Heart and Aging Research in Genomic Epidemiology Consortium (CHARGE),; Genetic and Environmental Risk in AD/Defining Genetic, Polygenic and Environmental Risk for Alzheimer's Disease Consortium (GERAD/PERADES),, Pilotto A, Bullido MJ, Peters O, Crane PK, Bennett D, Bosco P, Coto E, Boccardi V, De Jager PL, Lleo A, Warner N, Lopez OL, Ingelsson M, Deloukas P, Cruchaga C, Graff C, Gwilliam R, Fornage M, Goate AM, Sanchez-Juan P, Kehoe PG, Amin N, Ertekin-Taner N, Berr C, Debette S, Love S, Launer LJ, Younkin SG, Dartigues JF, Corcoran C, Ikram MA, Dickson DW, Nicolas G, Campion D, Tschanz J, Schmidt H, Hakonarson H, Clarimon J, Munger R, Schmidt R, Farrer LA, Van Broeckhoven C, C O'Donovan M, DeStefano AL, Jones L, Haines JL, Deleuze JF, Owen MJ, Gudnason V, Mayeux R, Escott-Price V, Psaty BM, Ramirez A, Wang LS, Ruiz A, van Duijn CM, Holmans PA, Seshadri S, Williams J, Amouyel P,

Schellenberg GD, Lambert JC, Pericak-Vance MA. Genetic meta-analysis of diagnosed Alzheimer's disease identifies new risk loci and implicates Aβ, tau, immunity and lipid processing. Nat Genet. 2019 Mar;51(3):414-430. doi: 10.1038/s41588-019-0358-2. Epub 2019 Feb 28.

III. Faculty Biography

Dr. Alison Goate, DPhil, completed her education in the U.K. where she obtained a Bacheors of Science in Biochemistry from the University of Bristol and a PhD/D.Phil in molecular cell biology from Oxford University. She first worked on the genetics of Alzheimer's disease in the lab of Dr. John Hardy at Imperial College London. In 1992 she joined the faculty at Washington University in St. Louis where she spent more than 20 years. In 2015, she moved to the Icahn School of Medicine to become the Director of the Ronald M. Loeb Center for Alzheimer's disease. She is a renowned neuropsychiatric researcher and molecular geneticist whose pioneering work falls within two areas: gene discovery and modeling disease mutations. She is best known for identifying the first gene mutation linked to an inherited form of Alzheimer's disease, and for identifying a network of microglial expressed genes regulated by the transcription Pu.1/SPI1 that influence risk for late onset AD. Dr. Goate has published more than 500 papers in major journals including *Nature, Nature Neuroscience, Science, Nature Genetics, Neuron, Proceedings of the National Academy of Sciences, Molecular Psychiatry,* and *Biological Psychiatry*. She has won multiple awards for her work including the Potamkin Award from the American Academy of Neurology (1994), the MetLife Award (1994) and the Khalid Iqbal Lifetime Achievement Award from the Alzheimer's Association (2015). She was elected a fellow of the American Association for the Advancement of Science in 2012 and a member of the National Academy of Medicine in 2016.

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's 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 Education 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 **Jean Paul Vonsattel** 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
2017	Eliezer Masliah	Disease Modifying Therapeutical Approaches for Synucleinopathies of the Aging Population
2018	Rebecca D. Folkerth	Reading Tea Leaves: Patterns of Injury in the Pediatric Nervous System
2019	Jean Paul Vonsattel	Approaching the Challenge of Determining Mechanism Through Neuropathology

SAUL R. KOREY LECTURE

Approaching the Challenge of Determining Mechanism Through Neuropathology

Time: 10:30 am – 11:30 am

Date: Saturday, June 8, 2019

Jean Paul Vonsattel, MD, *Columbia University, New York, NY*

I. Learning Objectives

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

1. Describe the pathologic data that reveal insights into the causes of hypokinetic versus hyperkinetic disorders.
2. Explain how "basal ganglia" degeneration can cause an imbalance of outputs, either positive or negative.
3. Contrast sequelae of successful or failed therapeutic intervention.

II. Abstract & Relevant References

The novel molecular techniques applied for investigating the pathogenesis of neurodegenerative diseases provide a constant flow of new data, the interpretations of which are often challenging, or to some extent confusing. To learn from past experiences, selected clinicopathologic observations and interpretationsare used that form the basis of our current understanding of the roles of the basal ganglia.

Thus, proposed is to briefly review how previous generations of neuropathologists coped with the emerging multifaceted data to ultimately figure out which primary or secondary centers of the brain are involved in the occurrence of gradually worsening, differential or overlapping movements disorders. The attempted review focuses in parallel on the neuropathologic findings and clinical correlations pertaining to the pathogenesis of hypokinesia, as in Parkinsonism for example, or of hyperkinesia, as in Huntington disease.

Despites the limitations of the conventional techniques applied, the neuropathologic phenotypes recorded and the modus operanndi can provide critical clues as to the mechanisms underlying neurodegeneration, which can help triage and interpret molecular findings, and ultimately contribute to the development of therapies beyond pallidotomy or deep brain stimulation.

References:

1. Blocq P, Marinesco G. Sur un cas de tremblement parkinsonien hémiplégique symptomatique d'une tumeur du pédoncule cérébral. Comptes Rendus Des Séances De La Société De Biologie Et De Ses Filiales. 1893;5:105-11. PubMed PMID: 2417.
2. Marinesco G. Sur la présence des corpuscules acidophiles paranucléolaires dans les cellules du locus niger et du locus coeruleus. Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences. 1902;135:1000-2. PubMed PMID: 2420.
3. Lewy FH. Zur pathologischen Anatomie der Paralysis agitans. Deutsche Zeitschrift für Nervenheilkunde. 1913;50:50-5. PubMed PMID: 2252.
4. Kiesselbach G. Anatomischer Befund eines Falles von Huntingtonscher Chorea. MonatsschrPsychiatNeurol. 1914;35:525-43.
5. Hunt JR. Progressive atrophy of the globus pallidus (Primary atrophy of the pallidal system). Brain. 1917;40:58-148. PubMed PMID: 310.
6. Trétiakoff C. Contribution à l'étude de l'anatomie pathologique du locus niger de Soemmering avec quelques déductions relatives à la pathogénie des troubles du tonus musculaire et de la maladie de Parkinson. Paris: Jouve & Cie, éditeurs; 1919.

7. Goldstein K. Über anatomische Veränderungen (Atrophie der Substantia nigra) bei postencephalitischem Parkinsonismus. Zeitschrift für die gesamte Neurologie und Psychiatrie. 1922;76(1):627-32. PubMed PMID: 4084.
8. Geddes JF, Hughes AJ, Lees AJ, Daniel SE. Pathological overlap in cases of parkinsonism associated with neurofibrillary tangles. A study of recent cases of postencephalitic parkinsonism and comparison with progressive supranuclear palsy and Guamanian parkinsonism-dementia complex. Brain. 1993;116:281-302. PubMed PMID: 429.
9. DeLong MR, Wichmann T. Circuits and circuit disorders of the basal ganglia. Archives of Neurology. 2007;64:20-4. PubMed PMID: 3495.
10. Greenfield JG, Bosanquet FD. The brain-stem lesions in parkinsonism. Journal of Neurology Neurosurgery & Psychiatry. 1953;16:213-26. PubMed PMID: 4086.

III. Faculty Biography

Dr. Vonsattel's main focus of interest is the neuropathology of neurodegenerative diseases, particularly Alzheimer disease, frontotemporal lobar degeneration, Parkinson disease, and associate diseases causing Parkinsonism including essential tremor; and Huntington disease. He is the director of the New York Brain Bank at Columbia University, Director of Neuropathology in the Taub Institute at Columbia University, and also the director of the Alzheimer's Research Center Neuropathology Core at Columbia University Medical Center. He developed new standards, which gained wide-acceptance, for banking postmortem, diagnostically well-characterized brain and organs samples optimally prepared for basic research.

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 Education Committee.

We are pleased to have **Kwanghun Chung** 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
1993	W. Ian McDonald	The Clinical and Pathological Dynamics of Multiple Sclerosis
1995	Leroy Hood	Deciphering the Human Genome: Implications for Medicine of the 21st Century
1996	Martin Raff	Programmed Cell Death--Mechanisms and Social Controls
1997	Michael Goedert	Tau Pathology as the Common Denominator between Alzheimer's Disease and other Neurodegenerative Disorders
1998	James Eberwine	Single Cell Molecular Neuropathology
1999	Richard T. Johnson	Viral Pathogenesis, an Overview
2000	Seymour Benzer	The Neuropathology of Drosophila
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	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
2010	Mark Gilbert	RTOG: Clinical Trials and the Increasing Role of Neuropathology
2011	Kevin P. Campbell	Mechanistic and Molecular Insights into the Pathogenesis of Glycosylation – Deficient Muscular Dystrophy
2012	Robert H. Brown, Jr.	The Pathogenesis of ALS
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
2017	M. Beatriz S. Lopes	An Update of the WHO Classification of Tumors of the Pituitary Gland, 4th Edition
2018	Mario L. Suvà	Deciphering Single-Cell Regulatory Programs in Adult and Pediatric Gliomas
2019	Kwanghun Chung	Rapid and Holistic 3D Imaging of Large-Scale Tissues

MATTHEW T. MOORE LECTURE

Rapid and Holistic 3D Imaging of Large-Scale Tissues

Time: 8:45 am – 9:35 pm
Date: Sunday, June 9, 2019
Kwanghun Chung, PhD, *Massachusetts Institute of Technology, Cambridge, MA*

I. Learning Objectives

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

1. Define 3D imaging of tissues.
2. Explain the underlying principles of 3D tissue transformation techniques.
3. Explain the underlying principles of rapid tissue labeling methods.
4. Discuss the unique advantages of holistic and rapid intact tissue imaging and phenotyping.

II. Abstract & Relevant References

Holistic measurement of diverse functional, anatomical, and molecular traits that span multiple levels, from molecules to cells to an entire system, remains a major challenge in biology. In this talk, I will introduce a series of technologies including CLARITY (Chung, 2013), SWITCH (Murray, 2015), MAP (Ku, 2016), stochastic electrotransport (Kim, 2015), and SHIELD (Park, 2019) that enable integrated multiscale imaging and molecular phenotyping of both animal tissues and human clinical samples. I will discuss how we engineer (1) the physicochemical properties of brain tissues, (2) molecular interactions, and (3) molecular transport all together to achieve integrated brain-wide molecular phenotyping at unprecedented speed and resolution. I will also discuss how these tools can be deployed synergistically to study a broad range of biological questions. We hope that these new technologies will accelerate the pace of discovery in biomedical research.

References:

1. Young-Gyun Park*, Chang Ho Sohn*, Ritchie Chen*, Margaret McCue, Gabrielle T. Drummond, Taeyun Ku, Dae Hee Yun, Nicholas B. Evans, Hayeon Caitlyn Oak, Wendy Trieu, Heejin Choi, Xin Jin, Varoth Lilascharoen, Ji Wang, Matthias C. Truttmann, Helena W. Qi, Hidde L. Ploegh, Todd R. Golub, Shih-Chi Chen, Matthew P. Frosch, Heather J. Kulik, ByungKook Lim, **Kwanghun Chung**†, "Protection of tissue physicochemical properties using polyfunctional crosslinkers", ***Nature Biotechnology***, 2018, doi:nbt.4281
2. Taeyun Ku, Justin Swaney, Jeong-Yoon Park, Alexander Albanese, Evan Murray, Jae Hun Cho, Young-Gyun Park, Vamsi Mangena, Jiapei Chen, and **Kwanghun Chung**. "Multiplexed and scalable super-resolution imaging of three-dimensional protein localization in size-adjustable tissues", ***Nature Biotechnology***, 2016, 34(9), 973-81.
3. Evan Murray, Jae Hun Cho, Daniel Goodwin, Taeyun Ku, Justin Swaney, Sung-Yon Kim, Heejin Choi, Jeong-Yoon Park, Austin Hubbert, Meg McCue, Young-Gyun Park, Sara Vassallo, Naveed Bakh, Matthew Frosch, Van J. Wedeen, H. Sebastian Seung, and **Kwanghun Chung**. Simple, scalable proteomic imaging for high-dimensional profiling of intact systems, ***Cell,*** Dec 3:163(6): 1500-14. doi: 10.1016/j.cell.2015.11.025. PubMed PMID: 26638076.
4. Sung-Yon Kim, Jae Hun Cho, Evan Murray, Naveed Bakh, Heejin Choi, Kimberly Ohn, Sara Vassallo, Luzdary Ruelas, Austin Hubbert, Meg McCue, Philipp Keller and **Kwanghun Chung**. **Stochastic electrotransport selectively enhances the transport of highly electromobile molecules**, ***PNAS***, 2015 Nov 17: 112(46): E6274-83. doi: 10.1073/pnas.1510133112. Epub 2015 Nov 2. PubMed PMID: 26578787; PubMed Central PMCID: PMC4655572.
5. **Kwanghun Chung**, Jenelle Wallace, Sung-Yon Kim, Sandhiya Kalyanasundaram, Aaron Andalman, Tom J. Davidson, Kelly A. Zalocusky, Joanna Mattis, Sally Pak, Viviana Gradinaru, Hannah Bernstein, Julie Mirzabekov, Charu Ramakrishnan, and Karl Deisseroth, "Structural and molecular interrogation of intact biological systems", ***Nature***, 2013, 497, 332-337

III. Faculty Biography

Kwanghun Chung is currently an Assistant Professor of Chemical Engineering at MIT, as well as a Core Member of the Institute for Medical Engineering and Science (IMES). He is also a Core Member of the Picower Institute for Learning and Memory, and an Associate Member of the Broad Institute. He received his B.S. in Chemical Engineering from Seoul National University in 2005, and then moved to Georgia Institute of Technology for his Ph.D. training under the mentorship of Dr. Hang Lu, where he developed automated and integrated microsystems for high-throughput imaging, molecular/behavioral phenotyping, and cell microsurgery of a broad range of living systems. Following his graduation in 2009, Dr. Chung joined the Karl Deisseroth Lab at Stanford University for post-doctoral training in 2010, where he invented a novel technology termed CLARITY, which enables system-wide structural and molecular analysis of large-scale intact biological samples. In 2013, Dr. Chung established his independent group at MIT and has been leading an interdisciplinary team to develop and apply novel technologies for holistic understanding of large-scale complex biological systems. Chung was the recipient of the NIH New Innovator Award 2016, the Mcknight Technological Innovations in Neuroscience Award 2016, the Packard Fellowships for Science and Engineering Award 2015, the NARSAD Young Investigator Award 2015, the Yumin Awards for Creativity 2014, the Searle Scholars Award 2014, and the BWF Career Award at the Scientific Interface 2012.

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Award for Meritorious Contributions to Neuropathology

Friday, June 7, 2019
11:30 am – 11:45 am
Honoring Eileen Bigio, MD
Presented by: Qinwen Mao, MD, PhD

Saturday, June 8, 2019
11:30 am – 11:45 am
Honoring Raymond Sobel, MD
Presented by: Jeffrey Golden, MD

AWARD 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. Eileen Bigio** and **Dr. Raymond Sobel**. 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

Year	Recipient
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
2017	Ronald C. Kim
	Harry V. Vinters
2018	Hannah C. Kinney
	Brian N. Harding
2019	Eileen Bigio
	Raymond Sobel

AWARD FOR MERITORIOUS CONTRIBUTIONS TO NEUROPATHOLOGY

Biography: Eileen Bigio, MD

Dr. Bigio graduated from the University of Michigan in 1975 with a degree in Medical Technology and worked for six years in Ann Arbor and Galveston, TX. As the daughter of two teachers, Eileen had known she did not want to teach, so when she reached the limits of her interest in medical technology, she returned to school in 1981 for her medical degree. Even as she started a family she 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. During her residency she became intrigued by Alzheimer disease when the family of a wealthy Galveston woman had her body exhumed for an autopsy to prove she had dementia. Later, at an annual Texas Society of Pathology meeting, she heard talks by Dr. Charles White and Dr. Dennis Burns from UT Southwestern Medical School in Dallas and learned that UT Southwestern had just been awarded an NIA ADC. She applied for and was accepted into a Neuropathology training program customized for her by Drs. White and Burns. All three, coincidentally, were the same age. From the beginning of her neuropathology training, Eileen's 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.

In 2001 she was recruited to lead the Neuropathology Core of the Northwestern University Feinberg Alzheimer Disease Center in Chicago. 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. Despite her earlier avoidance of teaching as a profession, she found she had an instinct for it, and she developed an ACGME-accredited Neuropathology Fellowship training program at Northwestern University Feinberg School of Medicine in 2008. Of her over 200 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 also published the first case of what is now called Globular Glial Tauopathy, and later the first case of what is now called FTLD-FET (FTLD-FUS), NIFID. 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 has been on review panels for the Brain and Tissue Repository Contract applications and for ADNI.

She was named the Paul E. Steiner Research Professor of Pathology in 2012, renewed in 2015 and 2018. Since 2014 she has been recognized yearly by Thomson Reuters as being one of the Northwestern Feinberg School of Medicine physicians having highly cited papers (top 1% most cited). Dr. Bigio has served on the Program Committee, Awards Committee, and Professional Affairs Committee of the American Association of Neuropathologists, has chaired or co-chaired many platform sessions, and since 2014 has been an Executive Council Member-At-Large for the AANP. In 2020 she will be Vice-President, alongside her chairman, Dan Brat, who will be President, of the AANP.

Dr. Eileen Bigio "Contributions to the Field", written by Qinwen Mao, MD, PhD

Early career exploration. Eileen Bigio was born in a small town in Michigan. As a child, she was full of energy and curiosity. Her favorite activity was building things with her dad in the basement to unleash her inner curiosity and creativity. As she grew older, her dream was to be either a medical technologist or doctor, and eventually, she chose the field of medical technology. Eileen attended the University of Michigan and received her undergraduate degree, a B.S. in Medical Technology, in 1975. She worked as a medical technologist at the University of Michigan hospital in Ann Arbor, and then at UT Medical Branch in Galveston, Texas. It was while working in Galveston that she found her job to not be challenging enough and finally decided to go back to medical school at age 28. She considered herself a "geriatric" freshman med student. During her pathology residency at UTMB, from 1985 to 1989, she became interested in neuropathology, under the mentorship of Dr. Jerry Campbell. She became particularly intrigued by Alzheimer disease when the family of a wealthy deceased Galvestonian had her body exhumed for a brain autopsy to prove she had dementia, in order to contest her will.

A pioneer in FTLD research. During her 4th year of the then 5-year Pathology residency, she was inspired by talks given by Dr. Charles White and Dr. Dennis Burns from UT Southwestern at the annual Texas Society of Pathology meeting. When Dr. White informed the attendees that UT Southwestern had just been awarded an NIA ADC, Eileen decided that she needed to do a neuropathology fellowship and that Dallas was the obvious place to go. She stayed on as faculty at UT Southwestern as Dr. White's assistant in the Neuropathology Core of the UTSW ADC. At UTSW, Eileen began focusing on frontotemporal lobar degeneration. This was partly sparked by a platform presentation she made at the 1998 AANP meeting about dementia in PSP, when Dennis Dickson got up afterward and said he thought some of the cases she presented might be CBD instead of PSP. She started studying FTLD and the UTSW brain autopsy cases that had "unsatisfying" diagnoses, and at the 2001 AANP meeting, she presented the finding that FTLD-U, now FTLD-TDP, was the most common FTLD, previously thought to be "dementia lacking distinctive histology." Around that time, she also published the first case of what is now known as Globular Glial Tauopathy, and later, the first case of what is now known as FTLD-FET (FTLD-FUS), NIFID.

A contributor to the academic community. In 2001, she was recruited to lead the Neuropathology Core of the Northwestern Alzheimer Disease Center, now called the Mesulam Center for Cognitive Neurology and Alzheimer's Disease. With Northwestern ADC's focus on primary progressive aphasia (PPA) resulting in more FTLD brain autopsies than the usual ADC, and the presence of Dr. Teepu Siddique at Northwestern offering the opportunity to acquire brain/spinal cord autopsies on ALS patients, it was the perfect fit for Eileen. Over the years, together with the Northwestern ADC group she has published extensively on the underlying pathology of PPA, which is often more severe in language-related regions of the brain. More recently, with them she has published on the pathologic findings of a group of subjects known as "SuperAgers," whose brains seem to have more von Economo neurons than the brains of normal, non-cognitively impaired elderly individuals (von Economo neurons are a type of neuron Bill Seeley has resurrected that are linked to frontotemporal dementia). Later collaborations included those with Dr. Tanya Simuni on autopsies of patients with movement disorders. She has also extensively collaborated with Ian Mackenzie, Manuela Neumann, and Rosa Rademakers on many clinicopathologic/genetic investigations of FTLD-linked disorders. She is the author of over 200 scientific publications. Since 2014, she has been recognized yearly by Thomson Reuters as being one of Northwestern Feinberg School of Medicine's highly cited physicians. The AANP has been at the center of Eileen's academic life. She has served on the Program Committee, the Awards Committee, and the Executive Committee, has chaired or co-chaired many platform sessions, and will be its Vice President in 2020, alongside the president, Dan Brat.

A mentor to the younger generation. Eileen 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 instituted the ACGME-accredited Neuropathology Fellowship training program at Northwestern in 2008, which is the only Neuropathology fellowship program in Illinois. She is a brilliant teacher who is loved by trainees and students alike. She is very generous with her time when teaching. She has the mysterious ability to present complicated concepts in a simple, clear, and humorous way. She is always the first person to reply to emails regarding an abstract or manuscript, with detailed edits and suggestions in beautiful writing. She has provided professional help to numerous colleagues, junior faculty, fellows, and residents on campus. She always makes time to talk to medical school students who contact her for career guidance or summer fellowship opportunities. She shares with them her passion for neuropathology and for unraveling the mysteries of dementia and provides them with lab experience as much as possible.

Passion and compassion. Eileen makes changes in the work place to facilitate better communication and efficiency. She opens doors and creates a communication-friendly space. She is hands-on and is always the first person to find where a communication breakdown may be occurring (and then proceeds to fix whatever issues arise). In the last few years, she has suffered from multiple health problems requiring medical attention. After each surgery or hospitalization, she got back on her feet right away and with full energy. There is nothing that can defeat her passion for her job. She is the mother at the work place whom colleagues and co-workers go to for suggestions and support when they have issues at work or at home. Outside of work, she loves her family unconditionally and enjoys travelling, glass fusing, genealogy, and wine-making.

Eileen is knowledgeable, passionate, generous, understanding, and kind—someone who I am proud to consider my mentor, colleague, and friend. I have learned a great deal, not only about neuropathology but also about life, from her. Eileen represents a spirt of excellence and excitement for neuropathology. She sets a great example for all of us in that sense and is thus a very worthy recipient of the Award for Meritorious Service.

Biography: Raymond Sobel, MD

Raymond A. Sobel, MD was born in Los Angeles and was raised in Burbank, California. In his early years, he played the trumpet in various school and local groups. He attended Stanford University where he played in the Stanford Orchestra but later focused on pre-med studies. He graduated with a BS in Chemistry and Biology in 1972. He received his MD degree from the University of California San Francisco School of Medicine in 1976 and trained in anatomic pathology at UC Davis and UCSF. His exposure to neuropathology began at UCSF with Dr. Jeannette Townsend and formal training at UC Davis with Drs. William G. Ellis and Surl L. Nielsen. At that time, his research projects included studies of CNS coccidioidomycosis and toxic effects on CNS white matter in patients treated with amphotericin B methyl ester. He presented a poster on the latter topic at his first American Association of Neuropathologists meeting in New Orleans in 1980. Dr. Sobel has attended every AANP meeting since then. He subsequently trained in neuropathology at Stanford with Drs. Lucien Rubinstein, Mary Herman, and Lysia Forno and worked on a project on GFAP in hepatic encephalopathy with Drs. Forno, Lawrence Eng and Steven DeArmond; the latter led to his first publication in *JNEN* in 1981.

Following the encouragement of several mentors to pursue additional laboratory research, Dr. Sobel then moved to Boston for an immunopathology fellowship in the Department of Pathology at Massachusetts General Hospital with Dr. Robert Colvin. For 11 years at MGH, Dr. Sobel continued to work in diagnostic neuropathology under the mentorship of Drs. E.P. Richardson and E. Tessa Hedley-Whyte and to perform immunopathology research. He worked with Professor Marjorie Lees on experimental autoimmune encephalomyelitis (EAE) induced with myelin proteolipid protein (PLP); she was the co-discoverer of PLP and a cherished mentor. He also studied infection of the CNS by what was then called HTLV-III in the initial stages of the HIV/AIDS epidemic. His MGH years were highlighted by immersion in the rich immunology environment at Harvard and exposure to the giants of clinical neurology at MGH including Drs. Raymond D. Adams and C. Miller Fisher. He also witnessed the early stellar career trajectories of some of the current leaders of neuropathology including Drs. Ann McKee, David Louis, John M. (Jack) Lee and Jeffrey Golden. Collaborations with the Harvard immunologist Professor Vijay Kuchroo began in 1990 and have continued to the present, resulting in more than 60 publications.

In 1992, Dr. Sobel returned to Stanford to continue clinical practice, initially along with Drs. Dikran Horoupian, Maie K. Herrick and Lysia Forno. He continues to serve as Professor of Pathology (Neuropathology) at the Stanford University School of Medicine and as the neuropathologist at the Palo Alto VA Health Care System. His early exposure to research on CNS infections and EAE led to continuing emphasis in those areas in his laboratory. In addition to Dr. Kuchroo, he has worked with collaborators at Stanford, including Drs. Eugene Butcher, May Han, Larry Steinman and David Stevens, Dr. Arlene Sharpe at Harvard, Dr. Scott Zamvil at UCSF, their trainees, and colleagues at other institutions.

Dr. Sobel participated in numerous committees of the AANP and chaired the Program and Nominating Committees; he served as AANP Vice-President in 2002 and President in 2012. He has served on various Stanford and VA committees, Editorial Boards and Grant Review Committees of the National MS Society and the NIH. He was on the Editorial Board (1991-2004), and served as Associate Editor (2005-2007), and then Editor-in-Chief (2007-2016) of the *JNEN*. In addition to clinical duties, he continues to serve as Deputy Editor of the *JNEN* and to teach neuropathology to students and trainees in pathology, neurology, neurosurgery, and neuropsychology at Stanford and the VA and to pursue his research on the pathogenesis of demyelinating diseases.

Dr. Raymond Sobel "Contributions to the Field", written by Jeffrey Golden, MD

Dr. Raymond Sobel has made numerous and broad ranging contributions to neuropathology. Scientifically he has published important papers in the fields of infectious diseases, oncology, neurodegeneration and most significantly immunology. Through his meticulous work he has helped characterize the pathobiology underlying multiple sclerosis in several animal models, and most significantly experimental autoimmune encephalomyelitis (EAE). He is lauded by his collaborators to bring new dimensions to their studies and new insights into our understanding of immunologically mediated nervous system disorders. Beyond his science, Dr. Sobel has been an active member of the AANP, having never missed a meeting since first attending in 1980 and serving numerous leadership roles including the AANP President in 2012 (Chicago, IL for the record). Finally, Dr. Sobel served as the Editor-in-Chief of our Journal for a decade, from 2007-2016. As the Editor he was exemplary at being fair with both authors and reviewers. During this time, he meticulously read and edited every manuscript and deftly navigated the journals' relationships with several publishers and the association leadership. Dr. Sobel's leadership and extreme dedication were instrumental to the Journal's continued success. This contribution alone to the AANP would be worthy of meritorious recognition, but as outlined above, is but one piece of the many contributions Dr. Sobel has made to neuropathology.

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

What Every Neuropathologist Needs to Know

Saturday, June 8, 2019

WHAT EVERY NEUROPATHOLOGIST NEEDS TO KNOW

What Every Neuropathologist Needs to Know About Muscle

Time: 4:45 pm – 5:15 pm

Steven Moore, MD, PhD, *The University of Iowa, Iowa City, IA*

I. Learning Objectives:

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

1. Apply best practices of muscle biopsy processing to consistently prepare tissue of the highest quality for diagnostic evaluation.
2. Construct a diagnostic approach to best evaluate individual neuromuscular disease cases.
3. Recall classic patterns of skeletal muscle pathology that may be utilized as biomarkers of neuromuscular disease.

II. Abstract and Relevant Resources

Muscle biopsy evaluation has a long history of contributing information critically important for the diagnosis of neuromuscular disorders. Structural, ultrastructural, histochemical, and enzyme histochemical pathology are all used to classify disease. As the genetic basis for some neuromuscular disorders unfolded, biopsy pathology took on the role of predicting the underlying mutant gene. The additional tool of immunohistochemistry became particularly helpful in the diagnosis of genetic and inflammatory myopathies. Technological advances in molecular genetic evaluation have altered the landscape and, in some instances, pushed muscle biopsy pathology into the role of confirming the pathogenesis of novel gene variants or variants of unknown significance. However, diagnostic approaches vary widely among clinicians who evaluate neuromuscular disease. Some patients will undergo extensive clinical and laboratory evaluation prior to the muscle biopsy. In other patients a biopsy will be performed after only cursory clinical observations.

In order to best serve patients and clinical colleagues, neuropathologists practicing muscle pathology should rely on old-school acumen to optimally prepare skeletal muscle for pathologic evaluation and to recognize classic patterns of neuromuscular pathology. The toolbox utilized by individual neuropathologists may vary widely depending on their training, practice volume, case mix, and laboratory resources. However, considerable diagnostic mileage can be derived from a relatively small, standard set of tools. Diagnostic approaches can be individualized to best evaluate specific muscle biopsies. A broad spectrum of neuromuscular disease examples will be shown as a guide to what every neuropathologist needs to know about muscle.

Web-based resources

1. Gene Table of Neuromuscular Disorders. http://www.musclegenetable.fr
2. GeneReviews. https://www.ncbi.nlm.nih.gov/books/NBK1116/
3. Leiden Muscular Dystrophy Pages. http://www.dmd.nl
4. Online Mendelian Inheritance in Man. https://www.ncbi.nlm.nih.gov/omim
5. Monoclonal Antibodies for Muscular Dystrophy Research. http://www.glennmorris.org.uk/mabs/WCIND.htm
6. Developmental Studies Hybridoma Bank. http://dshb.biology.uiowa.edu

Textbook and other resources

1. Dubowitz V, Sewry CA, and Oldfors A. Muscle Biopsy: A Practical Approach, 4th edition, Saunders, 2013.
2. Engel AG and Franzini-Armstrong C. Myology. 3rd Edition. McGraw-Hill, New York, 2004.
3. Carpenter S and Karpati G, Pathology of Skeletal Muscle, 2nd edition, Oxford University Press, 2001.
4. Amato AA and Russell JA, Neuromuscular Disorders, 2nd edition, McGraw Hill, 2016.
5. Heffner RR Jr., Moore SA, and Balos LL. *Muscle Biopsy in Neuromuscular Diseases*. Chapter 4, in Sternberg's Diagnostic Surgical Pathology, 6th edition. Mills SE, ed. Wolters Kluwer, pages 113-147, 2015.
6. Romansky SG. *Neuromuscular diseases*. Chapter 35, in Potter's Pathology of the Fetus, Infant, and Child, 2nd edition, Gilbert-Barness E, ed. Mosby, pages 1899-1957, 2007.
7. Cai C, Anthony DC, and Pytel P. A pattern-based approach to the interpretation of skeletal muscle biopsies. Mod Pathol. 32:462-483, 2019.

III. Faculty Biography:

Dr. Moore is a Professor in the Department of Pathology at the University of Iowa. He is also Co-Director of the NIH-funded Wellstone Muscular Dystrophy Cooperative Research Center (MDCRC) at Iowa. Originally from Indiana where he obtained a bachelor's degree at Purdue University and both PhD and MD degrees at Indiana University School of Medicine, he moved to Iowa in 1982 for a residency in anatomic pathology followed by a fellowship in neuropathology, both at the University of Iowa. Starting around 1997, Dr. Moore's clinical and research interests increasingly focused on neuromuscular disorders. His clinical service responsibilities include muscle and nerve biopsy diagnostics and molecular genetic testing for FSHD. The Iowa Wellstone MDCRC was first funded in 2005. One component of the MDCRC is a biorepository of muscle biopsies and cultured fibroblasts. Clinical and basic science projects in the MDCRC focus on the dystroglycanopathies. The biorepository resources support basic science research as well as assay development for the use of muscle biopsy endpoints in clinical trials.

WHAT EVERY NEUROPATHOLOGIST NEEDS TO KNOW

What Every Neuropathologist Needs to Know: Nerve

Time: 5:15 pm – 5:45 pm

Peter Pytel, MD, *The University of Chicago, Chicago, IL*

I. Learning Objectives:

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

1. Explain what to communicate to the treating clinician as to what can be expected from a tissue biopsy on a patient with peripheral neuropathy.
2. Explain how to make basic decisions regarding specimen triage of peripheral nerve biopsies.
3. Identify the most common patterns of morphologic change observed in peripheral nerve biopsies.

II. Abstract and Relevant Resources

Peripheral neuropathy is one of the most common neurologic diseases and can have very diverse etiologies. These include metabolic disease processes like diabetes, nutritional deficiencies, toxic damage, infections, autoimmune conditions, vasculitis, amyloid, and genetic defects. For many patients a diagnosis and treatment plan can be developed based on the clinical history, physical exam, electrophysiologic testing and laboratory studies but in some situations a tissue biopsy may still be performed. The two main pathologic specimens are skin biopsies processed according to special protocols for assessment of cutaneous nerve endings and peripheral nerve biopsies that most often target the sural nerve. The pathologist has to make key decisions regarding specimen triage upon receipt of a peripheral nerve biopsy. These decisions are complicated by the fact that there are no uniformly accepted guidelines for the processing of nerve biopsies. Instead, techniques like morphometry, teased fiber preparations and electron microscopy are variably employed at different institution. Ultimately, the clinical context has to be considered in making an educated decision regarding tissue processing. The most important commonly observed abnormalities influencing patient care are inflammatory features, vasculopathic changes and amyloid deposition. In some cases, the identification of demyelinating features or distinctive ultrastructural alterations can provide useful clues to the diagnosis. Inherited neuropathies are quite common with an incidence of approximately 1:3,000 and have been linked to mutations in over fifty genes. Nowadays, molecular studies rather than biopsies are usually performed as the preferred diagnostic test leaving biopsies as modality for those rare cases in which molecular testing is inconclusive because of variants of uncertain significance. New insights into the key pathophysiologic processes like Wallerian degeneration, axonopathy and axon-Schwann cell interaction continue to improve our understanding of peripheral neuropathies. The indication for tissue biopsies is evolving but in the appropriate context these samples can still yield crucial information for patient management.

References:

1. Adachi H, et al. Adult-onset Krabbe disease presenting with an isolated form of peripheral neuropathy. Muscle Nerve. 2016 Jun;54(1):152-7
2. Barohn RJ, Amato AA. Pattern-recognition approach to neuropathy and neuronopathy. Neurol Clin. 2013 May;31(2):343-61.
3. Chen P, Piao X, Bonaldo P. Role of macrophages in Wallerian degeneration and axonal regeneration after peripheral nerve injury. Acta Neuropathol. 2015 Nov;130(5):605-18.
4. Collins MP, Hadden RD. The nonsystemic vasculitic neuropathies. Nat Rev Neurol. 2017 Apr 27;13(5):302-316.
5. Conforti L, Gilley J, Coleman MP. Wallerian degeneration: an emerging axon death pathway linking injury and disease. Nat Rev Neurosci. 2014 Jun;15(6):394-409.

6. Duchesne M, et al. Nerve Biopsy Is Still Useful in Some Inherited Neuropathies. J Neuropathol Exp Neurol. 2018 Feb 1;77(2):88-99
7. Fukuda Y, Li Y, Segal RA. A Mechanistic Understanding of Axon Degeneration in Chemotherapy-Induced Peripheral Neuropathy. Front Neurosci. 2017 Aug 31;11:481.
8. Graf J, Imboden J. Vasculitis and peripheral neuropathy. Curr Opin Rheumatol. 2019 Jan;31(1):40-45.
9. Jiang QL, Pytel P, Rowin J. Disseminated intravascular large-cell lymphoma with initial presentation mimicking Guillain-Barré syndrome. Muscle Nerve. 2010 Jul;42(1):133-6.
10. Kanda T. Usefulness of sural nerve biopsy in the genomic era. Neuropathology. 2009 Aug;29(4):502-8. doi: 10.1111/j.1440-1789.2009.01009.x. Epub 2009 May 22.
11. Katona I, Weis J. Diseases of the peripheral nerves. Handb Clin Neurol. 2017;145:453-474.
12. Landowski LM, et al. Axonopathy in peripheral neuropathies: Mechanisms and therapeutic approaches for regeneration. J Chem Neuroanat. 2016 Oct;76(Pt A):19-27.
13. Lunn ER, et al. Absence of Wallerian Degeneration does not Hinder Regeneration in Peripheral Nerve. Eur J Neurosci. 1989;1(1):27-33.
14. Mathis S, et al. Value of nerve biopsy in the management of peripheral neuropathies. Expert Rev Neurother. 2018 Jul;18(7):589-602.
15. Nathani D, et al. Vasculitic neuropathy: Comparison of clinical predictors with histopathological outcome. Muscle Nerve. 2019 Jan 31.
16. Sopacua M, et al. Small-fiber neuropathy: Expanding the clinical pain universe. J Peripher Nerv Syst. 2019 Mar;24(1):19-33.
17. Sucheston-Campbell LE, et al. Genome-wide meta-analyses identifies novel taxane-induced peripheral neuropathy-associated loci. Pharmacogenet Genomics. 2018 Feb;28(2):49-55.
18. Piccione EA, et al. Nerve pathologic features differentiate POEMS syndrome from CIDP. Acta Neuropathol Commun. 2016 Oct 31;4(1):116.

III. Faculty Biography:

Dr. Peter Pytel is Professor of Pathology at the University of Chicago where he stayed on as faculty member after completing his residency and fellowship training. He participates in the bone and soft tissue and pediatric pathology services. He also runs all aspects of the neuropathology service including the examination of autopsy brains, neuromuscular biopsies, brain tumors and NGS-based molecular profiling of CNS neoplasms. His academic and research interests encompass neurofibromatosis-associated lesions, gliomas and neuromuscular pathology.

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Diagnostic Slide Session

Saturday, June 8, 2019

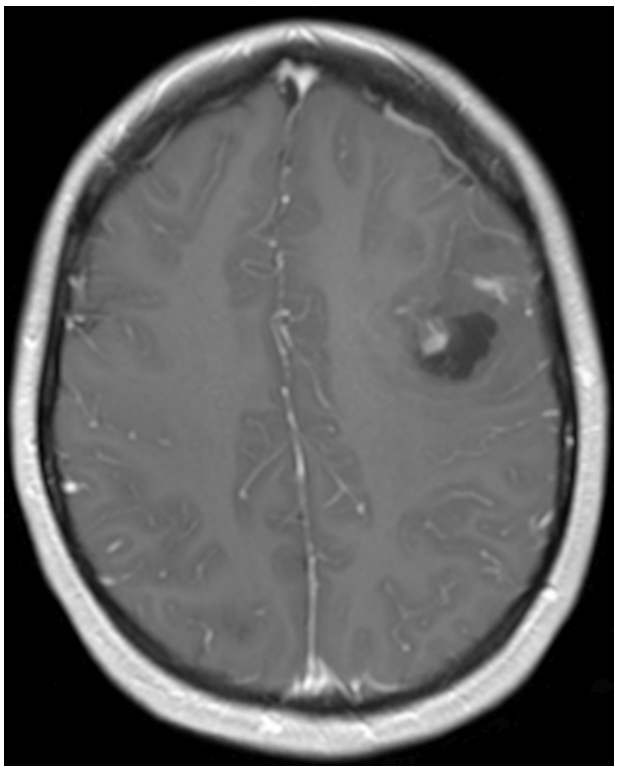
Learning Objectives:

1. *Recognize patterns of neuroanatomic involvement and types of cellular reactions of infectious brain diseases due to viruses, bacteria, and protozoa, and guide confirmation of diagnosis with available molecular analytic tools.*
2. *Describe the features of rare neurodegenerative disorders with atypical patterns of degeneration, including accumulation of materials in glial and/or neuronal cells, and their underlying genetic bases.*
3. *Delineate important exceptions to genotype-phenotype correlations, as well as potentially overlapping histologic findings, among tumors of the pituitary, central nervous system, and cranial tissues coming to neuropathological evaluation*
4. *Cite a differential diagnosis of myopathic disorders characterized by tubular aggregates.*
5. *Explain means of distinguishing host from donor-derived cell types in stem cell transplantation-related disorders.*

60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019
CASE 2019-1

Submitted By:
Catherine Gestrich DO, Audrey Jajosky MD, PhD, Navid Sadri MD, PhD, Marta Couce MD, PhD, and Mark Cohen MD
University Hospitals Cleveland Medical Center/Case Western Reserve

Clinical History:
Our patient is a 22-year-old female with no significant past medical history who presented to the Emergency Department following two witnessed generalized tonic-clonic seizures. MRI demonstrated an expansile mass located in the left frontal lobe, insula and external capsule. Within the mass, there was a 1.6 x 2.1 cm cystic area located in the left frontal lobe which contained a 7 x 9 mm enhancing lesion. The remainder of the mass demonstrated no enhancement.



Material Submitted:
1. H&E section of left frontal mass; Diagnostic MRI

Points for Discussion:
1. Differential diagnosis
2. Diagnostic work-up
3. Prognosis

60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019
CASE 2019-2

Submitted By:
Romain Cayrol and Hannes Vogel
Department of Pathology, Stanford University

Clinical History:
The patient was a 6-year-old girl with a history of regression of milestones beginning at approximately one year of age and a febrile seizure that became generalized tonic/clonic. She was noted to have a dystonic movement disorder but was eventually diffusely hypotonic, confined to bed and developed joint contractures. She was noted to have a laryngeal cleft and developed intermittent exotropia, hearing loss and hirsutism. She had late eruption of her primary teeth at about 3 1/2 years. Laboratory study results included normal lactate, ceruloplasmin, copper; normal SCN1A sequence and deletion analysis; severe ketonuria with mild elevation of 3-OH-glutaric acid; normal karyotype; normal SNP microarray; initial whole exome sequencing confirmed that she was a carrier for biotinidase deficiency and a variant of unknown significance (VUS) in the TYMP gene associated with thymidine phosphorylase deficiency and MNGIE disease, and a VUS in the NDUFAF5 gene associated with mitochondrial complex 1 deficiency; she and her mother were carriers for the common cystic fibrosis mutation deltaF508.

Brain MRI had shown abnormal T2 hyperintensity in the basal ganglia, dorsal brainstem, and dentate nuclei with mild thinning of the corpus callosum, decreased white matter volumes of the cerebral hemispheres, and resultant mild ventriculomegaly.

She developed worsening feeding difficulties requiring a gastrostomy tube, and chronic lung disease from aspiration with recurrent pneumonia, who presented to the hospital with acute respiratory failure, and three weeks later expired after failed attempts at extubation.

Autopsy Findings:
Postmortem examination of the brain showed bilateral and symmetrical frontal lobe atrophy and venticulomegaly.

Material submitted:
1. 1 H&E stained section of basal ganglia is provided for review

Points for discussion:
1. Diagnosis
2. Genetic association

60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019
CASE 2019-3

Submitted By:
Emily A. Sloan MD/PhD, David Solomon MD/PhD, and Marta Margeta MD/PhD
Department of Pathology, University of California San Francisco

Clinical History:
The patient is a 62-year-old man with a history of hypertension and bilateral ischemic optic neuropathy resulting in legal blindness, who presented to UCSF Neurology clinic with slowly progressive low back pain, shooting lower leg pains, and worsening gait. Neurologic examination demonstrated significant weakness in a distal-dominant pattern, most prominent in the right tibialis anterior, right extensor hallucis longus, and bilateral toe flexors, with steppage gait on the right. CSF analysis was remarkable for persistent leukocytosis (range 29-195/µl), elevated protein (maximum 2880 mg/dl), and IgM/IgG antibodies against West Nile Virus. Subsequent electromyogram and nerve conduction studies demonstrated a pattern of abnormal findings consistent with bilateral 5th lumbar (L5) and 1st sacral (S1) radiculopathies.

Magnetic resonance imaging of the lumbar spine revealed marked diffuse thickening of the cauda equina nerve roots, with faint enhancement on post-contrast imaging and progressive effacement of the CSF space over a 16-month period. PET-CT scan showed diffuse hypermetabolic activity within the T12 - L1 spinal cord that extended through the conus and lumbar nerve roots. The patient underwent biopsy of the S1 sensory nerve root.

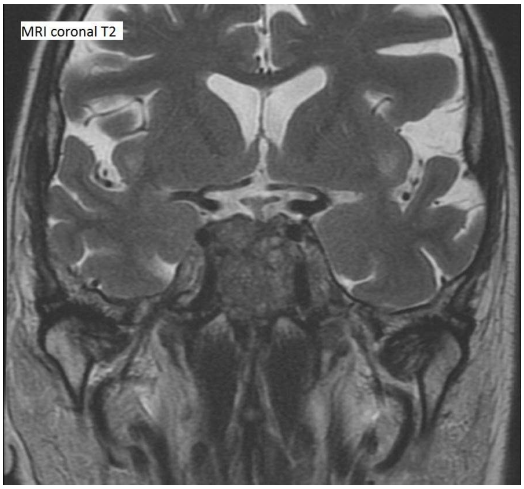
Material Submitted:
1. One H&E stained slide of the S1 nerve root biopsy (digital)

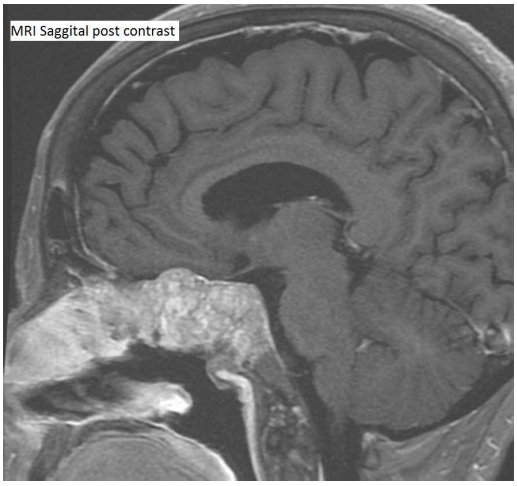
Points for Discussion:
1. Differential diagnosis and ancillary testing
2. Pathogenesis and implications

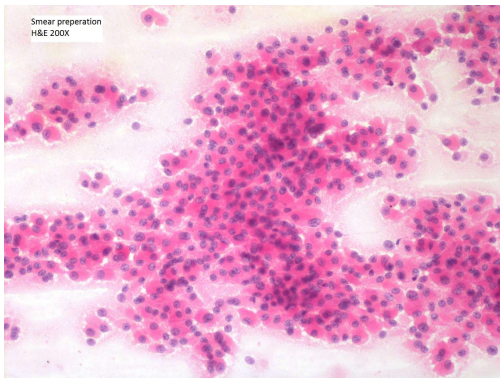
60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019
CASE 2019-4

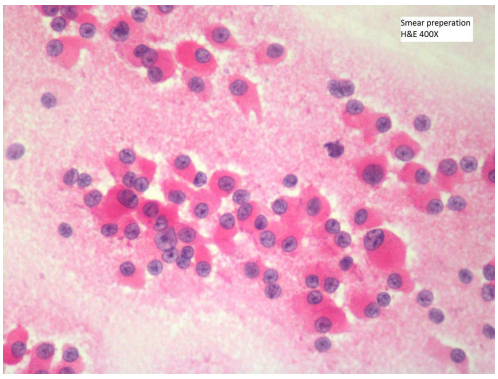
Submitted By:
Amir Banihashemi, MD; Mary Fowkes, MD, PhD
Department of Pathology, Icahn School of Medicine at Mount Sinai

Clinical History:
67-year-old female with no significant past medical history who initially presented with bitemporal hemianoptic field defect 12 years ago and found to have a sella/suprasellar heterogeneous mass on Head MRI at that time. Despite multiple surgical interventions (4 times) and radiation therapy, the tumor has continued to grow and now extends through the sphenoid, ethmoid and cavernous sinuses as well as upper nasal cavity.









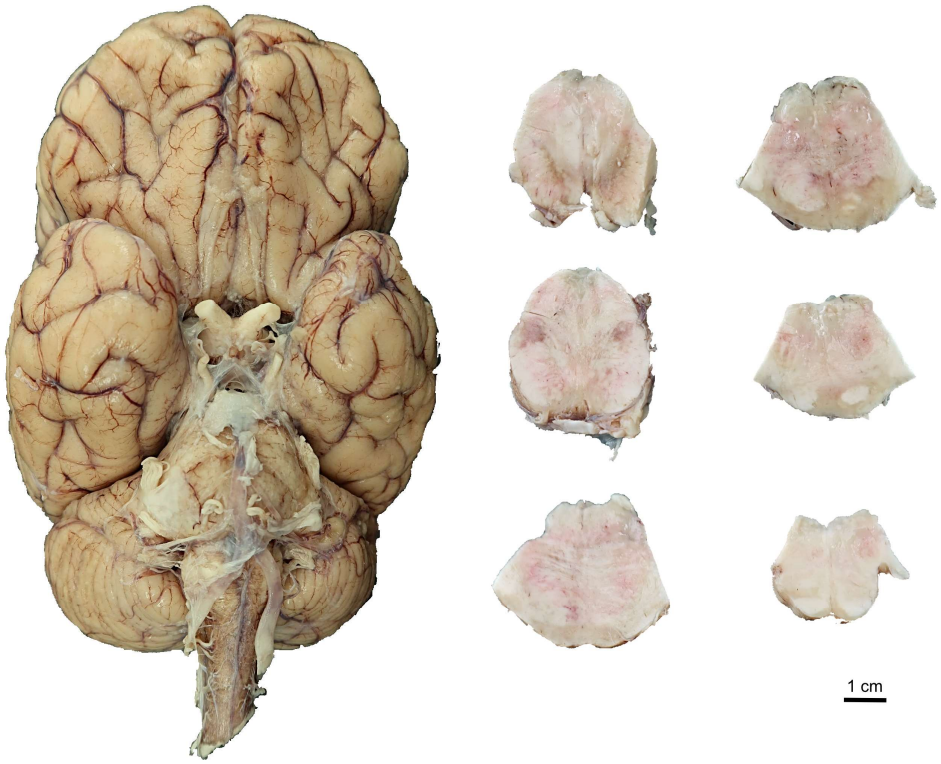
Material Submitted:
1. One representative H&E slide
2. Representative MRI images prior to last operation
3. Microscopic images of smear preparation from recent resection

Points for Discussion:
1. Differential diagnosis
2. Immunohistochemical work-up
3. Molecular findings

60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019
CASE 2019-5

Submitted By:
Richard A. Hickman, M.B.Ch. B & James E. Goldman, M.D., Ph.D.,
Irving Medical Center, Columbia University

Clinical History:
39-year-old, HIV+, man presented with repeated bouts of fevers and altered mental status, requiring hospitalization four times at an outside hospital. CSF infectious workups were negative. On the most recent admission, cranial imaging revealed a 'brainstem mass' at an outside hospital and the patient was transferred to our institution, requiring intubation. Despite numerous courses of antibiotic therapies, he died. An autopsy (brain-only) was requested to ascertain the cause of death.



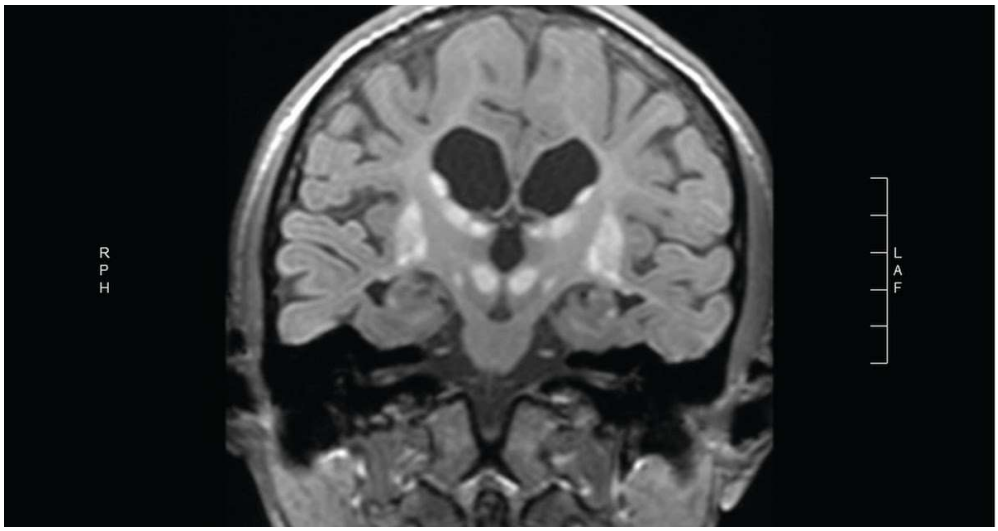
Material Submitted:
1. Gross photographs of the base of the brain and transverse sections of the brainstem
2. Luxol Fast Blue/ H&E stained section of the midbrain (right half)

Points for Discussion:
1. Diagnosis and differential diagnosis
2. Ancillary tests

60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019
CASE 2019-6

Submitted By:
Julieann C. Lee[1] and Joanna J. Phillips[1,2]
1. Department of Pathology, University of California, San Francisco, CA
2. Department of Neurological Surgery, University of California, San Francisco, CA

Clinical History:
The decedent was a 23-year-old woman. Her head circumference was below average, and there were early developmental delays. MRI at 10 months of age demonstrated vermian hypoplasia and diminished myelination. She developed and gained skills in the first decade of life, with subsequent progressive motor regression beginning at age 10. By her late teens she was almost entirely wheelchair bound and was fed primarily by a gastric tube. She became increasingly nonverbal, with dystonia and ballistic movements. Serial MRIs demonstrated progressive volume loss most notable in the periventricular white matter, thalamus, midbrain, and pons. There were bilateral T1 hyperintense signal abnormalities within the caudate, putamen, globus pallidus, thalamus, subthalamic nuclei, hippocampal cortex, red nucleus, substantia nigra, and cortical spinal tract. CT imaging did not show basal ganglia calcifications. Her peripheral iron and magnesium levels were unremarkable. Her eye exam did not reveal retinopathy, Kayser-Fleischer rings, or cataracts. She became anemic in the setting of menorrhagia, dehydrated, and lethargic with episodes of emesis, and began home hospice care. There has been no one else in the family with similar clinical findings.



Autopsy Findings:
Autopsy findings included aspiration pneumonia and cachexia. Gross evaluation of the brain showed hydrocephalus ex vacuo with marked volume loss, particularly involving the white matter of the cerebrum, cerebellum, and brainstem. There was reduced volume of the cerebellum and brainstem, with severe hypoplasia/atrophy of the cerebellar vermis.

Material Submitted:
1. H&E section including the right insular cortex, putamen, and globus pallidus
2. Magnetic resonance image showing T1 hyperintense signal abnormalities

Points for Discussion:
1. Differential diagnosis
2. Immunohistochemistry, special stains, and molecular evaluation

60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019
CASE 2019-7

Submitted By:
Jason A. Gregory, CPT USA, MD, John Crary, MD, PhD, Jorge Trejo-Lopez, MD, and Anthony T. Yachnis, MD
Department of Pathology, Immunology, and Laboratory Medicine, University of Florida

Clinical History:
An 80-old male with a 6-year history of clinical Parkinson's disease passed away after approximately 6 month of increasing somnolence and confusion. Disturbances of tremor and gait were initially well controlled by anti-parkinsonian pharmacotherapy. However, in the three to four years prior to death the patient developed increasing forgetfulness and had several falls. In addition to progression of the movement disorder, the patient experienced progressive cognitive decline with decreased levels of attention and concentration, disorientation to person and place, and difficulty with spontaneous speech. The prior medical history included lung and colon cancer, diabetes, hypertension, and coronary artery disease. CT imaging showed focal encephalomalacia of the right basal ganglia and left internal capsule but was otherwise within normal limits.

Autopsy findings:
Gross examination revealed a 1270 gram brain with mild frontotemporal atrophy and cingulate gyrus atrophy. There was moderate ventriculomegally with hydrocephalus ex vacuo. Moderate hypopigmentation of the substantia nigra and locus coeruleus was noted. The remainder of the cerebrum and cerebellum appeared grossly normal.

Material Submitted:
1. H&E-stained section of the midbrain
2. H&E-stained section of the mid-frontal cortex
3. Gross image of the brain
4. Gross images of the pons and midbrain

Points for Discussion:
1. Differential diagnosis and ancillary studies
2. Pathogenesis

60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019

CASE 2019-8

Submitted By:
Kyle S. Conway, Sandra Camelo-Piragua, Kathryn McFadden
University of Michigan

Clinical History:
This patient is a 16-year-old male who presented with sudden onset of swelling in the hands and eyes. His creatine phosphokinase (CPK) was 870 IU/L in the Emergency Department and fluctuated between 600 and 900 over a period of several months. His ED labs were remarkable for a WBC of 20.0 and platelets of 138. MRI showed enlarged inguinal, external iliac, and popliteal lymph nodes, but no evidence of changes in the musculature. He was referred to neurology for his muscle weakness and hematology/oncology for his leukocytosis and thrombocytopenia. A muscle biopsy of the right vastus lateralis was performed.

Material Submitted:
1. Right vastus lateralis, muscle biopsy: (1) H&E (frozen) (2) Gomori trichrome (frozen)

Points for Discussion:
1. Workup and differential diagnosis based on the H&E and trichrome findings
2. Potential genetic findings in this patient and their correlation with the clinical and histopathologic findings

60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019
CASE 2019-9

Submitted By:
J. Stephen Nix[1], Lisa M. Rooper[1], Analiz Rodriguez[2], Murat Gokden[2]
[1]Johns Hopkins School of Medicine
[2]University of Arkansas for Medical Sciences

Clinical History:
A woman in her early forties presented with right-sided headache, heaviness in the head, tongue tingling and numbness, and vomiting. After an initial impression of Bell's palsy in the Emergency Department, imaging showed a mass involving the V2 division of the trigeminal nerve, eroding into the right maxillary sinus, with expansion of the right foramen rotundum. After an initial resection extending up to the foramen rotundum and subsequent gamma-knife therapy, her complaints continued, and the mass was found to now extend into the cranial cavity, abutting the right internal carotid artery and involving the clivus, sphenoid body, and petrous apex. The right temporal lobe exhibited extensive surrounding vasogenic edema. A second, more extensive resection was performed. Despite subsequent radiation and chemotherapy, the tumor continued growing and the patient died as a consequence of mass effect and herniation.

Material Submitted:
1. 1 H&E-stained paraffin section

Points for Discussion:
1. Differential diagnosis
2. Additional work-up

60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019
CASE 2019-10

Submitted By:
Klonoski, Joshua M[1], Marsden, Lily[2], Palmer, Cheryl A[1]
[1]University of Utah Department of Pathology, Huntsman Cancer Institute
[2]Utah Office of the Medical Examiner

Clinical History:
A middle-aged man from rural Utah with a history of an NSTEMI, reflux, hyperlipidemia, hypertension, depression and Poland syndrome presented by ambulance to the ER for wheezing and hyperventilation. He had visited the ER several times over the previous 5 days for a reported industrial work place accident for which he received dexamethasone. In the ER, he continued to complain of severe muscle spasms and paresthesias in his neck, back and right arm, and reported that he had also been unable drink fluids due to these spasms. Physical exam showed him to be afebrile, mildly dehydrated and tachypneic with good oxygen saturation. After admission, he became acutely delirious prompting transfer to a higher acuity hospital. Upon arrival he demonstrated florid psychosis, dysphasia, dystonic posturing, akathisia and orofacial dyskinesias. Electrolytes were normal but his Cr, BUN and CPK were elevated. Following intubation and sedation, brain and C-spine MRIs and a lumbar puncture were normal. An EEG showed generalized slowing and disorganization consistent with encephalopathy. During repeat interviews with his family, they also reported a witnessed ground level fall, possible auditory hallucinations, travel history to the Pacific Northwest and a grouse hunt. By day 3 of admission his blood pressures began fluctuating and he developed a temperature of 40°C. Over the following 48 hours his condition deteriorated and he became unresponsive with EEG showing status epilepticus and bitemporal lobe edema on MRI. On day 10, his MRI showed diffuse edema in the pons and midbrain, bilateral thalamic and temporal pole hyperintensities with worsening leptomeningeal enhancement and corticospinal tract and cranial nerve enhancement in CN III and V.

His blood and CSF cultures as well as PCR and serology tests were negative for bacteria, viruses, fungi, syphilis, *Francisella*, *Borrelia*, *Leptospira*, *Ehrlichia* and typhoid. Vitamin levels, thyroid hormones, toxicology and drug studies were also normal. An ANA was 1:160 but all other autoimmune and demyelinating evaluations were negative.

Given his poor prognosis, he was placed on comfort care and passed away on hospital day 15.

Autopsy Findings:
The Utah State Department of Health and the CDC were consulted, and an autopsy was performed by the Utah Medical Examiner's office with neuropathology evaluation by the University of Utah. The autopsy was remarkable for cerebral edema but no other significant gross pathology. Pending studies at the time of death included a 14-3-3/tau and tests performed by the CDC.

Material Submitted:
2. H&E section of cerebellum

Points for Discussion:
1. Explain the differential diagnosis for rapidly progressing encephalopathy
2. Ancillary studies

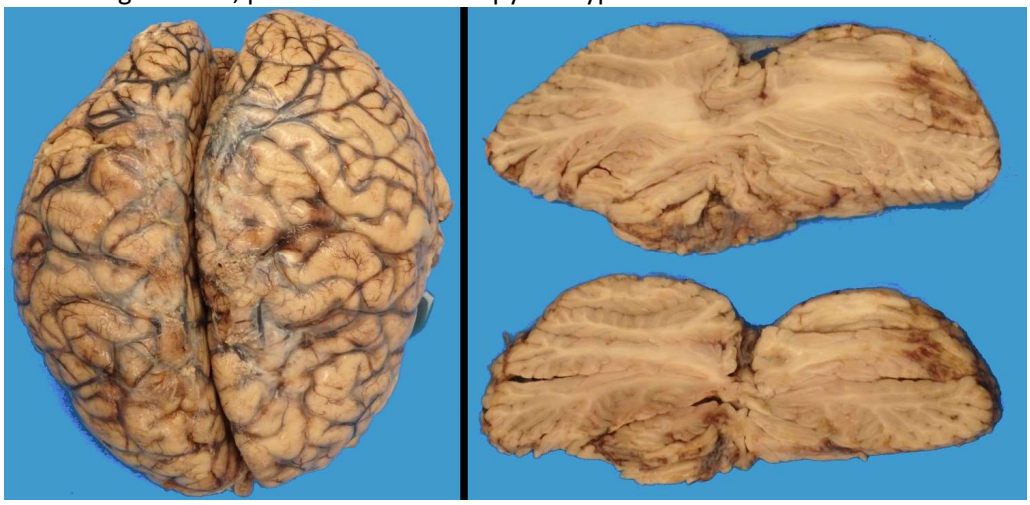
60th ANNUAL DIAGNOSTIC SLIDE SESSION 2019

CASE 2019-11

Submitted By:
Dale Davis, M.A. [1], Todd Williams, M.D. [1], Roosecelis B. Martines, M.D., Ph.D. [2], Peter Stenzel, M.D., Ph.D. [1], Matthew Wood, M.D., Ph.D. [1]
[1]Department of Pathology, Oregon Health & Science University
[2]Infectious Disease Pathology Branch, Centers for Disease Control and Prevention

Clinical History:
The patient is a 66-year-old male with a history of T-cell prolymphocytic leukemia and type 2 diabetes mellitus who was found collapsed and was admitted for presumed bacterial meningitis. His medical history was complicated by frequent loss to follow-up, varied adherence to medications, and *Nocardia* pneumonia and cavitary lung nodules in mid-2017. During admission, the patient remained intubated with a Glasgow Coma Scale ranging from 2 to 6. A bronchoalveolar lavage culture was positive for *Aspergillus fumigatus*. Cerebrospinal fluid analysis showed 2384 nucleated cells, 488 RBCs, 5% lymphocytes, 86% neutrophils, glucose 69, and total protein 687. CSF cultures and PCR-based studies for viral, fungal, bacterial, and mycobacterial organisms were negative. There was no clinical improvement on treatment with antibiotics and steroids; he was transitioned to comfort care and died 10 days after admission. The patient immigrated from Mexico approximately 25 years ago and worked in restaurants and as a landscaper. He traveled to California and western Oregon but had no known recent international travel.

Autopsy Findings:
The brain showed effaced gyri, narrowed sulci, an absence of leptomeningeal exudates, softening of the periventricular white matter in both hemispheres, and bilateral cerebellar hemispheric hemorrhagic lesions (fixed brain weight, 1533 g). The body examination revealed purulent material in the bronchioles of the lower lung lobes, distal bronchiectasis, and multiple subcentimeter lung nodules, positive on microscopy for hyphal forms.



Material Submitted:
1. H&E stained slide of a representative cerebellar lesion, and gross images of brain autopsy findings.

Points for Discussion:
1. Determine differential diagnosis
2. Analyze results of ancillary diagnostic studies
3. Final diagnosis

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

Presidential Symposium

Sunday, June 9, 2019

Learning Objectives:

1. *Describe new microscopic methodologies for visualization of tissue architecture and cellular and subcellular structures.*
2. *Explain how new technologies provide for 3D imaging of large-scale tissues*
3. *Outline advances in high-resolution optical techniques.*
4. *Cite 2-3 examples of the application of new technologies to research and/or clinical practice.*

PRESIDENTIAL SYMPOSIUM

Neuropathology for the Future: Knowing Where to Look and New Ways to Look

Time: 8:05 am – 8:45 am

Matthew P. Frosch, MD, PhD, *Massachusetts General Hospital, Boston, MA*

I. Learning Objectives:

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

1. Compare principles of tissue sampling for both focal and diffuse processes
2. Infer what we don't see as pathologist but might have importance for understanding disease mechanisms and diagnoses
3. Discuss how emerging scientific methods may change how neuropathologists examine tissue and make diagnoses

II. Abstract and Relevant Resources

Diagnostic neuropathology has drawn on the gross and microscopic examination of tissue to build effective tools for disease identification, classification and predictors of clinical course and outcome. Methods including electron microscopy, immunohistochemistry and more recently molecular studies have enhanced our ability to provide informative reporting which drives clinical care and informs patients, families and physicians. At the same time, we don't commonly think about the implicit problems in how we sample tissue specimens, what our sampling does to shape our interpretation of what we see, and what we miss through out sampling. While not yet deployed in the arena of diagnostics, there are methods for ex vivo tissue imaging as well as novel methods for treating tissue to change aspects of its physical structure while maintaining critical biological information. The goal of this talk is to use a few examples, in part drawing on the issues raise by our studies of cerebral amyloid angiopathy (CAA), to highlight the problems inherent in our current approaches. This will lead to similar extensions to include these newer methods – which will be expanded upon in the subsequent talks of the Presidential Symposium.

References:

1. Wilkinson EJ, Hause L. Probability in lymph node sectioning. Cancer. 1974 May; 33(5):1269-74.
2. Pugh TD, King JH, Koen H, Nychka D, Chover J, Wahba G, He YH, Goldfarb S. Reliable stereological method for estimating the number of microscopic hepatocellular foci from their transections. Cancer Res. 1983 Mar;43(3):1261-8.
3. Chung K, Deisseroth K. CLARITY for mapping the nervous system. Nat Methods. 2013 Jun;10(6):508-13.
4. Chen F, Tillberg PW, Boyden ES. Optical imaging. Expansion microscopy. Science. 2015 Jan 30;347(6221):543-8.
5. Kasthuri N, Hayworth KJ, Berger DR, Schalek RL, Conchello JA, Knowles-Barley S, Lee D, Vázquez-Reina A, Kaynig V, Jones TR, Roberts M, Morgan JL, Tapia JC, Seung HS, Roncal WG, Vogelstein JT, Burns R, Sussman DL, Priebe CE, Pfister H, Lichtman JW. Saturated Reconstruction of a Volume of Neocortex. Cell. 2015 Jul 30;162(3):648-61.
6. Murray E, Cho JH, Goodwin D, Ku T, Swaney J, Kim SY, Choi H, Park YG, Park JY, Hubbert A, McCue M, Vassallo S, Bakh N, Frosch MP, Wedeen VJ, Seung HS, Chung K. Simple, Scalable Proteomic Imaging for High-Dimensional Profiling of Intact Systems. Cell. 2015 Dec 3;163(6):1500-14.
7. Lauer A, van Veluw SJ, William CM, Charidimou A, Roongpiboonsopit D, Vashkevich A, Ayres A, Martinez-Ramirez S, Gurol EM, Biessels GJ, Frosch M, Greenberg SM, Viswanathan A. Microbleeds on MRI are associated with microinfarcts on autopsy in cerebral amyloid angiopathy. Neurology. 2016 Oct 4;87(14):1488-1492

8. van Veluw SJ, Charidimou A, van der Kouwe AJ, Lauer A, Reijmer YD, Costantino I, Gurol ME, Biessels GJ, Frosch MP, Viswanathan A, Greenberg SM. Microbleed and microinfarct detection in amyloid angiopathy: a high-resolution MRI-histopathology study. Brain. 2016 Dec;139(Pt 12):3151-3162.
9. van Veluw SJ, Kuijf HJ, Charidimou A, Viswanathan A, Biessels GJ, Rozemuller AJ, Frosch MP, Greenberg SM. Reduced vascular amyloid burden at microhemorrhage sites in cerebral amyloid angiopathy. Acta Neuropathol. 2017 Mar;133(3):409-415.

III. Faculty Biography:

Dr. Frosch received his undergraduate degree from Amherst College, followed by his MD and PhD (Biophysics) degrees from Harvard University. He then trained in Anatomic Pathology and Neuropathology at Brigham and Women's Hospital. He is currently an active clinical and experimental neuropathologist, serving as Director of the C.S. Kubik Laboratory for Neuropathology at Massachusetts General Hospital with responsibilities for the clinical neuropathology service and the MGH Neuropathology Training Program. In addition, he is the Neuropathology Core Leader for the Massachusetts Alzheimer Disease Research Center. His research has focused on human tissue and animal models of neurodegenerative diseases, with an emphasis on cerebral amyloid angiopathy. He also participates in extensive interdisciplinary collaborations focused on clinco-pathologic and radiographic-pathologic correlations as well as studies developing new methods for anatomic and pathologic understanding of the brain in health and disease. He is an Associate Director of the Harvard-MIT Division of Health Sciences and Technology, with significant teaching and administrative contributions. As member of the AANP since fellowship, he has been honored to deliver the Saul Korey Memorial Lecture previously and has been grateful for the opportunity to serve the AANP and his colleagues as President of the AANP from 2018-2019.

PRESIDENTIAL SYMPOSIUM

Expansion Microscopy

Time: 10:20 am – 11:10 am

Edward Boyden, PhD, *Massachusetts Institute of Technology, Cambridge, MA*

I. Learning Objectives

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

1. Describe principles of how expansion microscopy chemistry enhances resolution of imaging.
2. Explain how to use expansion microscopy in pathology experiments.
3. Plan expansion microscopy workflows in the biology laboratory.

II. Abstract & Relevant References

Recently our group developed a new method for imaging, with nanoscale spatial precision, the identity and location of proteins, nucleic acids, and other kinds of biomolecules in 3-D throughout intact cells and tissues, by physically expanding such samples in an isotropic fashion. By embedding biological specimens in a swellable polymer, anchoring key biomolecules or labels to the polymer, mechanically homogenizing the specimens, and then swelling the samples isotropically (Science 347(6221):543-8), we found that it was possible to physically swell samples by ~4.5x in linear dimension, enabling nanoscale imaging of complex biological systems in 3-D –- and on ordinary diffraction-limited microscopes. Since then, we have been working to improve the expansion factor further, aiming for ~10x-100x expansion in linear dimension, which would ideally give an effective resolution in the nanometers to low tens of nanometers. We have also been working to incorporate multiplexed imaging of biomolecules into the expansion microscopy context. We have also developed protocols for expansion microscopy of paraffin-embedded, fresh frozen, and other kinds of pathology specimens. Finally, we present progress on our ongoing project to develop a method of in situ sequencing of nucleic acids (e.g., RNA) throughout individual cells throughout intact tissues, by fusing expansion microscopy with fluorescent in situ sequencing (FISSEQ, developed by the Church lab at Harvard), which we call expansion sequencing. Our hope is that this toolset will enable the powerful, democratized identification and localization of perhaps thousands of different kinds of biomolecule, with nanoscale precision, throughout cells and tissues- a key step towards understanding the configuration of complex biological systems in normal and disease states.

***References*:**

1. Chen, F.*, Tillberg, P.W.*, Boyden, E.S. (2015) Expansion Microscopy, Science 347(6221):543-548. (*, equal contribution)
2. Tillberg, P.W.*, Chen, F.*, Piatkevich, K.D., Zhao, Y., Yu, C.-C., English, B.P., Gao, L., Martorell, A., Suk, H.-J., Yoshida, F., DeGennaro, E.M., Roossien, D.H., Gong, G., Seneviratne, U., Tannenbaum, S.R., Desimone, R., Cai, D., Boyden, E.S. (2016) Protein-retention expansion microscopy of cells and tissues labeled using standard fluorescent proteins and antibodies, Nature Biotechnology 34:987–992. (*, co-first authors)
3. Chen, F.*, Wassie, A.T.*, Cote, A.J., Sinha, A., Alon, S., Asano, S., Daugharthy, E.R., Chang, J.-B., Marblestone, A., Church, G.M., Raj, A., Boyden, E.S. (2016) Nanoscale Imaging of RNA with Expansion Microscopy, Nature Methods 13(8):679-84. (*, co-first authors)
4. Chang, J.-B., Chen, F., Yoon, Y.-G., Jung, E. E., Babcock H., Kang J.-S., Asano S., Suk H.-J., Pak N., Tillberg P.W., Wassie A., Cai D., Boyden E.S. (2017) Iterative expansion microscopy, Nature Methods 14:593-599.
5. Wassie AT*, Zhao Y*, Boyden ES (2018) Expansion microscopy: principles and uses in biological research, Nature Methods 16(1):33-41. (*, equal contributors)
6. Asano SM*, Gao R*, Wassie AT*, Tillberg PW, Chen F, Boyden ES (2018) Expansion Microscopy: Protocols for Imaging Proteins and RNA in Cells and Tissues, Current Protocols in Cell Biology 80(1):e56. (*, co-first authors)

7. Ruixuan Gao*, Shoh M. Asano*, Srigokul Upadhyayula*, Igor Pisarev, Daniel E. Milkie, Tsung-Li Liu, Ved Singh, Austin Graves, Grace H. Huynh, Yongxin Zhao, John Bogovic, Jennifer Colonell, Carolyn M. Ott, Christopher Zugates, Susan Tappan, Alfredo Rodriguez, Kishore R. Mosaliganti, Shu-Hsien Sheu, H. Amalia Pasolli, Song Pang, C. Shan Xu, Sean G. Megason, Harald Hess, Jennifer Lippincott-Schwartz, Adam Hantman, Gerald M. Rubin, Tom Kirchhausen, Stephan Saalfeld, Yoshinori Aso, Edward S. Boyden**, Eric Betzig** (2019) Cortical column and whole-brain imaging with molecular contrast and nanoscale resolution, Science 363(6424):eaau8302. (*, equal contribution, **, co-corresponding)

III. Faculty Biography:

Ed Boyden is Y. Eva Tan Professor in Neurotechnology at MIT, associate professor of Biological Engineering and Brain and Cognitive Sciences at MIT's Media Lab and McGovern Institute for Brain Research, and was recently selected to be an Investigator of the Howard Hughes Medical Institute (2018). He leads the Synthetic Neurobiology Group, which develops tools for analyzing and repairing complex biological systems such as the brain, and applies them systematically to reveal ground truth principles of biological function as well as to repair these systems. These technologies include expansion microscopy, which enables complex biological systems to be imaged with nanoscale precision; optogenetic tools, which enable the activation and silencing of neural activity with light; robotic methods for directed evolution that are yielding new synthetic biology reagents for dynamic imaging of physiological signals; novel methods of noninvasive focal brain stimulation; and new methods of nanofabrication using shrinking of patterned materials to create nanostructures with ordinary lab equipment. He co-directs the MIT Center for Neurobiological Engineering, which aims to develop new tools to accelerate neuroscience progress. Amongst other recognitions, he has received the Canada Gairdner International Award (2018), the Breakthrough Prize in Life Sciences (2016), the BBVA Foundation Frontiers of Knowledge Award (2015), the Carnegie Prize in Mind and Brain Sciences (2015), the Jacob Heskel Gabbay Award (2013), the Grete Lundbeck Brain Prize (2013), the NIH Director's Pioneer Award (2013), the NIH Director's Transformative Research Award (three times, 2012, 2013, and 2017), and the Perl/UNC Neuroscience Prize (2011). He was also named to the World Economic Forum Young Scientist list (2013) and the Technology Review World's "Top 35 Innovators under Age 35" list (2006), and is an elected member of the American Academy of Arts and Sciences (2017), the National Academy of Inventors (2017), and the American Institute for Medical and Biological Engineering (2018). His group has hosted hundreds of visitors to learn how to use new biotechnologies, and he also regularly teaches at summer courses and workshops in neuroscience, and delivers lectures to the broader public (e.g., TED (2011), TED Summit (2016), World Economic Forum (2012, 2013, 2016)). Ed received his Ph.D. in neurosciences from Stanford University as a Hertz Fellow, working in the labs of Jennifer Raymond and Richard Tsien, where he discovered that the molecular mechanisms used to store a memory are determined by the content to be learned. In parallel to his PhD, as an independent side project, he co-invented optogenetic control of neurons, which is now used throughout neuroscience. Previously, he studied chemistry at the Texas Academy of Math and Science at the University of North Texas, starting college at age 14, where he worked in Paul Braterman's group on origins of life chemistry. He went on to earn three degrees in electrical engineering and computer science, and physics, from MIT, graduating at age 19, while working on quantum computing in Neil Gershenfeld's group. He has contributed to over 140 peer-reviewed papers and 180 granted patents, and given over 450 invited talks on his group's work. He has co-founded four startup companies. Long-term, he hopes that understanding how the brain generates the mind will help provide a deeper understanding of the human condition, and perhaps help humanity achieve a more enlightened state.

PRESIDENTIAL SYMPOSIUM

Histologic Validation of High-Resolution Ex Vivo Neuroimaging

Time: 11:10 am – 12:00 pm

Jean Augustinack, PhD, *Massachusetts General Hospital, Boston, MA*

I. Learning Objectives

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

1. Summarize the factors needed to generate high resolution post mortem neuroimaging
2. Distinguish the differences between ex vivo MRI and in vivo MRI parameters and advantages.
3. Explain how to appraise pathologic diseases to formulate a hypothesis that is well suited to an ex vivo MRI approach.

II. Abstract & Relevant References

New advancements in MRI such as improved radio frequency coils, higher field strengths and refined pulse sequences, have propelled modern brain mapping and have made validation to biological standards – histology and pathology – possible. Ex vivo (post mortem) imaging has yielded the visualization of several architectonic features in the human brain – the stria of Gennari in visual cortex, the entorhinal islands, the perirhinal columns in the parahippocampal gyrus, and several strata of the hippocampus. More importantly, these early ex vivo studies put neuroanatomical descriptions at the neuroimaging forefront for validation and this approach has resulted in more precise segmentations in the human brain. The ensuing application to neuroimaging software for in vivo analyses has created detailed parcellations of the hippocampal/subicular subfields, amygdala nuclei and thalamic nuclei, to name a few examples. The ex vivo imaging approach has been applied to several neurodegenerative diseases and conditions as well, including Alzheimer's disease, cerebral amyloid angiopathy, and multiple sclerosis, among others, where subsequent histopathologic studies have validated post mortem neuroimaging observations. Several findings in disease have demonstrated increased sensitivity for diagnosis – including an improved accuracy of Alzheimer's disease diagnosis because of hippocampal subfields segmentation, alterations in white matter, or small structural changes that predict Alzheimer's disease. Such findings have produced inroads to better diagnoses, analyses and applications in neurodegenerative disease and prompted the development of higher resolution in vivo imaging.

References:

1. Augustinack JC, van der Kouwe AJ, Blackwell ML, Salat DH, Wiggins CJ, Frosch MP, Wiggins GC, Potthast A, Wald LL, Fischl BR. Detection of entorhinal layer II using 7Tesla magnetic resonance imaging. Ann Neurol. 2005 Apr;57(4):489-94.
2. Hinds O, Polimeni JR, Rajendran N, Balasubramanian M, Wald LL, Augustinack JC, Wiggins G, Rosas HD, Fischl B, Schwartz EL. The intrinsic shape of human and macaque primary visual cortex. Cereb Cortex. 2008 Nov;18(11):2586-95.
3. Augustinack JC, van der Kouwe AJW, Fischl B. Medial Temporal Cortices in Ex Vivo Magnetic Resonance Imaging, Journal of Comparative Neurology 521:4177–4188, 2013 (review)
4. Iglesias JE, Augustinack JC, Nguyen K, Player, CM, Player A, Wright M, Roy N, Frosch MP, McKee AC, Wald LL, Fischl B, Van Leemput K and for the Alzheimer's Disease Neuroimaging Initiative. Neuroimage. A computational atlas of the hippocampal formation using ex vivo, ultra-high resolution MRI: Application to adaptive segmentation of in vivo MRI, 2015; 115: 117–137.
5. Yu L, Dawe RJ, Buchman AS, Boyle PA, Schneider JA, Arfanakis K, Bennett DA. Ex vivo MRI transverse relaxation in community based older persons with and without Alzheimer's dementia. Behav Brain Res. 2017 Mar 30;322(Pt B):233-240.
6. Saygin ZM, Kliemann D, Iglesias JE, van der Kouwe AJW, Boyd E, Reuter M, Stevens A, Van Leemput K, McKee A, Frosch MP, Fischl B, Augustinack JC; Alzheimer's Disease Neuroimaging Initiative. High-resolution

magnetic resonance imaging reveals nuclei of the human amygdala: manual segmentation to automatic atlas. Neuroimage. 2017 Jul 15;155:370-382.
7. van Veluw SJ, Reijmer YD, van der Kouwe AJ, Charidimou A, Riley GA, Leemans A, Bacskai BJ, Frosch MP, Viswanathan A, Greenberg SM. Histopathology of diffusion imaging abnormalities in cerebral amyloid angiopathy. Neurology. 2019 Feb 26;92(9):e933-e943.

III. Faculty Biography:

Dr. Augustinack received her Bachelor of Science degree from the University of Wisconsin and her doctorate from the University of Iowa in the Department of Anatomy and Cell Biology. While at the University of Iowa she worked with Dr. Gary Van Hoesen on the architecture and vulnerability of the human perirhinal cortex in Alzheimer's disease. She subsequently completed her post-doctoral fellowship in the Alzheimer's Unit in the Department of Neurology at the Massachusetts General Hospital. While a post-doctoral fellow, she focused on the cytopathology of tau in Alzheimer's disease. In 2004, she joined the Martinos Center for Biomedical Imaging in the Department of Radiology at the Mass General Hospital as Instructor where she has applied her histopathology experience to high-resolution neuroimaging. Currently, she is Assistant Professor in the Department of Radiology at Harvard Medical School and Massachusetts General Hospital.

2018 DONATIONS

A special 'thank you' to members who contributed generous donations to the AANP in 2018.

Dennis Dickson
James Goldman
E Tessa Hedley-Whyte
Qinwen Mao
Douglas Miller
Suzanne Mirra
E. Kelly Mrachek
Kathy Newell
Kiyomitsu Oyanagi
Arie Perry
Gerald Reis
Ralf Schober
Matthew Wood

ABSTRACT AUTHOR INDEX

NOTES

NOTES