Alzheimer's Disease Center Fall Meeting 2019
NP Core Leaders Meeting

Celebrating Neuropathology Cores Contributions outside of ADC network

Julie A. Schneider, M.D. M.S.
The Deborah R. And Edgar D. Jannotta Presidential Professor,
Pathology (Neuropathology) and Neurological Sciences
Associate Director, Rush Alzheimer's Disease Center,
Rush University Medical Center

Impact of ADC Neuropath Cores

Synergizing with other centers, outside researchers and outside studies, cross disciplinary

NEUROPATHOLOGY ACROSS ADC AND NON-ADC STUDIES AND PARTNERSHIPS

NEUROPATHOLOGY Informing on animal models

THE SCIENCE OF RESILIENCE is started from the neuropathology…

Neuropathology Advancing work on **DIVERSITY AND SEX**

INFLUENCE ON NOMENCLATURE both for AD and other ADRD

NEUROPATHOLOGY AND **sophisticated epidemiologic analytic methodologies**

PATHOLOGY ACROSS ADC AND NON-ADC STUDIES AND PARTNERSHIPS

Neurology. 2007 Dec 11;69(24):2197-204. Epub 2007 Jun 13.

Mixed brain pathologies account for most dementia cases in community-dwelling older persons.

Schneider JA[1], Arvanitakis Z, Bang W, Bennett DA.

Author information

1 Rush Alzheimer's Disease Center, Rush University Medical Center, Armour Academic Center, 600 S. Paulina Street, Suite 1022F, Chicago, IL 60612, USA. julie_a_schneider@rush.edu

Acta Neuropathol. 2018 Sep;136(3):377-388. doi: 10.1007/s00401-018-1872-5. Epub 2018 Jun 18.

Non-Alzheimer's contributions to dementia and cognitive resilience in The 90+ Study.

Robinson JL[1], Corrada MM[2], Kovacs GG[1,3], Dominique M[1], Caswell C[4], Xie SX[4], Lee VM[1], Kawas CH[5], Trojanowski JQ[6].

Author information

1 Department of Pathology and Laboratory Medicine, Center for Neurodegenerative Disease Research, Institute on Aging, University of Pennsylvania, Philadelphia, PA, USA.
2 Department of Neurology, Department of Epidemiology, Institute for Memory Impairments and Neurological Disorders, University of California at Irvine, Irvine, CA, USA.
3 Institute of Neurology, Medical University of Vienna, Vienna, Austria.
4 Department of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, PA, USA.
5 Department of Neurology, Department of Neurobiology and Behavior, Institute for Memory Impairments and Neurological Disorders, University of California at Irvine, Irvine, CA, USA.
6 Department of Pathology and Laboratory Medicine, Center for Neurodegenerative Disease Research, Institute on Aging, University of Pennsylvania, Philadelphia, PA, USA. trojanow@upenn.edu.

J Neuropathol Exp Neurol. 2014 Jan;73(1):72-80. doi: 10.1097/NEN.0000000000000028.

Neuropathologic heterogeneity does not impair florbetapir-positron emission tomography postmortem correlates.

Dugger BN[1], Clark CM, Serrano G, Mariner M, Bedell BJ, Coleman RE, Doraiswamy PM, Lu M, Fleisher AS, Reiman EM, Sabbagh MN, Sadowsky CH, Schneider JA, Zehntner SP, Carpenter AP, Joshi AD, Mintun MA, Pontecorvo MJ, Skovronsky DM, Sue LI, Beach TG.

Author information

1 From the Avid Radiopharmaceuticals (CMC, ML, APC, ADJ, MAM, MJP, DMS), Philadelphia, Pennsylvania; Banner Sun Health Research Institute (BND, GS, MM, MNS, LIS, TGB), Sun City, Arizona; Biospective Inc. and Montreal Neurological Institute (BJB, SPZ), McGill University, Montreal, Canada; Duke University Medical Center (REC, PMD), Durham, North Carolina; Banner Alzheimer's Institute (ASF, EMR), Phoenix, Arizona; Nova SE University (CHS), Ft Lauderdale, Florida; and Rush University Medical Center (JAS), Chicago, Illinois.

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Neurobiology of Disease

Reduced Efficacy of Anti-Aβ Immunotherapy in a Mouse Model of Amyloid Deposition and Vascular Cognitive Impairment Comorbidity

Erica M. Weekman,[1,2] Tiffany L. Sudduth,[1,2] Carly N. Caverly,[1,2] Timothy J. Kopper,[2] Oliver W. Phillips,[1,2] Dave K. Powell,[3,4] and Donna M. Wilcock[1,2]

[1]Sanders-Brown Center on Aging, [2]Department of Physiology, [3]Magnetic Resonance Imaging and Spectroscopy Center, [4]Department of Biomedical Engineering, University of Kentucky, Lexington, Kentucky 40536

Hyperhomocystinemia (via diet) & AD (APP/PS1) model (Wilcock lab)

Amyloid movement to the vasculature with microbleeds and inflammation;

<u>Reduced cognitive efficacy of anti-amyloid therapies in this model despite amyloid clearance</u>

Exacerbated cerebrovascular adverse events

Resilience

Neurology. 1996 Mar;46(3):707-19.

Cerebral amyloid deposition and diffuse plaques in "normal" aging: Evidence for presymptomatic and very mild Alzheimer's disease.

Morris JC[1], Storandt M, McKeel DW Jr, Rubin EH, Price JL, Grant EA, Berg L.

Author information

1 Alzheimer's Disease Research Center, Department of Neurology, Washington University School of Medicine, St. Louis, M0 63110, USA.

J Neuropathol Exp Neurol. 2003 Nov;62(11):1087-95.

Neuropathology of cognitively normal elderly.

Knopman DS[1], Parisi JE, Salviati A, Floriach-Robert M, Boeve BF, Ivnik RJ, Smith GE, Dickson DW, Johnson KA, Petersen LE, McDonald WC, Braak H, Petersen RC.

Author information

1 Department of Neurology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55905, USA. knopman@mayo.edu

Neurobiol Aging. 2013 Jan;34(1):157-68. doi: 10.1016/j.neurobiolaging.2012.03.004. Epub 2012 May 2.

Cellular, synaptic, and biochemical features of resilient cognition in Alzheimer's disease.

Arnold SE[1], Louneva N, Cao K, Wang LS, Han LY, Wolk DA, Negash S, Leurgans SE, Schneider JA, Buchman AS, Wilson RS, Bennett DA.

Author information

1 Department of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104, USA. steven.arnold@uphs.upenn.edu

Sci Rep. 2016 Jun 14;6:27812. doi: 10.1038/srep27812.

Preserved neurogenesis in non-demented individuals with AD neuropathology.

Briley D[1], Ghirardi V[1], Woltjer R[2], Renck A[1], Zolochevska O[1], Taglialatela G[1], Micci MA[3].

Author information

1 Mitchell Center for Neurodegenerative diseases, Department of Neurology, University of Texas Medical Branch, Galveston, TX, USA.
2 Department of Pathology, Oregon Health &Science University, OR, USA.
3 Department of Anesthesiology, University of Texas Medical Branch, Galveston, TX, USA.

Sex, diversity,and neuropathology

Neurology. 2015 Aug 11;85(6):528-34. doi: 10.1212/WNL.0000000000001834. Epub 2015 Jul 15.

Mixed pathology is more likely in black than white decedents with Alzheimer dementia.

Barnes LL[1], Leurgans S[2], Aggarwal NT[2], Shah RC[2], Arvanitakis Z[2], James BD[2], Buchman AS[2], Bennett DA[2], Schneider JA[2].

Author information

1 From Rush Alzheimer's Disease Center (L.L.B., S.L., N.T.A., R.C.S., Z.A., B.D.J., A.S.B., D.A.B., J.A.S.), the Department of Neurological Sciences (L.L.B., S.L., N.T.A., Z.A., A.S.B., D.A.B., J.A.S.), the Department of Behavioral Sciences (L.L.B.), Family Medicine (R.C.S.), Internal Medicine (B.D.J.), and Pathology (J.A.S.), Rush University Medical Center, Chicago, IL. lbarnes1@rush.edu.

2 From Rush Alzheimer's Disease Center (L.L.B., S.L., N.T.A., R.C.S., Z.A., B.D.J., A.S.B., D.A.B., J.A.S.), the Department of Neurological Sciences (L.L.B., S.L., N.T.A., Z.A., A.S.B., D.A.B., J.A.S.), the Department of Behavioral Sciences (L.L.B.), Family Medicine (R.C.S.), Internal Medicine (B.D.J.), and Pathology (J.A.S.), Rush University Medical Center, Chicago, IL.

J Alzheimers Dis. 2019;68(1):145-158. doi: 10.3233/JAD-180992.

Neuropathological Diagnoses of Demented Hispanic, Black, and Non-Hispanic White Decedents Seen at an Alzheimer's Disease Center.

Filshtein TJ[1], Dugger BN[2], Jin LW[2,3], Olichney JM[4], Farias ST[4], Carvajal-Carmona L[5], Lott P[6], Mungas D[4], Reed B[7], Beckett LA[8], DeCarli C[4,9].

Author information

1 Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA.
2 Department of Pathology and Laboratory Medicine, School of Medicine, University of California, Davis, Sacramento, CA, USA.
3 UC Davis MIND Institute, Sacramento, CA, USA.
4 Department of Neurology, University of California, Davis, Sacramento, CA, USA.
5 Department of Biochemistry and Molecular Medicine and Genome Center, University of California, Davis, Sacramento, CA, USA.
6 Genome Center, University of California, Davis, Sacramento, CA, USA.
7 Center for Scientific Review, Division of Neuroscience, Development and Aging, NIH, Bethesda, MD, USA.
8 Department of Public Health Sciences, Division of Biostatistics, University of California, Davis, Sacramento, CA, USA.
9 IDeA Laboratory, Center for Neuroscience, University of California, Davis, Sacramento, CA, USA.

Brain. 2019 Sep 1;142(9):2581-2589. doi: 10.1093/brain/awz206.

Sex differences in the genetic predictors of Alzheimer's pathology.

Dumitrescu L[1,2], Barnes LL[3], Thambisetty M[4], Beecham G[5,6], Kunkle B[6], Bush WS[7], Gifford KA[1], Chibnik LB[8,9], Mukherjee S[10], De Jager PL[11,12], Kukull W[13], Crane PK[10], Resnick SM[4], Keene CD[14], Montine TJ[15], Schellenberg GD[16], Deming Y[17], Chao MJ[18], Huentelman M[19], Martin ER[5,6], Hamilton-Nelson K[6], Shaw LM[16], Trojanowski JQ[16], Peskind ER[20], Cruchaga C[17], Pericak-Vance MA[6], Goate AM[18], Cox NJ[2], Haines JL[7], Zetterberg H[21,22,23,24], Blennow K[21,22], Larson EB[10,25], Johnson SC[26], Albert M[27]; Alzheimer's Disease Genetics Consortium and the Alzheimer's Disease Neuroimaging Initiative, Bennett DA[3], Schneider JA[3], Jefferson AL[1], Hohman TJ[1,2].

Nomenclature and new pathologies

Alzheimers Dement. 2012 Jan;8(1):1-13. doi: 10.1016/j.jalz.2011.10.007.

National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease.

Hyman BT[1], Phelps CH, Beach TG, Bigio EH, Cairns NJ, Carrillo MC, Dickson DW, Duyckaerts C, Frosch MP, Masliah E, Mirra SS, Nelson PT, Schneider JA, Thal DR, Thies B, Trojanowski JQ, Vinters HV, Montine TJ.

Author information

1 Department of Neurology, Massachusetts General Hospital, Harvard University, Boston, MA, USA.

Acta Neuropathol. 2014 Dec;128(6):755-66. doi: 10.1007/s00401-014-1349-0. Epub 2014 Oct 28.

Primary age-related tauopathy (PART): a common pathology associated with human aging.

Crary JF[1], Trojanowski JQ, Schneider JA, Abisambra JF, Abner EL, Alafuzoff I, Arnold SE, Attems J, Beach TG, Bigio EH, Cairns NJ, Dickson DW, Gearing M, Grinberg LT, Hof PR, Hyman BT, Jellinger K, Jicha GA, Kovacs GG, Knopman DS, Kofler J, Kukull WA, Mackenzie IR, Masliah E, McKee A, Montine TJ, Murray ME, Neltner JH, Santa-Maria I, Seeley WW, Serrano-Pozo A, Shelanski ML, Stein T, Takao M, Thal DR, Toledo JB, Troncoso JC, Vonsattel JP, White CL 3rd, Wisniewski T, Woltjer RL, Yamada M, Nelson PT.

Author information

1 Department of Pathology and Cell Biology and the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University Medical Center, New York, NY, 10032, USA, john.crary@mountsinai.org.

Brain. 2019 Jun 1;142(6):1503-1527. doi: 10.1093/brain/awz099.

Limbic-predominant age-related TDP-43 encephalopathy (LATE): consensus working group report.

Nelson PT[1], Dickson DW[2], Trojanowski JQ[3], Jack CR[4], Boyle PA[5], Arfanakis K[5,6], Rademakers R[2], Alafuzoff I[7], Attems J[8], Brayne C[9], Coyle-Gilchrist ITS[9], Chui HC[10], Fardo DW[1], Flanagan ME[11], Halliday G[12], Hokkanen SRK[9], Hunter S[9], Jicha GA[1], Katsumata Y[1], Kawas CH[13], Keene CD[14], Kovacs GG[15], Kukull WA[14], Levey AI[16], Makkinejad N[6], Montine TJ[17], Murayama S[18], Murray ME[2], Nag S[5], Rissman RA[19], Seeley WW[20], Sperling RA[21], White Iii CL[22], Yu L[5], Schneider JA[5].

Author information

1 University of Kentucky, Lexington, KY, USA.
2 Mayo Clinic, Jacksonville, FL, USA.
3 University of Pennsylvania, Philadelphia, PA, USA.
4 Mayo Clinic, Rochester, MN, USA.

ALZHEIMER'S DISEASE VS. ALZHEIMER'S DEMENTIA

Acta Neuropathol. 2016 Jan;131(1):87-102. doi: 10.1007/s00401-015-1509-x. Epub 2015 Dec 10.

Aging-related tau astrogliopathy (ARTAG): harmonized evaluation strategy.

Kovacs GG[1], Ferrer I[2], Grinberg LT[3,4], Alafuzoff I[5], Attems J[6], Budka H[7], Cairns NJ[8], Crary JF[9,10], Duyckaerts C[11], Ghetti B[12], Halliday GM[13], Ironside JW[14], Love S[15], Mackenzie IR[16], Munoz DG[17], Murray ME[18], Nelson PT[19], Takahashi H[20], Trojanowski JQ[21], Ansorge O[22], Arzberger T[23], Baborie A[24], Beach TG[25], Bieniek KF[18], Bigio EH[26], Bodi I[27], Dugger BN[25,28], Feany M[29], Gelpi E[30], Gentleman SM[31], Giaccone G[32], Hatanpaa KJ[33], Heale R[6], Hof PR[10], Hofer M[22], Hortobágyi T[34], Jellinger K[35], Jicha GA[36], Ince P[37], Kofler J[38], Kövari E[39], Kril JJ[40], Mann DM[41], Matej R[42], McKee AC[43], McLean C[44], Milenkovic I[45,46], Montine TJ[47], Murayama S[48], Lee EB[21], Rahimi J[45], Rodriguez RD[49], Rozemüller A[50], Schneider JA[51,52], Schultz C[53], Seeley W[3], Seilhean D[11], Smith C[14], Tagliavini F[32], Takao M[54], Thal DR[55,56], Toledo JB[21], Tolnay M[57], Troncoso JC[58], Vinters HV[59,60], Weis S[61], Wharton SB[37], White CL 3rd[33], Wisniewski T[62,63,64], Woulfe JM[65], Yamada M[66], Dickson DW[67].

Author information

1 Institute of Neurology, Medical University of Vienna, AKH 4J, Währinger Gürtel 18-20, 1097, Vienna, Austria. gabor.kovacs@meduniwien.ac.at.

2 Institute of Neuropathology, Bellvitge University Hospital, University of Barcelona, Hospitalet de Llobregat, Barcelona, Spain.

3 Department of Neurology, Memory and Aging Center, University of California, San Francisco, USA.

4 Department of Pathology, LIM-22, University of Sao Paulo Medical School, Sao Paulo, Brazil.

5 Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden.

6 Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK.

7 Institute of Neuropathology, University Hospital Zürich, Zurich, Switzerland.

8 Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO, USA.

9 Department of Pathology, Friedman Brain Institute, and the Ronald M. Loeb Center for Alzheimer's Disease, Icahn School of Medicine at Mount Sinai, New York, USA.

Moving neuropath data into population type epidemiologic analytic and genetic methodologies

Ann Neurol. 2007 Oct;62(4):406-13.

Pathological correlates of dementia in a longitudinal, population-based sample of aging.

Sonnen JA[1], Larson EB, Crane PK, Haneuse S, Li G, Schellenberg GD, Craft S, Leverenz JB, Montine TJ.

Author information

1 Department of Pathology, University of Washington, Seattle, WA, USA. jsonnen@u.washington.edu

The Statistical Modeling of Aging and Risk of Transition Project: Data Collection and Harmonization Across 11 Longitudinal Cohort Studies of Aging, Cognition, and Dementia.

Abner EL[1], Schmitt FA[2], Nelson PT[3], Lou W[4], Wan L[5], Gauriglia R[6], Dodge HH[7], Woltjer RL[8], Yu L[9], Bennett DA[10], Schneider JA, Chen R, Masaki K, Katz MJ, Lipton RB, Dickson DW, Lim KO, Hemmy LS, Cairns NJ, Grant E, Tyas SL, Xiong C, Fardo DW, Kryscio RJ.

Author information

1 Snders-Brown Center on Aging, University of Kentucky.
2 Oregon Center for Aging & Technology, Oregon Health & Science Univ
3 Rush Alzheimer's Disease Center, Rush University Medical Center.
4 Kuakini Medical Center.
5 Department of Neurology, Albert Einstein College of Medicine.
6 Department of Laboratory Medicine & Pathology, Mayo Clinic Jackson
7 Department of Psychiatry, University of Minnesota.
8 Alzheimer's Disease Research Center, Washington University.

Ann Neurol. 2018 Jul;84(1):10-22. doi: 10.1002/ana.25246. Epub 2018 Jun 26.

Combined neuropathological pathways account for age-related risk of dementia.

Power MC[1], Mormino E[2], Soldan A[3], James BD[4,5], Yu L[6], Armstrong NM[7], Bangen KJ[8,9], Delano-Wood L[8,9], Lamar M[4,10], Lim YY[11], Nudelman K[12], Zahodne L[13], Gross AL[7,14,15], Mungas D[16], Widaman KF[17], Schneider J[4,6,18].

Author information

1 Department of Epidemiology and Biostatistics, George Washington University Milken Institute School of Public Health, Washington, DC.
2 Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA.
3 Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD.
4 Rush Alzheimer's Disease Center, Rush University, Chicago, IL.
5 Department of Internal Medicine, Rush University, Chicago, IL.
6 Department of Neurological Sciences, Rush University, Chicago, IL.
7 Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.
8 VA San Diego Healthcare System, San Diego, CA.
9 Department of Psychiatry, University of California San Diego, San Diego, CA.
10 Department of Behavioral Sciences, Rush University Medical Center, Chicago, IL.
11 Florey Institute of Neuroscience and Mental Health, Parkville, VIC, Australia.
12 Department of Radiology and Imaging Sciences, Indiana University-Purdue University at Indianapolis, Indianapolis, IN.
13 Department of Psychology, University of Michigan, Ann Arbor, MI.
14 Johns Hopkins Center on Aging and Health, Baltimore, MD.
15 Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.
16 Department of Neurology, University of California-Davis, Davis, CA.
17 Graduate School of Education, University of California Riverside, Riverside, CA.
18 Department of Pathology, Rush University Medical Center, Chicago, IL.

PLoS Genet. 2014 Sep 4;10(9):e1004606. doi: 10.1371/journal.pgen.1004606. eCollection 2014 Sep.

Genome-wide association meta-analysis of neuropathologic features of Alzheimer's disease and related dementias.

Beecham GW[1], Hamilton K[1], Naj AC[2], Martin ER[1], Huentelman M[3], Myers AJ[4], Corneveaux JJ[3], Hardy J[5], Vonsattel JP[6], Younkin SG[7], Bennett DA[8], De Jager PL[9], Larson EB[10], Crane PK[11], Kamboh MI[12], Kofler JK[13], Mash DC[14], Duque L[14], Gilbert JR[1], Gwirtsman H[15], Buxbaum JD[16], Kramer P[17], Dickson DW[7], Farrer LA[18], Frosch MP[19], Ghetti B[20], Haines JL[21], Hyman BT[22], Kukull WA[23], Mayeux RP[24], Pericak-Vance MA[1], Schneider JA[25], Trojanowski JQ[26], Reiman EM[27]; Alzheimer's Disease Genetics Consortium (ADGC), Schellenberg GD[26], Montine TJ[28].

Author information

1 John P. Hussman Institute for Human Genomics, University of Miami, Miami, Florida, United States of America.
2 Division of Epidemiology, University of Pennsylvania, Philadelphia, Pennsylvania, United States of America.
3 Neurogenomics Division, Translational Genomics Research Institute, Phoenix, Arizona, United States of America.
4 Department of Psychiatry & Behavioral Sciences, University of Miami, Miami, Florida, United States of America.
5 Department of Molecular Neuroscience, University College London, London, United Kingdom.

Conclusions

By collaborating outside of the ADC –

Neuropathology cores have a tremendous opportunity to inform, further, and collaborate on scientific advances in AD