The State of the Knight ADRC
June 21st, 2016

John C. Morris, MD
Harvey A. and Dorismae Hacker Friedman
Distinguished Professor of Neurology
Disclosure Statement (2015-2016)

- Sources of Research Support
  1. National Institute on Aging (P50 AG05681; P01 AG03991; P01 AG026276; UF1 AG032438)
  2. Anonymous Foundation
  3. Alzheimer’s Association

- Consulting Relationships
  1. Lilly USA
  2. Takeda

- Industry-Sponsored Trials
  1. Eli Lilly

- Fees > $10,000
  None

- Stock Equity
  None

- Speaker’s Bureaus
  None

- Editorial Boards
  1. *Annals of Neurology*
  2. *Neurology Now*
## Changes in ADRC Investigators, Scholars, and Staff

<table>
<thead>
<tr>
<th>Additions</th>
<th>Fond Goodbyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Dru Branson</td>
<td>- Reneé Labarge</td>
</tr>
<tr>
<td>- Dr. Fanaye Dadi</td>
<td>- Dr. Brianne Newman</td>
</tr>
<tr>
<td>- Dr. Jee-young Han</td>
<td>- Liz Rourke</td>
</tr>
<tr>
<td>- Dr. Sarah Hartz</td>
<td>- Treacy Williams</td>
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<tr>
<td>- Debbie Kemp</td>
<td>- Faye Harvey</td>
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<tr>
<td>- Dr. Eric McDade</td>
<td>- Joyce Haynie</td>
</tr>
<tr>
<td>- Marta Santos</td>
<td>- Doris Jones</td>
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<td></td>
<td>- Erica Key</td>
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</table>
Our Unifying Theme

- The study of preclinical AD, using AD biomarkers
  - 4 grants that cover the lifespan

- Key questions
  - Does preclinical AD inevitably progress to symptomatic AD?
  - Can the period of transition from cognitive normality to symptomatic AD be characterized?

- The answers will be crucial for “secondary prevention” trials of putative disease-modifying drugs in cognitively normal older adults who are AD biomarker-positive
### Knight ADRC and Affiliated Grants

#### Antecedent Biomarkers for AD: The Adult Children Study
**JC Morris, PI (P01 AG025276)**
- **Project 1**: The natural history of Aβ accumulation in preclinical AD (Morris)
- **Project 2**: CSF Biomarkers of Antecedent AD (Fagan)
- **Project 3**: Behavioral and Neural Markers of Mental Control: Modeling, Imaging, & Enrichment (Balota)
- **Project 4**: Antecedent Imaging Biomarkers (Benzinger)
- **Project 5**: Aerobic Glycolysis in the Pathophysiology of AD (Vlassenko)

#### Knight ADRC
**JC Morris, PI (P01 AG03991)**
- **Project 1**: Cognitive and Functional Indicators of Transition to Symptomatic AD (Morris)
- **Project 2**: Sleep: Potential Prognostic and Theranostic Marker for Preclinical AD (Holtzman)
- **Project 3**: Identification of Genetic Variants Associated with Rate of Disease Progression (Cruchaga)
- **Project 4**: Imaging Markers of Neuronal Dysfunction in Preclinical AD (Benzinger)

#### Knight Alzheimer's Disease Research Center
**JC Morris, PI (P50 AG05681)**
- **Project 1**: Correlation of Tau PET Imaging with CSF AD Biomarkers (Fagan)
- **Project 2**: Synergy of Aβ Clearance Mechanisms in vivo (Cirrito)
- **Project 3**: Circadian Rhythms in Regulation of Aβ Pathology and Brain Oxidative Stress (Musiek)

#### Other affiliations:
- NACC, NCRAD, LOAD, ADCS, ADNI, GWAS, Alzheimer's Assn, AAA Board, NIH & Industry Clinical Trials, affiliated R01 & other grants

### Dominantly Inherited Alzheimer Network (DIAN)
**RJ Bateman, PI (UF1 AG032438)**
- **Project 1**: Correlation of Tau PET Imaging with CSF AD Biomarkers (Fagan)
- **Project 2**: Synergy of Aβ Clearance Mechanisms in vivo (Cirrito)
- **Project 3**: Circadian Rhythms in Regulation of Aβ Pathology and Brain Oxidative Stress (Musiek)

#### USA
- Brigham & Women's Hospital/MGH
- Butler H/Brown U
- Columbia U
- Indiana U
- USC
- U Pittsburgh
- Mayo Clinic – Jacksonville
- Washington U

#### United Kingdom
- ION-UC London

#### Australia
- Edith Cowan U – Perth
- U Melbourne
- U New South Wales – Sydney

#### Germany
- Univ Tübingen
- Ludwig-Maximilians-Universität – Munich

#### Argentina
- Inst Neurol Research – Buenos Aires

#### Japan
- Osaka City Univ
20 Years of Service to Our HASD/ACS EAC!
Secondary Prevention Trials in Alzheimer Disease
The Challenge of Identifying a Meaningful End Point

Richard J. Kryscio, PhD

From: John Morris
Sent: Monday, August 11, 2014 8:20 AM
To: 'kyrscio@email.uky.edu'
Cc: 'Roger Rosenberg'
Subject: Your editorial

Dick-
Thanks for your editorial in the August issue of JAMA Neurology regarding composite endpoints that are based on combinations of cognitive impairment across multiple domains for secondary prevention trials in AD. Thanks also for citing Chengjie!

I was curious that you cited the API trial in Colombia and the A4 trial in the US as examples of SPTs in AD, but not the Dominantly Inherited Alzheimer Network – Trial Unit (DIAN-TU). This omission is curious because the DIAN-TU was the first SPT to launch (1st participant consented Dec 31, 2012), has dosed more participants than API and A4 combined, and is the only SPT that simultaneously evaluates two anti-Abeta drugs.

-John
From: Kryscio, Richard [mailto:richard.kryscio@uky.edu]
Sent: Tuesday, August 12, 2014 6:42 AM
To: John Morris
Subject: RE: Your editorial

John:

The purpose of the editorial was to discuss statistical issues related to identifying endpoints for SPTs in AD with a focus on the A4 endpoint since the editorial accompanied the publication of the manuscript describing the A4 endpoint. With a constraint on number of words and number of references allowed for the editorial, I opted to quote as many.stat articles on the issue as possible instead of attempting to list all the SPTs in dementia. This assumes the interested reader would consult those stat articles for references to other SPTs. Therefore, I goofed in mentioning the API trial since that clearly opens the editorial to comments about the failure to mention other well run SPTs including the DIAN trial.

With apologies for the omission on the DIAN trial.

Dick
Knight ADRC Terminology

- Knight ADRC (rather than “KADRC”)
- Participants (rather than “subjects”)
- Alzheimer disease (rather than “Alzheimer’s Disease”)
  - AD is the brain disorder regardless of clinical status (preclinical versus symptomatic)
- Alzheimer disease dementia (rather than “DAT”)
  - Alternatively, “symptomatic AD” encompasses both MCI due to AD and AD dementia
- Cognitively normal (rather than “nondemented”)
WUSM (David Perlmutter, Dean)

Dept of Neurology (David Holtzman, Chair)

Section: Aging & Dementia (JCM)

Knight ADRC (JCM)

Memory Diagnostic Center (JCM/B. Joy Snider)

Memory & Aging Project (JCM)
The Operational Arm of Our Clinical Core is the Memory & Aging Project (MAP)

- MAP is the clinical research office for the ADRC, HASD, ACS, and Wash U DIAN site
- Leadership: JCM
  - Angela Oliver, Asst CL
  - Maria Carroll, Clin Ops Manager
- Nurse clinicians: E Cattoor, M Creech, P Kelly, D Kemp, M Santos, T Williams
- Social workers: B Fierberg, T Hosto
- Psychometric unit:
  - J Hassenstab, Leader; D Maue Dreyfus, Senior Psychometrician
  - J Fisher-Eastep, A Hernandez, J Petros
- Office: D Branson, T Earle, D Ritter
MAP Eligibility Criteria

- Age: 45 and older
- English speaking
- Available collateral source
- Clinically stable medical/psychiatric illnesses; conditions that could confound cognitive assessment (e.g., major affective disorder) or preclude longitudinal assessment (e.g., renal failure requiring dialysis) are excluded
- Willing and eligible to undergo longitudinal sleep and biomarker studies (MRI, PET, LP to collect CSF)
  - LP is not mandatory for African Americans
Limitations and Advantages of the MAP Cohort

- Any self-referred cohort of research volunteers that undergoes longitudinal biomarker studies, including LP, is NOT representative of the general population.

- MAP participants experience comorbid disorders (depression in 16%; stroke in 5%); likely representative of cohorts enrolled in longitudinal AD research.

- Advantage: comprehensively assessed, longitudinally followed cohort provides a perhaps unparalleled database of clinical, cognitive, genetic, structural/molecular imaging, and biofluid data.
  - To the extent our participants do not contribute these data, the value of the cohort is diminished.
## Clinical Core: Us vs Them

<table>
<thead>
<tr>
<th>Recruitment pool</th>
<th>MAP</th>
<th>Other ADCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-based self-referral for research only; no billing or disease management provided</td>
<td>Clinic-based; dx, CDR, basic psychometrics, imaging already available at entry into Clinical Core</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assessment personnel</th>
<th>MAP</th>
<th>Other ADCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physicians and trained nurse clinicians: single clinician conducts all interviews and exam, generates CDR and dx</td>
<td>Research assistants interview, generate CDR Neurologist: exam Cognitive batteries</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>MAP</th>
<th>Other ADCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single clinician at time of assessment; feedback to participant and family; no reference to psychometric performance, past CAs, etc</td>
<td>Consensus conference after assessment for dx, using cognitive test results (inc change from before), neuroimages, etc</td>
<td></td>
</tr>
</tbody>
</table>
Total number of active participants (N=871)
  - HASD/ADRC (65 y and older): 496
  - ACS (45 y and older): 283
  - DIAN (18 y and older): 92 (out of 455 total internationally)

Age range = 23-101

56% women

16% African American

Longest period of participation = 30 years (1 person)

Participants come from 24 states, including Idaho, Maine, California, and Texas
### Total Combined HASD and ADRC Registry (N = 496)

<table>
<thead>
<tr>
<th></th>
<th>CDR 0 N = 347</th>
<th>CDR 0.5 N = 79</th>
<th>CDR 1 N = 70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>76.8 ± 7.4</td>
<td>79.2 ± 8.0</td>
<td>80.9 ± 8.4</td>
</tr>
<tr>
<td>Education (y)</td>
<td>15.8 ± 2.6</td>
<td>15.6 ± 2.8</td>
<td>15.4 ± 2.8</td>
</tr>
<tr>
<td>Male (%)</td>
<td>42</td>
<td>51</td>
<td>49</td>
</tr>
<tr>
<td>African American (%)*</td>
<td>20</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.8 ± 1.4</td>
<td>26.8 ± 2.8</td>
<td>22.0 ± 4.0</td>
</tr>
<tr>
<td>Carriers of one or more APOE4 alleles</td>
<td>32</td>
<td>42</td>
<td>66</td>
</tr>
</tbody>
</table>

*19% of all participants are African American; metropolitan St. Louis is 18% African American
MAP Participants Meeting

- June 4th, 2016 (Doubletree Westport, 9–11 AM)
- 454 attendees (participants and family members)
- Agenda:
  I. Knight ADRC Update - John C. Morris, MD
  II. Retaining Participants in Knight ADRC Studies - Suzy Stark, PhD
  III. Imaging Advances - Beau Ances, MD, PhD
  IV. Dementia in Diverse Populations - Lenise Cummings-Vaughn, MD
  V. Clinical Trials Update - B. Joy Snider, MD, PhD
- Big thanks to all MAP/ADRC faculty and staff who attended and assisted; very big thanks to Ron Hawley and Angela Oliver
The Adult Children Study (ACS)

- First and only cohort of middle age and older research volunteers who are studied longitudinally with all of the following:
  - PET scans to detect amyloid-beta deposits (and now also to detect tau aggregates)
  - Cerebrospinal fluid concentrations of amyloid-beta and tau
  - Brain volume and cortical thickness
  - Brain connectivity
  - Genetic risk factors
  - Comprehensive clinical and cognitive assessments
ACS Grant Resubmission

- Submitted January 21\textsuperscript{st}, 2016
- 707 pages: 5 Cores, 3 Projects, and an Overall section
- Total funds requested (for the next 5 years): $11,854,211
- 177 publications generated during the last 5 years

### Active ACS Cohort (n=283) as of 12/31/2015

<table>
<thead>
<tr>
<th>Age at entry</th>
<th>Current Mean Age</th>
<th>%F</th>
<th>Education</th>
<th>MMSE</th>
<th>% APOE4+</th>
<th>%AA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parental History of AD N=159</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-54y, n=48</td>
<td>52.3 (5.2)</td>
<td>63</td>
<td>16.4 (2.2)</td>
<td>29.4 (0.8)</td>
<td>50</td>
<td>13</td>
</tr>
<tr>
<td>55-64y n=62</td>
<td>65.9 (4.7)</td>
<td>73</td>
<td>16.1 (2.6)</td>
<td>29.2 (1.1)</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>65-74, n=49</td>
<td>75.6 (4.8)</td>
<td>63</td>
<td>15.8 (2.4)</td>
<td>28.4 (3.3)</td>
<td>40</td>
<td>6</td>
</tr>
<tr>
<td>No Parental History of AD N=124</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-54y, n=26</td>
<td>57.7 (3.1)</td>
<td>73</td>
<td>16.6 (2.3)</td>
<td>29.5 (0.8)</td>
<td>27</td>
<td>8</td>
</tr>
<tr>
<td>55-64y, n=52</td>
<td>64.4 (4.8)</td>
<td>52</td>
<td>16.3 (2.3)</td>
<td>29.2 (1.1)</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>65-74y, n=46</td>
<td>75.0 (4.3)</td>
<td>39</td>
<td>16.4 (2.8)</td>
<td>29.0 (1.8)</td>
<td>24</td>
<td>11</td>
</tr>
</tbody>
</table>
ACS Participation in Study Procedures as of 12/31/2015*

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Initial (T1) assessment</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; follow-up (3 yrs)*</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; follow-up (6 yrs)*</th>
<th>3&lt;sup&gt;rd&lt;/sup&gt; follow-up (9 yrs)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET PIB (Project 1)</td>
<td>333/384 87%</td>
<td>235/254 91%</td>
<td>155/168 92%</td>
<td>64/85 75%</td>
</tr>
<tr>
<td>LP for CSF (Project 2)</td>
<td>341/384 88%</td>
<td>208/241 86%</td>
<td>131/139 94%</td>
<td>49/58 84%</td>
</tr>
<tr>
<td>Attentional Control (Project 3)</td>
<td>358/384 93%</td>
<td>242/257 94%</td>
<td>150/168 89%</td>
<td>54/73 74%</td>
</tr>
<tr>
<td>MRI (Project 4)</td>
<td>358/384 93%</td>
<td>253/257 98%</td>
<td>164/168 97%</td>
<td>84/85 98%</td>
</tr>
</tbody>
</table>

*Eligibility for follow-up can vary by procedure due to complicating factors (e.g., pacemaker for imaging studies), or previous refusal to complete a procedure.
ACS Grant Resubmission

- Changes:
  - Creation of an Imaging Core (Benzinger) to conduct both florbetapir/MRI and AV-1451 scans
  - Combine imaging science initiatives into Project 1 (Morris/Benzinger)
  - Two-stage review of P01s at NIA:
    - First stage = special emphasis panel similar to a regular Study Section; held May 3rd, 2016
    - Second stage = parent program project committee; planned for early/mid-August
**Snapshot of Other ADRC-Supported Studies**

**Imaging**
- ADNI2; ADNI3
- Stress & brain structure
- Brain metabolism
- GEPCI

- B. Ances
- D. Head
- A. Vlassenko
- D. Yablonskiy

**Genetics**
- AD
- FTD

- C. Cruchaga
- N. Ghoshal

**Cognition**
- Attention
- False hearing
- Prospective memory
- Memory collaboration

- D. Balota/J. Duchek
- M. Sommers
- J. Bugg
- M. McDaniel
- T. Morris

**Other**
- Driving
- Vision
- Tau kinetics

- C. Roe
- G. Van Stavern
- R. Bateman
8 currently active affiliated studies are recruiting

Comments from participants:
- “Which study is this for? I have been contacted a lot as of late.”
- “My calendar has a lot of study dates on it.”
- “Sounds like there is a lot of research right now.”

Survey on affiliated studies being developed by Drs. Susy Stark and Sarah Hartz
- Restrict # of studies?
- Incentives: determine how study results can be shared?
Kingshighway/Forest Park Pkwy Construction

- Conversion to a traditional intersection
- Work expected to begin in July for a ~1 year project
- Closures:
  - Forest Park west of Kingshighway will be closed
  - Kingshighway will be open with some lane closures
  - Forest Park between Kingshighway and Euclid will be 1 lane each way
- Knight ADRC working on directions for participants to our building (4488 Forest Park)
- Please take the construction into account when utilizing Knight ADRC participants and accommodate when possible!!
Knight ADRC Pilot Grant Program

- In the most recent ADRC grant cycle, 23 pilot grants awarded (21 from the P50, 2 from ADRC Director funds)

- Recipients come from: Neurology, Psychiatry, Radiology, Developmental Biology, Hematology, Cell Biology & Physiology, Chemistry, Occupational Therapy, Neurosurgery, Ophthalmology, and Pathology & Immunology

- These pilots generated 27 new grants totaling ~$21,000,000

- 2016-2017 pilots:
  - Thomas Brett: “Identification of cell surface TREM-2 ligands involved in Alzheimer disease pathogenesis”
  - Gregory Day: “Decoding clinical and genetic contributions in Alzheimer disease dementia (A2D2)”
  - Christina Lessov-Schlaggar: “Surveillance for Impending AD in Down Syndrome: A WU ADRC/IDDRCC Feasibility Study”
ADRC Productivity

- Sharing of data, tissue, and participants in the last year (individual participants are represented more than once)
  - Data from 21,558 participants
  - Tissue from 4,060 participants
  - Participants: 434 individuals contributed to affiliated studies

- Tracking the use of our resources is critical to support our existence as an NIA-funded ADRC
  - Resource sharing now must also be reported for our Program Project Grants (HASD and ACS)
Transdisciplinary Knight ADRC

- Faculty from 13 WUSM Departments/Divisions (Neurology, Neurosurgery, Psychiatry, Pathology & Immunology, Radiology, Medicine/Geriatrics, Biostatistics, Ophthalmology, Occupational Therapy, Physical Therapy, Emergency Medicine, Biochemistry & Biophysics, and Neuroscience) AND from 4 Schools on Danforth Campus (Law, Social Work, Engineering, and Arts and Sciences: Departments of Chemistry, Political Science, and Psychology)
Selected Highlights
**DIAN International Expansion**

- Currently, 17 active sites in the US, Australia, England, Germany, Argentina, and Japan

- Model for international expansion established by the 2 German sites and the DZNE → additional countries must obtain their own research support

- Additional sites launching DIAN
  - Japan (Hiroshi Mori, PI); Osaka City
    » 3 additional sites in Tokyo, Hirosaki, and Niigata
  - Korea (Jae-Hong Lee, PI)
    » Seoul
Financial support has also been provided by anonymous sources.

Director: Randy Bateman

*DIAN-TU Pharma Consortium*

**NATIONAL INSTITUTE ON AGING**
National Institutes of Health
U01 AG042791, R01 AG046179

**NIH** National Institutes of Health

**ACCELERATING MEDICINES PARTNERSHIP (AMP)**

**GHR FOUNDATION**

**alzheimer’s association**

**DIAN-TU** Dominantly Inherited Alzheimer Network Trials Unit

**U01 AG042791, R01 AG046179**
DIAN-TU Trial Status

- Present
  - Enrollment complete for first two drug arms!!
  - 24 active trial sites: 11 US, 3 Australian, 5 French, 3 Canadian, 1 UK, and 1 Spain

- Next steps
  - Funding received from the Alzheimer’s Association to start-up and launch the next generation of drug arms for the DIAN-TU trial (DIAN-TU NexGen)
  - DIAN-TU NexGen NIA grant resubmission - July, 2016

- DIAN: www.dian-info.org; DIAN Expanded Registry: www.DIANexr.org (or 844-342-6297)
What is the A4 Study?

- A4 = Anti-Amyloid Treatment in Asymptomatic Alzheimer’s
- To determine whether we can prevent memory loss in people who may be at a higher risk for developing AD before they show symptoms.
- Testing whether a new investigational treatment, an anti-amyloid antibody, can prevent memory loss associated with AD
- Cognitively normal older adults with elevated brain amyloid as shown by an Amyvid® scan are eligible; individuals will learn their Amyvid® results
  - 550 people will be randomized to active treatment (antibody)
  - 550 people will be randomized to placebo
A4 Fast Facts

● Participants
  – 65 – 85 years old
  – Normal thinking and memory abilities
  – Have a study partner
  – Willing and able to participate in all required procedures (brain MRI, brain Amyvid® scan, optional LP)

● 3.5 years with required monthly visits for antibody infusion

● Focus on diversity: many groups and individuals at higher risk for AD, but we don’t know why. Particular need for:
  – African Americans and Hispanic/Latino Americans
  – People over 75
  – People with a family history of AD

● Contact Erin Cattoor: 314-286-2303 or cattoore@abraxas.wustl.edu
Utility of Amyloid PET Scans

- The Division of Nuclear Medicine at Washington University provides scans for $4,300
- Neither Medicare nor any other 3rd party payer currently reimburses for these scans
- The Imaging Dementia-Evidence for Amyloid Scanning (IDEAS) study began 2016 to determine in the clinic whether amyloid scans in difficult-to-diagnose cases have a positive impact on patient outcomes
  - Enroll thousands of Medicare beneficiaries
    » Prodromal symptoms
    » Dementia of uncertain cause
  - Supported by CMS, Alzheimer Association, ACR, and ACRIN
  - 66 MDC referrals thus far; 32 have completed their scan
- [www.IDEAS-Study.org](http://www.IDEAS-Study.org)
Future Clinical Trials

- **LLCF or NAVIGATE-AD (Lilly):** Phase 2, Beta-site amyloid precursor protein cleaving enzyme (BACE) inhibitor
  - Oral administration, 3 or 12 mg/d
  - 55y-85y, MMSE 20-26, positive Amyvid PET
  - Endpoint: change in AV-1451 PET burden at 52 wk

- **Aducanumab or ENGAGE (Biogen):** Phase 3, human-derived monoclonal antibody to Aβ
  - Monthly infusion, 3 or 6 mg/kg (*APOE*4+); 6 or 10 mg/kg (*APOE*4−)
  - 50y-85y, CDR 0.5, MMSE 24-30, positive amyloid PET
  - Endpoint: change in CDR-SB at 78 wk

- **EARLY or A5 (Janssen/ATRI):** Phase 2b/3, BACE inhibitor
  - Oral administration, 10 or 25 mg/d
  - Asymptomatic (CDR 0), 60y-85y, positive amyloid PET or low CSF Aβ42
  - Endpoint: ADCS-PACC (preclinical Alzheimer cognitive composite): FSCRT, Logical Memory, Digit Symbol, MMSE) at 18 mo
Honors

- Randall Bateman, MD
  - 2015 MetLife Award in Medical Research
- Virginia Buckles, PhD
  - 2016 Harvey A. and Dorismae Hacker Friedman Award for Excellence in Service to Older Adults
- David Clifford, MD
  - 2016 Samuel R. Goldstein Leadership Award in Medical Student Education
- Janet Duchek, PhD
  - 2015 Emerson Electric Co Excellence in Teaching Award
- David Holtzman, MD, John Morris, MD, and Marcus Raichle, MD
  - 2015 Thomson Reuters Highly Cited Researchers
- Catherine Roe, PhD
  - 2015 Mentor of the Year for the ICTS Masters Program in Clinical Investigation
- Susan Stark, PhD
  - 2015 WUSM Award for Distinguished Community Service
- Chengie Xiong, PhD
  - 2016 Division of Biostatistics Faculty of the Year Award (3rd time since 2011!)
Seed money provided by the Hope Center (Benzinger/Morris), Avid, Dept of Radiology, ICTS, and the BJH Foundation

ADRC/HASD/ACS participants as of May 1, 2016
- 126 individuals (104 CDR 0, 18 CDR 0.5, 3 CDR1, 1 CDR 2)
- 61 ACS, 65 HASD/ADRC

Now formalized in HASD/ADRC through a competing revision to add new HASD Project 4 (Benzinger)
Tau Imaging at the Knight ADRC

- Brier et al., Science Transl Med 2016; “Tau and Aβ imaging, CSF measures, and cognition in Alzheimer’s disease”

- Gordon et al., Brain 2016; “The relationship between cerebrospinal fluid markers of Alzheimer pathology and positron emission tomography tau imaging”

- Wang et al., JAMA Neurol (in press); “The value of tau imaging in staging Alzheimer disease and revealing interactions between amyloid β and tau pathology”
PET Imaging of Tau Offers Marker of Alzheimer’s Disease Progression in Living Patients, New Study Found

BY JAMIE TALAN

PET IMAGING showing the average tau accumulation in the brains of Alzheimer's disease patients.
Other Selected Publications

- AD biomarkers, attentional control, and semantic memory retrieval: Synergistic and mediational effects of biomarkers on a sensitive cognitive measure in non-demented older adults
  - Aschenbrenner AJ et al., Neuropsychology 2015

- Neuropathologic assessment participants in two multi-center longitudinal observational studies: ADNI and DIAN
  - Cairns NJ et al., Neuropathology 2015

- Certified normal: AD biomarkers and normative estimates of cognitive functioning

- Three dimensions of the amyloid hypothesis: time, space, and ‘wingmen’
  - Musiek ES and Holtzman DM, Nat Neurosci 2015

- Longitudinal CSF biomarker changes in preclinical AD during middle age
  - Sutphen CL et al., JAMA Neurol 2015

- Longitudinal relationships among biomarkers for AD in the ACS
  - Xiong C et al., Neurology 2016
ADRC Partners

- St. Louis Chapter of the Alzheimer’s Association
- African American Advisory Board
- Links, Incorporated – St. Louis Chapter
- Harvey A. Friedman Center for Aging
- Hope Center for Neurological Disorders
- Barnes-Jewish Hospital Foundation
  - Tina Hissong
- Washington University
  - Strong institutional support from Chancellor Mark Wrighton, Dean David Perlmutter, and Dept Chair Dr. David Holtzman
  - Alumni and Development –David Blasingame, David Shearrer, Pam Morris, and Zach Silvers
  - Donors and friends, including Chuck and Joanne Knight, Mildred Poletsky, Daniel Brennan, Rodger and Paula Riney, David and Betty Farrell, and Fred Simmons and Olga Mohan
Outstanding AAAB

- Provides counsel on cultural sensitivity and outreach strategies and encourages research participation by African Americans
- Represents our research mission to the community
- Area leaders in education, diversity, the clergy, community advocacy, health care and media communications.

AAAB Chair: Pastor Douglass Petty, PhD

Vice Chair: Rev. C. Jessel Strong

Members: Benita Austin, Alexandre Carter, MD, PhD, Karen Collins, EdD, Beverly Foster, Ronald Gregory, EdD, Mary Harper-Thomas, Shawni Jackson-Triggs, Collins Lewis, MD, Martin Mathews, Norman R. Seay, Sallie Simmons, Jesse Swanigan, Sidney White
Norman R. Seay Lecture

- Norman R. Seay - Retired Educator, Community Activist and African American Advisory Board Chair Emeritus

- Upcoming: The 11th Annual Norman R. Seay Lecture, October 11th, 2015 (Farrell Center, WUSM)
  - Dr. Donna Masterman, Senior Medical Director in Neuroscience at Genentech
Knight ADRC Externship Experience

- Students and fellows from a wide range of educational backgrounds often seek Knight ADRC learning experiences through the Administration and Education Cores in consultation with the WUSM Curriculum Office and Human Resources

- 2016 summer students
  - Rachel Bailey, UMKC undergrad (McDade)
  - Samantha Donaldson, Fort Zumwalt high school student (Day)
  - Dane Fickes, STLCOP student (Gordon)
  - Kelly Fredericksen, Elmhurst College grad (Snider)
  - Lindsey Friedman, George Washington Univ MS student (Morris/Head)
  - Chunyu Ma, WU Biostat MS student (Roe)
  - Darcy Shulman, Denison Univ undergrad (Roe)

- Knight ADRC visiting scholars
  - Ryoko Ihara, MD, PhD, University of Tokyo; Arrived Spring 2015
  - Hongbo Luo, PhD, Jincheng Hospital of Lanzhou; Arrived Summer 2015
  - Jee-young Han, MD, Seoul National University; Arriving Summer 2016
News
ADC Review Panel

- Convened by NIA to provide recommendations to shape the future of the ADC program
- Goal: provide recommendations regarding how the ADCs can best support AD research and facilitate the implementation of the primary NAPA goal to prevent and effectively treat AD (and related dementias) by 2025
- Chaired by Barry Greenberg, PhD (Toronto Dementia Research Alliance)
  - All members currently external to the ADC program
  - Includes individuals from academia, industry, government, and non-profit foundations
- Will provide final recommendations to NIA in March 2017
Good News at NIA

Note: 2017 projection does NOT include the additional $400 million for AD research proposed by the Senate Appropriations Committee
## Good News at NIA

NIA Percentile Paylines (FY2016)

<table>
<thead>
<tr>
<th>Pay line for CSR-reviewed applications</th>
<th>&lt;$500k, General</th>
<th>&lt;$500k, AD</th>
<th>&gt;=$500k, General</th>
<th>&gt;=$500k, AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>All applications except N.I. or E.S.I. R01s</td>
<td>7%</td>
<td>18%</td>
<td>4%</td>
<td>15%</td>
</tr>
<tr>
<td>N.I. R01s</td>
<td>10%</td>
<td>21%</td>
<td>7%</td>
<td>18%</td>
</tr>
<tr>
<td>E.S.I. R01s</td>
<td>12%</td>
<td>23%</td>
<td>9%</td>
<td>20%</td>
</tr>
</tbody>
</table>
We Have Been Fortunate

- Total dollars to Washington University in FY 2016 for Alzheimer-related research: $57,874,725

- Total AD-related dollars to other universities in FY2016
  - Saint Louis University: $205,727
  - University of Illinois (all): $7,848,190
  - University of Kansas (all): $4,434,625
  - University of Missouri (all): $1,348,117
Bolus of RFAs

- 12 RFAs released by NIA (and NINDS) in Fall 2015
  - Health Disparities in AD (R01 and R03)
  - Caregiving for AD (R01 and R21)
  - Aging Research on Stress and Resilience to Address Health Disparities (R01)
  - AD in the Context of the Aging Brain (R01)
  - Epidemiology of AD and Cognitive Resilience (R01)
  - Novel Approaches to Diagnosing AD (R01)
  - Molecular/Cellular Mechanisms of the Etiology of AD (R01)
  - Pilot Clinical Trials for AD (R01)
  - Phase III Clinical Trials for AD (R01)
  - Vascular Contributions to AD (R01)
Bolus of RFAs

- Even more in 2016!
  - From Association to Function in the Alzheimer's Disease Post Genomics Era (R01 and R21)
  - Impact of Aging in Human Cell Models of Alzheimer's Disease (R01)
  - Adult Maturational Changes and Dysfunctions in Emotion Regulation (R01 and R21)
Famous People from Akron
Thank You!!!