

Novel Protein Biomarkers for Alzheimer Disease in Cerebrospinal Fluid

Symptomatic Alzheimer disease (AD) affects ~5 million individuals in the U.S. The term 'symptomatic' is important because the pathological plaques and tangles of AD begin to form in the brain about 10-15 years before the first problems appear. When we account for individuals suffering from this "pre-clinical" phase of AD, the number of people estimated to have AD today is much greater than 5 million.

Why do we care about "preclinical" AD? One important difference between "preclinical" and symptomatic AD appears to be loss of brain cells (neurons) and the connections between them (synapses) that allow our brains to process information. If we can treat people with "preclinical" AD *before* they lose neurons and synapses in large numbers (or with early AD, before losses are severe), we believe we will have better luck in preserving brain function.

One major hurdle, then, is identifying those people who appear normal (or have only subtle memory problems), but actually have "preclinical" or early AD. To accomplish this, we must develop new diagnostic tests that can distinguish "preclinical" and early AD from healthy aging. Ideally, a test might also indicate risk of progression to more severe stages.

The goal of investigator Dr. Richard Perrin's study is to identify such a test, using proteins found in the cerebrospinal fluid (CSF). Currently, a few CSF

proteins ("biomarkers") are known to distinguish a *group* of individuals with plaques and tangles from a *group* of people with healthy brains, but these biomarkers show considerable test score overlap (in the middle range) between groups. Consequently, only very high or very low test scores might reasonably be used to guide individual diagnosis.

To begin this study, Dr. Perrin's team took advantage of these existing biomarkers to select two groups of participants: those with early symptomatic AD (and test scores suggestive of plaques and tangles) and those without symptoms (and test scores suggestive of no plaques and tangles). In CSF samples from the two groups, they measured 777 proteins and identified 149 that were present in different amounts between the two groups.

In the next phase, they will evaluate approximately 8 of these 149 candidate biomarkers for their ability to (1) diagnose early and preclinical AD, and (2) predict risk of progression, by testing more than 300 CSF samples generously donated by Washington University Alzheimer's Disease Research Center study volunteers.

As a final aim, they will apply state-of-the-art mass spectrometry to study several candidate biomarkers in atomic detail; this work may enable them to measure these biomarkers more precisely, and may provide insight into the pathological processes that underlie AD.

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HELP US GO GREEN

In order to save paper and printing costs, the ADRC has created a *Horizons* newsletter e-mail list. You can sign up for this e-mail list and opt out of receiving a paper copy of our newsletter by contacting Ron Hawley (hawleyr@abraxas.wustl.edu or 314-286-2468). Include your name and the e-mail address where you'd like the newsletter sent.

E-mail addresses will not be shared with any other parties and will be used only to send you our ADRC *Horizons* newsletter.



Volunteers Needed for ADRC Studies

Do you know of someone who might consider volunteering for a research project on cognitive aging?

The primary project of the ADRC is in need of new volunteers:

The **Memory & Aging Project** enrolls persons aged 65+, both those with mild memory problems and those who are cognitively healthy.

If you know of a potential volunteer, please ask that person to call the ADRC at 314-286-2683. Thank you!

Memory Day 2009 Through New Eyes

by Hyun Jung Kim

As a social work intern at the Memory and Aging Project, I attended Missouri Memory Day on March 11, 2009 in Jefferson City. Missouri Memory Day 2009 invited Alzheimer advocates, including individuals living with Alzheimer's disease (AD), families, caregivers, friends, students and professionals, to share personal stories of Alzheimer's disease with state representatives and senators at the state capitol. Throughout the day, I heard powerful messages of hope for a future without AD.

Alzheimer's advocates from all around Missouri met with state legislators to talk about issues related to care and support for those living with AD. As one voice together, we advocated for Alzheimer's service grants, designed to provide community-based services such as adult education classes for individuals with early memory loss, respite assistance for family caregivers, care consultations with master's level counselors, MedicAlert + Safe Return membership, community education classes and outreach to underserved areas.

Due to the economic downturn, there was concern of cutting the Alzheimer's service grants from the state budget this year. However, Alzheimer's advocates asserted that cutting these programs and services would not only negatively affect individuals with AD, their families and caregivers, but also would bring more economic and social burden on public health institutions.

As we arrived in Jefferson City, we participated in an opening ceremony in the capitol rotunda to commemorate families and friends affected by AD. Those participating in the ceremony came from all over the state and from all walks of life. The power of togetherness was so strong that we truly believed we could positively affect the legislators' decisions concerning Alzheimer's service grants. Following the ceremony in the rotunda, we formed groups with 5-10 individuals according to our districts to meet with our state representatives and senators. When my group members went to meet our representative, she was in session. However, her administrative assistant invited us to the session to meet her. She welcomed us and spoke about the reason why we were there in front of all the House of Representatives. After a short introduction, a few representatives came to us and encouraged us in what we were doing. At the end of the day, we heard amazing news. They had passed the Alzheimer's service grants bill for this fiscal year.

As a Memory and Aging Project intern, I comprehend the great need for both research and resources to combat Alzheimer's disease. One of the avenues utilized by social workers to change policy is to enlighten and educate people, thus empowering individuals to actually participate in the government policy-making process. Through Missouri Memory Day 2009, I experienced the power of unity and togetherness to build support and commit resources to assist all those who are living with AD. Therefore, we should take a proactive stance with regard to issues related to Alzheimer's disease. Our voice and our engagement in advocacy for policy can make a positive difference!

Hyun Jung Kim was a social work practicum student with the Memory & Aging Project/ADRC in the spring of 2009. Hyun Jung will graduate from the George Warren Brown School of Social Work, Washington University, in August 2009.

FOR YOUR CALENDAR

7th Leonard Berg Symposium

“Presymptomatic Detection of Dominantly Inherited
Alzheimer's Disease”

October 1-2, 2009

Eric P. Newman Education Center
Washington University School of Medicine

The Berg Symposia were established to honor the founding director of our
Alzheimer's Disease Research Center, Dr. Leonard Berg.

Please follow the links at www.alzheimer.wustl.edu for more information.
Registration is open!

4th Annual

Norman R. Seay Lecture

November 17, 2009

4:00 - 5:00 pm

Reception immediately following

Washington University School of Medicine

Featuring Guest Lecturer
Orien Reid, MSW



**National Advisory Council on Aging
National Institutes of Health Council of Councils
Former Chair of the National Board of Directors of the
Alzheimer's Association and of
Alzheimer's Disease International**

2009 Alzheimer's Association

Memory Walk

St. Louis - Forest Park
Saturday, Sept. 12th

The Memory & Aging Project forms a Memory Walk team each year to support the event and to raise money. Register online to join our team, or contact Barbie Kuntemeier at 314-286-2882 for more information about the MAP team.

Please visit www.alzstl.org for more information and to register to walk.

Enrolling Clinical Trials for Alzheimer's Disease (AD) through the Memory and Aging Project/Alzheimer's Disease Research Center (ADRC)

All study procedures are for research only and are at no cost to participants

Name of Investigational Agent	Inclusion Criteria	Exclusionary Criteria	Exclusionary meds	Study Design	Refer patients to:
Elan Passive Immunization (HRPO #08-0450 and 08-0455) Intravenous medication to try to prevent amyloid from depositing in the brain.	50-89 years old Mild to moderate Alzheimer's (Mini Mental score of 16-26) Ability to have MRI	Strokes or mini-strokes on MRI. Weight above 264 lbs. Immune or autoimmune problems. Heart attack in last 2 years. Smoking more than 20 cigarettes/day. Prior treatment with an Alzheimer's vaccine.	Steroids in last 90 days. Chemotherapy in the last 3 years. Gingko and huperzine. Narcotic pain medications.	20 visits with 6 intravenous (in the vein) infusions over 83 weeks. The study has 7 brain MRI's, 5 ECG's (heart tracings), and numerous paper-pencil test sessions.	Study Coordinators Mary Coats, RN, MSN, GCS 314-286-2303 Christy Tomlinson, RN, MSN, GCS 314-286-2364
Wyeth Vaccine (HRPO #07-0852) Vaccine trial to assess the safety, tolerability and effectiveness of ACC-001. ACC-001 may prevent amyloid from depositing in the brain.	50-85 years old Mild to moderate Alzheimer's (Mini Mental score of 16-26 at screening) Stable on Alzheimer's medications for 120 days	Unable to have an MRI. History of stroke, encephalitis, seizures, auto immune disease, recent heart attack, uncontrolled blood pressure, alcohol or tobacco abuse, multiple allergies, cancer in the last 5 years.	Prior exposure to an Alzheimer's disease immunotherapeutic or vaccine	24 visits with 5 injections over 2 years. This includes 6 brain MRI's, 6 ECG's (heart tracings), and 2 lumbar punctures (spinal taps). Blood draws and paper-pencil tests may also be done at study visits.	Study Coordinator Vicki Weir, RN, MSG, BC 314-286-1973
Lilly Gamma Secretase Inhibitor (HRPO #08-0507) Oral medication may decrease amyloid production and slow down disease progression.	55+ years old Mild to moderate Alzheimer's (Mini Mental score of 16-26) If on Aricept, must be on 10mg dose.	Severe or multiple drug allergies, caregiver contact less than 10 hours/week, Serious or unstable illness, Cancer or serious brain disease in last 5 years	Exposure to Alzheimer's vaccine. Exposure to AD antibody in last 18 months	21 visits over 92 weeks. All participants will get drug at sometime during the study. Open label extension is planned. 4 physical exams, 14 blood draws, ECG's (heart tracings) at 19 visits. Optional MRI, lumbar puncture, and genetics substudies.	Study Coordinator Sue Neidenbach RN, MSN 314-286-2477

Alzheimer's Documentary Wins Awards

In the winter and spring of 2009, a documentary entitled "Alzheimer's Disease: Facing the Facts" aired on PBS affiliate stations nationwide. This video, which focuses on Alzheimer's disease research and healthy brain aging, has won two prestigious awards:

- ◆ 2009 Emmy Award for Documentary Program, National Academy of Television Arts & Sciences, Boston/New England Chapter
- ◆ Fall 2008 CINE Golden Eagle Award for Documentary Short

Produced for the National Institute on Aging's designated Alzheimer's Disease Centers through a grant from the MetLife Foundation, this film features several Washington University ADRC investigators. It originated as two separate videos, "Shining a Light on Alzheimer's Disease Through Research" and "Taking the Steps to Healthy Brain Aging." Copies of these individual DVDs are available at no cost from the Alzheimer's Disease Education and Referral Center (ADEAR) at www.nia.nih.gov/alzheimers.

Comings

- Carolyn Dufault - Psychometrician
- Peggy Kelly - Research Patient Coordinator
- Amy Thebeau - Medical Assistant, Memory Diagnostic Center

Goings

- Jane Sundermann - Psychometrician - left for the University of Denver to pursue a Ph.D. in Clinical Psychology
- Shirlene Taylor - Data Processing - retired in April after 41 years of dedicated service to Washington University!

HBO comes to St. Louis: “The Alzheimer’s Project” Documentary Screening

On May 4, 2009, a special screening of part of HBO’s new documentary series, “The Alzheimer’s Project,” was held at the Missouri History Museum.

Approximately 350 guests enjoyed a reception filled with brain-healthy foods such as blueberries, salmon, and green tea before viewing Part I of “Momentum in Science,” the portion of the documentary series that covers new discoveries and theories in the field of AD research.

This film prominently features investigators and their research

from our Alzheimer’s Disease Research Center here in St. Louis.

Following the 1-hour screening, a panel consisting of Dr. John C. Morris, Dr. David Holtzman, Dr. Randy Bateman, and Dr. Alison Goate discussed the film and answered audience questions.

The entire 4-part documentary series, along with supplementary videos, is available for free online streaming and can be viewed in its entirety at www.hbo.com.



L to R: Dean Larry Shapiro, Dr. David Holtzman, Dr. John Morris, Dr. Alison Goate, Dr. Randy Bateman (photo by David Preston, courtesy of HBO)

Awards & Honors

James Galvin, MD, MPH, was elected as an active member of the American Neurological Association.

Nupur Ghoshal, MD, received the Harvey A. Friedman Center for Aging Kopolow Award at the 9th Annual Friedman Conference on April 21, 2009. This award recognizes a resident, post-residency fellow, or non-tenured junior faculty member in Geriatric Neurology, Geriatric Psychiatry, or Geriatric Medicine who demonstrate achievement in direct patient care; in didactic learning exercises or in rounds, conferences, or national and international meetings; and in patient-oriented or basic research that addresses aging issues.

David Holtzman, MD, was elected to the Institute of Medicine.

John C. Morris, MD, was the 29th T.S. Srinivasan Orator in February 2009 in Chennai, India.

Catherine Roe, PhD, received the Harvey A. Friedman Center for Aging Friedman Award at the 9th Annual Friedman Conference on April 21, 2009. This award recognizes a non-physician who has made outstanding contributions to patient-oriented care, education, or research on aging or aging issues.

Henry “Roddy” Roediger, PhD, received the Arthur Holley Compton Faculty Achievement Award in December 2008.

Eugene Rubin, MD, PhD, was awarded the Distinguished Educator Award for House Staff Teaching from the Washington University School of Medicine in January 2009.

Consuelo Wilkins, MD, was selected for induction into the Alpha Omega Alpha Honor Medical Society.

It was announced that the Healthy Aging and Senile Dementia (HASD) program project directed by **Dr. John C. Morris** has been re-funded by the National Institute on Aging. HASD has been continuously funded since 1984.

In a paper in the *Journal of Alzheimer’s Disease* entitled “Alzheimer’s Disease Research: Scientific Productivity and Impact of the Top 100 Investigators in the Field,” the ADRC’s **Dr. John C. Morris, Dr. Nigel Cairns, and Dr. Alison Goate** were listed among the top 100 most prolific AD investigators. *Journal of Alzheimer’s Disease* 16 (2009) 451-465.

HORIZONS is the newsletter of the **Alzheimer's Disease Research Center (ADRC)** — a research program in the Department of Neurology, Washington University School of Medicine, funded by grants from the National Institute on Aging and private donations. The ADRC supports and promotes interdisciplinary research on Alzheimer's Disease. The Memory & Aging Project (MAP) — the clinical research office of the ADRC — provides expert clinical assessments of cognitive functioning in normal aging and dementia.

John C. Morris, MD, Director, ADRC, & Director, MAP

Eugene M. Johnson, PhD, Associate Director, ADRC

David M. Holtzman, MD, Associate Director, ADRC

Alison Goate, DPhil, Associate Director, ADRC, and Genetics Core Leader

Virginia Buckles, PhD, Executive Director, ADRC

Martha Storandt, PhD, Psychometric Core Leader

Nigel J. Cairns, PhD, MRCPATH, Neuropathology Core Leader

Mark Mintun, MD, & Denise Head, PhD, Imaging Core Leader and Co-Leader

Chengjie Xiong, PhD, Data Management and Biostatistics Core Leader

Monique Williams, MD, African American Satellite Leader

James E. Galvin, MD, MPH, Education Core/Rural Satellite Leader

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