

## Reflecting on Alzheimer's Disease: Perspectives from a Korean Neurologist Visiting the ADRC

The word 'nomang' in Korean means senility or a decline of mental faculties. In the past, we considered dementia as the state of having been captured by an evil spirit. Of course, due to recent studies and an emphasis on educating the public, many people now recognize it as the obvious organic disease that it is.

In 2004, the Korean Ministry of Health and Welfare reported that there would be 340,600 patients with dementia in Korea, representing 8.4% of people over 65 years of age in Korea. Korea already was considered an Aging Society in 2000 and soon will become an Aged Society (in 2008, Korean people over 65 years old made up 10.3% of the general population). Due to the rapidly changing population composition, the welfare of seniors is beginning to be regarded as one of the most important policies, and the issue of dementia is high on the list of concerns. Accordingly, the government became involved in the long-term care of seniors in July 2008; under this system, the nation and society bear the burdens of long-term care of the elderly with diseases such as

stroke and dementia. In addition, the Clinical Research Center for Dementia of South Korea (CREDOS), funded by the Korean Ministry of Health and Welfare, has been conducting a 9-year longitudinal study to investigate the epidemiological characteristics of dementia in Korea with a focus on prevention using the nationwide hospital- and community-based cohort from 2005.

However, there are yet some caregivers, such as sons and daughters, who ask me not to tell their loved ones with dementia that their diagnosis is dementia. They worry that their loved ones with mild dementia, who may have some insight into the fact that problems are occurring, might become upset upon hearing that they are demented, or 'captured by an evil spirit.' While having observed the methods of the Washington University ADRC for about three months now, I have experienced that doctors, patients, and their caregivers are up front about the diagnosis of dementia.

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The 7<sup>th</sup> Leonard Berg Symposium, "Presymptomatic Detection of Dominantly Inherited Alzheimer's Disease," was held on October 1-2 and attracted over 200 attendees, some from as near as Washington University's campus and others from as far as Australia, England, Japan, Belgium, and Spain. An associated poster session allowed twenty poster presenters to display current research pertaining to dominantly inherited forms of Alzheimer's disease as well as other forms of dementia.



Keith Johnson, William Klunk, Alison Goate, and Randall Bateman on Q&A panel at the 7th Leonard Berg Symposium

## A New ADRC Project: Antisense Oligonucleotide Therapy for Dementia

Dr. Timothy Miller, MD, PhD, Assistant Professor of Neurology at Washington University, is developing a novel treatment for dementia. One of the main components of “tangles” associated with Alzheimer’s disease is a protein called tau. He will be testing whether decreasing the levels of tau prevents the behavioral abnormalities in an APP transgenic mouse model. To decrease tau, Dr. Miller’s group will use antisense oligonucleotides, which are DNA-like chemicals that bind to and inactivate the signal used to make the tau protein. Similar antisense oligonucleotides could readily be developed for use in humans and, if this work is positive, could translate quickly into a novel

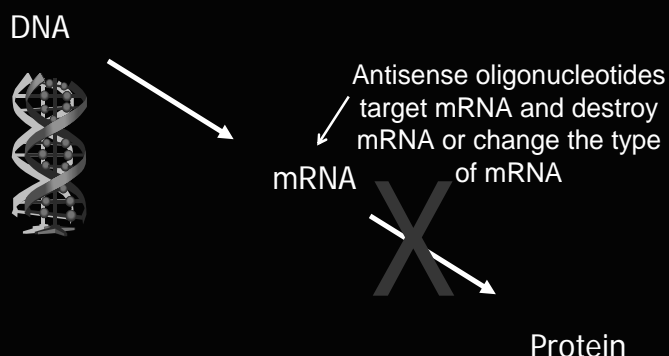
therapy for Alzheimer’s disease.

For some patients with frontotemporal dementia (FTD), increased levels of a particular form of tau cause FTD. For these patients, Dr. Miller believes that it will be protective to change the particular form of tau rather than decreasing overall levels of tau. To test this hypothesis, he will evaluate the effect of behavior after treating FTD model mice with antisense oligonucleotides. These antisense oligonucleotides affect the way tau is processed and thus change the forms of tau. Similar antisense oligonucleotides could readily be developed for use in humans; thus, this work could pave the way for a novel therapy for FTD.

### 2009 Poletsky Award Winner

The Richard & Mildred Poletsky Education Fund was established in 1995 to award a \$1,000 gift to support education and career development for a promising graduate student or post-doctoral fellow working in the field of Alzheimer’s disease or related dementias. The 2009 Poletsky Award winner is Elizabeth Mulligan, a 4<sup>th</sup>-year graduate student in the clinical psychology program in the Department of Psychology. Beth received her B.A. in Psychology from Williams College and her M.A. in Clinical Psychology from Washington University. She is now a Ph.D. candidate working on her thesis, “Grief among dementia caregivers: A comparison of two assessment systems.”

### Loss of mRNA Causes Loss of Proteins



### Would you like to make a gift in support of the ADRC?

You may support our research, education and service goals by joining the *Friends of the ADRC*. Members of the *Friends* are entitled to attend periodic *Friends Receptions*, and their donations support both the infrastructure upon which the ADRC depends, as well as specific research and educational projects of the Center. To join, simply call 314-286-2683.



L to R: John C. Morris, MD; Mrs. Mildred Poletsky; Beth Mulligan; James E. Galvin, MD

## Reflecting on Alzheimer's Disease

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Korean caregivers appear less comfortable receiving a dementia diagnosis for their loved ones, often preferring that it remain a secret. I agree that this open conversation is important to the people who have to prepare for the remainder of their lives after the diagnosis of dementia. Such openness and planning may be impossible for those who believe that patients with dementia are captured by an evil spirit.

While health policies and academic studies are important and necessary for helping patients with dementia, the general public's recognition and understanding of dementia still must not be overlooked.

Meanwhile, we must not make the person who began to forget forgotten.

\*Yong Soo Shim, MD, is a Korean neurologist currently acting as a visiting scholar to the ADRC. He moved to St. Louis with his wife and two children in August 2009.

## 4th Annual Norman R. Seay Lecture

The ADRC was proud to continue its Norman R. Seay Lecture Series this fall in honor of local civil rights leader and founding chair of the ADRC's African American Advisory Board, Mr. Norman R. Seay. The featured speaker for the 4th annual lecture, Ms. Orien Reid, has served as an active leader and volunteer with the Alzheimer's Association and other related organizations. Speaking from these experiences and from her role as a caregiver to family members with Alzheimer's disease, Ms. Reid addressed the audience about the importance of eliminating myths associated with AD, especially among minority populations, so that people with AD can begin to receive better care.



L to R: Consuelo Wilkins, Orien Reid, Norman Seay, David Holtzman, John C. Morris

## Breakfast Panel Emphasizes Minority Community Recognition and Involvement

The morning following the 4th Annual Norman R. Seay Lecture, the ADRC hosted a breakfast for key members of the African American community. "The Impact of Alzheimer's Disease on African Americans: A Breakfast Panel" drew leaders from all walks of life, including the President of the Mound City Bar Association, the President of the Archway Links, and the President and CEO of the *Saint Louis American* newspaper.

The panel consisted of figureheads both locally and nationally. Representing support from the national level was Dr. Marie Bernard, Deputy Director of the National Institute on Aging. She was accompanied on the panel by Orien Reid, the 2009 Norman R. Seay lecturer, Ida Goodwin Woolfolk, community leader and Chair of the ADRC's African American Advisory Board, Dr. John C. Morris, Director of the ADRC, and Douglas Petty, Pastor of Fresh Start Bible Church and Vice Chair of the ADRC's African American Advisory Board. The panel led a discussion regarding the importance of including African Americans in Alzheimer's research so that research results are generalizable to that population, and how to engage minorities in research who may still have a lingering fear of research due to past discrimination and injustice.



L to R: Marie Bernard, Orien Reid, Ida Goodwin Woolfolk, John C. Morris, Pastor Douglas Petty

**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\*\*

<b>Name of Investigational Agent</b>	<b>Inclusion Criteria</b>	<b>Exclusionary Criteria</b>	<b>Exclusionary meds</b>	<b>Study Design</b>	<b>Refer patients to:</b>
<p><b>Elan Passive Immunization</b> (HRPO #08-0450 and 08-0455)</p> <p>Intravenous medication to try to prevent amyloid from depositing in the brain.</p>	<p>50-89 years old</p> <p>Mild to moderate Alzheimer's (Mini Mental score of 16-26)</p> <p>Ability to have MRI</p>	<p>Strokes or mini-strokes on MRI.</p> <p>Weight above 264 lbs. Immune or auto-immune problems.</p> <p>Heart attack in last 2 years. Smoking more than 20 cigarettes/day. Prior treatment with an Alzheimer's vaccine.</p>	<p>Steroids in last 90 days. Chemotherapy in the last 3 years. Gingko and huperzine. Narcotic pain medications.</p>	<p>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.</p>	<p><b>Study Coordinators</b></p> <p>Mary Coats, RN, MSN, GCS 314-286-2303</p> <p>Christy Tomlinson, RN, MSN, GCS 314-286-2364</p>
<p><b>Wyeth Vaccine</b> (HRPO #07-0852)</p> <p>Vaccine trial to assess the safety, tolerability and effectiveness of ACC-001. ACC-001 may prevent amyloid from depositing in the brain.</p>	<p>50-85 years old</p> <p>Mild to moderate Alzheimer's (Mini Mental score of 16-26 at screening)</p> <p>Stable on Alzheimer's medications for 120 days</p>	<p>Unable to have an MRI.</p> <p>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.</p>	<p>Prior exposure to an Alzheimer's disease immunotherapeutic or vaccine</p>	<p>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.</p>	<p><b>Study Coordinator</b></p> <p>Pam Millsap, MSN 314-286-2363</p>
<p><b>Bristol-Myers Squibb Secretese Inhibitor for Prodromal Alzheimer's Disease</b> (HRPO #09-0833)</p> <p>Oral medication may decrease amyloid production and slow down disease progression.</p>	<p>45-90 years old</p> <p>Very mild AD (Mini Mental Score of 24-30)</p> <p>Women must be postmenopausal or surgically sterile</p> <p>In good general health</p>	<p>History of stroke, peptic ulcer, GI bleeding or inflammatory bowel disease, HIV, kidney disease, syphilis and/or insulin dependent diabetes.</p> <p>History of significant drug allergy.</p>	<p>Cannot be taking memantine (Namenda®), ginkgo.</p> <p>There are many medications participants cannot be taking at screening and during the study. Coordinators will review medications at screening.</p>	<p>13 visits over 52 weeks. The first 24 weeks after screening is the treatment phase (active drug or placebo). The following 24 weeks is observational follow-up. The study includes: 3 lumbar punctures, 10 ECGs, 4 MRIs of the brain and Memory and thinking tests and/or interviews at every visit.</p>	<p><b>Study Coordinators:</b></p> <p>Christy Tomlinson, RN, MSN, GCS 314-286-2364</p> <p>Pamela Jackson RN, MA 314-286-2409</p>

## 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!*

## Awards & Honors

**Michael Gitcho, PhD**, from the ADRC's Neuropathology Core was honored as having the most cited publication in the *Annals of Neurology* in 2008: TDP-43 A315T mutation in familial motor neuron disease. Gitcho MA, Baloh RH, Chakraverty S, Mayo K, Norton JB, Levitch D, Hatanpaa KJ, White CL 3rd, Bigio EH, Caselli R, Baker M, Al-Lozi MT, Morris JC, Pestronk A, Rademakers R, Goate AM, Cairns NJ. *Ann Neurol*. 2008 Apr; 63(4):535-8.

**Ronald Hawley**, the ADRC's Multimedia Programmer, represented Washington University at "Focus on Teaching and Technology: A Regional Conference" hosted by the University of Missouri – St. Louis on October 15-16, 2009. Mr. Hawley presented on navigating the digital video divide.

A paper from the lab of **David Holtzman, MD**, was published in the journal *Science* in September: Kang JE, Lim MM, Bateman RJ, Lee JJ, Smyth LP, Cirrito JR, Fujiki N, Nishino S, Holtzman DM. (2009) Amyloid- $\beta$  Dynamics Are Regulated by Orexin and the Sleep-Wake Cycle. *Science*. DOI: 10.1126/science.1180962

**John C. Morris, MD**, was designated as a top clinical provider for the Washington University School of Medicine Faculty Practice Plan in FY '09, indicating that he was rated in the top 10% of all medical school faculty according to patient satisfaction surveys. Dr. Morris also presented two named lectures: 1) The inaugural Ellen S. Dickinson Medical Science Symposium Lecture, September 21, 2009, at Ohio Wesleyan University in Delaware,

### Comings

Natalie Selsor - Research Coordinator

Cherese Fisher - Medical Assistant for the Memory Diagnostic Center

Joyce Haynie - MAP Nurse Clinician

Allison Brauch - MAP Nurse Clinician

Krista Moulder - Senior Staff Scientist

### Goings

Vicki Weir, a MAP nurse clinician, left to pursue an opportunity in neurosurgery.

## 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.



Ohio; and 2) the Soriano Lecture on October 13, 2009, at the 134th Meeting of the American Neurological Association in Baltimore, Maryland. He also was awarded a competitive supplement by the National Institute on Aging with funds provided by the American Recovery and Reinvestment Act (ARRA). These funds will supplement the Healthy Aging and Senile Dementia program project award for execution of Project 1: Preclinical Alzheimer's Disease Predicts Post-Stroke Dementia.

**Mario Ortega**, a graduate student in Dr. Denise Head's lab, received the Chancellor's Fellowship at Washington University for 2009-2014.

**Joseph L. Price, PhD**, received the Cortical Discover award given by the Cajal Club, a long-standing organization of neuroanatomists.

**Eugene Rubin, MD, PhD**, ADRC clinician, has an award named in his honor. The Gene Rubin Award annually recognizes a psychiatry resident in an early stage of training who demonstrates excellence in teaching and demonstrates excellent potential for an academic career involving teaching and educational administration. Funds for the award were raised by a "challenge" donation made by Dr. Rubin and his wife, which was matched by former housestaff.

**Monique M. Williams, MD**, will be collaborating with colleagues at Tuskegee University's Center for Bioethics in Research and Health Care on a GO grant from the National Center on Minority Health and Health Disparities to examine bioethical issues related to minority research participation. Dr. Williams will serve as project director for the Washington University site.

*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; Administration Core and Clinical Core Leader

**Eugene M. Johnson, PhD**, Associate Director, ADRC

**David M. Holtzman, MD**, Associate Director, ADRC

**Alison Goate, DPhil**, Associate Director, ADRC; Genetics Core Leader

**Virginia Buckles, PhD**, Executive Director, ADRC

**Martha Storandt, PhD**, Psychometric Leader

**Nigel J. Cairns, PhD, FRCPath**, 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

**Anne Fagan, PhD**, Biomarker Core Leader



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