BU ADC Bulletin

Boston University Alzheimer's Disease Center

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BOSTON UNIVERSITY SCHOOL of Medicine

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In This Issue:

ADC Researchers Brief Congressional Task Force

On Tuesday, January 16, 2007, Dr. Robert Green, Director of the Boston University Alzheimer's Disease Center (BU ADC) Clinical Core, and Dr. Robert Stern, Associate Director of the BU ADC Clinical Core, gave a joint presentation to the Bipartisan Congressional Task Force on Alzheimer's Disease. Dr. Green gave an overview of Alzheimer's disease (AD), and he spoke about risk factors relating to AD in special populations. Dr. Green also presented new findings in the genetics of AD (see "New Alzheimer's Gene Discovery" feature article in this issue). Dr. Stern presented information pertaining to recent advances in the diagnosis and treatment of AD as well as the important public health issue of AD among minority populations. In particular, he emphasized the need to diminish health care and research disparities among African-American elders.

Both Drs. Green and Stern emphasized the critical need to increase National Institutes of Health (NIH) funding for AD research. Former BU ADC trainee Dapo Akinleye discussed the importance of an NIH diversity training grant that supported a portion of his graduate education. He received his Master's in Public Health from the Boston University School of Public Health while working with Dr. Green at the BU ADC. Mr. Akinleye described to the Congressional Task Force his experiences working in

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Dapo Akinleye, Dr. Robert Stern, Congressman Edward Markey (D-Mass.), and Dr. Robert Green, (left to right).

New Alzheimer's Gene Discovery

In conjunction with colleagues from the University of Toronto and Columbia University, senior researchers affiliated with the Boston University Alzheimer's Disease Center have uncovered a major new gene associated with Alzheimer's disease (AD). Published in the February 2007 issue of *Nature Genetics*, data from four different ethnic groups support a link between the SORL1 gene and late-onset AD. This discovery is only the second gene to be linked to late-onset AD. Apolipoprotein E (APOE), identified in 1993, was the first late-onset AD gene to be discovered.

This new genetic discovery was uncovered when the international research group found that variants of the SORL1 gene are more common among people with late-onset AD as compared to healthy adults of the same age. The international research team believes that these SORL1 variations may be more common in people with AD because the SORL1 gene is functioning improperly. Through the amyloid precursor protein, SORL1 may increase amyloid beta peptides in the brain. Increased amyloid beta peptides are a key neuropathological feature of AD.

The SORL1 finding is based on a five-year study that involved DNA samples from more than 6,000 research volunteers. These data are particularly unique because most prior studies on the genetics of AD have focused on White populations of European ancestry. In contrast, the SORL1 discovery was replicated across four distinct ethnic and racial groups, including Whites of European ancestry, African-Americans, Caribbean-Hispanics, and Israeli-Arabs.

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New Clinical Services at the ADC

In this issue of the BU ADC Bulletin, we are pleased to highlight the opening of two new BU ADC-affiliated clinics, including the *Alzheimer's Disease Clinical & Research Program Clinic* at Boston University Medical Center in Boston, MA and the Edith Nourse Rogers Memorial Veterans Hospital *Geriatric Research, Education, & Clinical Center Memory Diagnostic Clinic* in Bedford, MA. These services are in addition to those already offered by BU ADC-affiliated clinics at Boston University Neurology Associates in Boston, MA and Weymouth, MA. For more information on all BU ADC-affiliated clinics, log onto our website (www.bu.edu/alzresearch).

Alzheimer's Disease Clinical & Research Program Clinic at the Boston University Medical Center, Boston, MA

Dr. Robert Stern (neuropsychologist), Dr. Anil Nair (neurologist), and Mr. Eric Steinberg (nurse practitioner) provide compassionate care for older adults with memory complaints and other cognitive problems at the *Alzheimer's Disease Clinical & Research Program (ADCRP) Clinic*. This team of experienced and knowledgeable professionals provides a comprehensive evaluation, which includes extensive interviews with the patient and family members, neuropsychological assessment (such as tests of memory and language), a neurological examination, and related diagnostic tests (such as brain imaging and blood work).

In most circumstances, all aspects of the clinical evaluation are conducted on the same day. An additional appointment is held one or two weeks later to review the results of the evaluation and treatment recommendations with the patient and family members.

The *ADCRP Clinic* provides medical treatment and follow-up care for Alzheimer's disease, frontal dementias, Lewy body disease and related disorders. This clinic also provides assessment of the cognitive and thinking skills necessary for safe driving along with consultation and support for the patient and family about the difficult decision to stop driving.

In addition to assessment services, the clinic provides assistance to patients and their families for long-term care planning, caregiver support, education, and referrals for community resources, such as adult day programs. These clinical services are affiliated with the research component of the ADCRP, which carries out many clinical trials in Alzheimer's disease. These trials provide interested patients with the opportunity to participate in cutting-edge Alzheimer's research.

The *ADCRP Clinic* welcomes new referrals from patients, families, or health care providers. To request an appointment or make a referral, please call 617-638-7100.

The Memory Diagnostic Clinic at the Edith Nourse Rogers Memorial Veterans Hospital, Bedford, MA

The Edith Nourse Rogers Memorial Veterans Hospital is pleased to announce that their new *Memory Diagnostic Clinic* is open and accepting new veteran referrals. The *Memory Diagnostic Clinic*, headed by Dr. Maureen O'Connor (neuropsychologist) and Dr. Andrew Budson (neurologist), provides comprehensive evaluation, diagnosis, and treatment of adults with Alzheimer's disease, dementia, and other related memory disorders. The multidisciplinary team consists of neurologists, neuropsychologists, and nurse practitioners who are experts in the diagnosis and treatment of memory disorders, and who are committed to enhancing the knowledge of the patient, caregivers, medical professionals, and the public through both clinical and research methods. An evaluation typically takes place in one day over the course of several hours and includes a neurological examination, a neuropsychological evaluation, laboratory assessments and neuroimaging tests as needed.

When all tests are completed the patient is scheduled for a return

Clinical Services continued on page 4 >

Drs. Maureen O'Connor and Andrew Budson in front of the Memory Diagnostic Clinic in Bedford, MA.

Research Update

Early Alzheimer's Neuropathological Changes Observed in Posterior Cortex

Dr. Ann McKee was selected to present "Early Tau Alterations are Prominent in Posterior Association Cortex in Preclinical Alzheimer's Disease" as a platform presentation at the American Academy of Neurology meeting, scheduled April 28th-May 5th. Over 10,000 researchers attend this annual national meeting. Dr. McKee's research study, using the BU ADC Brain Bank, identified major biological changes in early stage Alzheimer's disease in an area of the brain that has previously been overlooked. Collaborators of this project include investigators and staff from the Framingham Heart Study, including Dr. Philip Wolf, Dr. Rhoda Au, Jonathan Drake, Hyo Lee, and Carol Kubilus, and BU ADC Director, Dr. Neil Kowall.

Advancement in Tracking Brain Response to Drug Therapy

Dr. Brandon Ally, an investigator in Dr. Andrew Budson's Cognitive Neuroscience Laboratory, was awarded a 2006 ADC Pilot Grant to investigate electrophysiological biomarkers of patient response to drug therapy. Preliminary results are promising, illustrating that areas of the brain critical to memory function show an improved response after 8 weeks of cholinesterase inhibitor therapy. Figure A shows the brain activity of Alzheimer's disease patients prior to beginning therapy. Figure B shows improved brain activation after 8 weeks of therapy. The laboratory is continuing to recruit participants for this study.

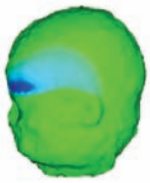

Figure A

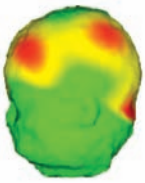

Figure B

New Drug Target for Alzheimer's Disease

Drs. Rina Yamin and Carmela Abraham reported in the *Journal of Neurochemistry* on the discovery of a novel enzyme, APEH, that can remove the toxic amyloid protein. There is ample evidence that the amyloid protein plays a major role in the development of Alzheimer's disease pathology and symptoms. Currently, the normal function of this enzyme is unknown, but studies using brain tissues from the BU ADC Brain Bank demonstrate that the level of the enzyme in Alzheimer's disease brains is five times lower than that found in healthy age-matched controls. Thus, APEH may become a new therapeutic target for Alzheimer's disease. Reference: Yamin, R, Bagchi, S, Hildebrant, R, Scaloni, A, Widom, RL, and Abraham, CR. Acyl Peptide Hydrolase, a Serine Proteinase Isolated from Conditioned Medium of Neuroblastoma Cells, Degrades the Amyloid ß Peptide. *Journal of Neurochemistry*, 2007; 100:458-467.

New Faculty

The BU ADC is pleased to welcome Ms. Christine Chaisson as the new Data Core Leader. Ms. Chaisson is an Assistant Research Professor of Public Health (Biostatistics) and Acting Director of the Data Coordinating Center, a data management resource center for Boston University Medical Center. Ms. Chaisson's team creates and maintains database applications for the BU ADC's participant registry (i.e., Health Outreach Program for the Elderly) and the Brain Bank. She and her team perform subject tracking, data entry, and data reporting. Ms. Chaisson also assists with form development for data collection, and she creates analytic datasets for BU ADC investigators and trainees.

Ms. Christine Chaisson

Race and Self-Perceived Risk for Alzheimer's Disease Associated with Study Dropout

Dr. Anil Nair's abstract, "Race and Low Self-Perceived Risk for Alzheimer's Disease are Associated with Higher Dropout in REVEAL study," was selected as a platform presentation at the International Conference on Prevention of Dementia. This meeting will be held in Washington, DC, June 9th-12th. Findings from this study suggest that race and lower self-perceived risk are associated with increased study dropout among family members of Alzheimer's disease patients who choose to get genetic susceptibility testing. Collaborators of this project include BU ADC investigators and staff, including Susan Hiraki, Winston Chung, Clara Chen and the BU ADC Clinical Core Director, Dr. Robert Green.

< *ADC Researchers continued from page 1*

the African-American community and methods for overcoming the reluctance of this population to seek medical care for this devastating disease.

Massachusetts Congressman Edward Markey, who invited the BU ADC researchers to present at the Congressional briefing, expressed his appreciation to the speakers and provided strong support for the need for increased federal funding of AD research and clinical care. Congressman Markey has been a leading national advocate for new grant programs for AD research and additional funding for the NIH.

Drs. Robert Stern and Robert Green

"This invitation was an honor for our entire institution as it recognized the groundbreaking work in AD being carried out at Boston University Medical Center," said Dr. Green. "The experience of briefing Congress also gave us a rare opportunity to speak directly to the people who are deliberating about the NIH budget, particularly funding for AD, about the critical need for increased funding at this time. We appreciate the leadership of Congressman Markey in rallying efforts to preserve and extend research to defeat AD."

< *Clinical Services continued from page 2*

visit to review results from the evaluation, ask questions, and receive treatment recommendations. The *Memory Diagnostic Clinic* provides education and information to patients and their caregivers concerning diagnosis, family planning, and patient care. This clinic also offers interventions for patients and caregivers as appropriate, including time limited individual and family psychoeducation, cognitive rehabilitation, and caregiver groups. In addition, linkage to community resources for additional care is provided.

The *Memory Diagnostic Clinic* welcomes new referrals. You must be a veteran to be seen in this clinic. The clinic is open Mondays from 9am to 3pm. For general information please contact Victoria Henehan at 781-687-3240, Monday through Friday, 8:00am – 4:30pm.

Drs. St. George-Hyslop and Lindsay Farrer at the recent Alzheimer's Disease Center Lecture Series.

< *Gene Discovery continued from page 1*

Dr. Lindsay Farrer, Chief of the Genetics Program at Boston University School of Medicine, led the local research effort. The University of Toronto research team was led by Dr. Peter St. George-Hyslop, Director of the Centre for Research in Neurodegenerative Diseases, and the Columbia University Medical Center research team was led by Dr. Richard Mayeux, Co-Director of the Taub Institute of Research on Alzheimer's Disease and the Aging Brain.

In March, Dr. St. George-Hyslop presented the SORL1 research findings at the Boston University Alzheimer's Disease Center lecture series, where he emphasized that additional data supporting SORL1's association with AD are needed. "This finding demonstrates the importance of international collaboration and is exciting preliminary information that needs to be validated."

Dr. Farrer believes this discovery is an important advancement in the understanding of genetics and AD, but he cautions that much more work lies ahead. "While we have identified several variants in SORL1 that show the same pattern of association across multiple ethnic groups with very different genetic makeup and lifestyle characteristics, we have not yet discovered the mechanism linking SORL1 gene variants to altered functioning of the SORL1 protein that may accelerate the process leading to AD."

Actively Recruiting Studies

Study Type	Study Title	Study Description
Memory & Cognition	HOPE: Health Outreach Program for the Elderly	This longitudinal study increases our understanding of age-related changes in memory and thinking. It serves as the BU ADC's main research registry, where participants agree to be contacted regarding other BU ADC-approved studies.
	Understanding False Memory in AD	This study seeks to better understand why patients with Alzheimer's disease (AD) and other dementias frequently remember things that never happened. The ultimate goal of this NIA-sponsored study is to provide the basis for ways to reduce false memories in patients with dementia.
Caregiving Support & Education	CARE-Plus	This caregiver-based study is seeking to determine whether an educational intervention can reduce behavior problems in patients with AD and improve caregivers' emotional well-being. It consists of a 5-week group intervention which offers 90-minute weekly sessions on AD, its symptoms, and tips for improving communication and interactions with the family member. It also focuses on family members' feelings about their own caregiving skills. The individual with AD is not involved in this study.
Genetics	MIRAGE: Multi-Institutional Research in Alzheimer's Genetic Epidemiology	This longstanding study evaluates the association between genetic (hereditary) and non-genetic risk factors for AD. The study is currently recruiting people with a diagnosis of probable AD who also have an unaffected sibling who would be willing to participate with them. The study is being conducted at multiple sites in the United States and abroad.
	REVEAL III: Risk Evaluation and Education for Alzheimer's Disease	This study is a multi-center, nationwide research project. The goal of REVEAL-III is to provide healthy adults with genetic susceptibility testing and information about their chances to develop AD.
Treatment	DHA * new study	This new study is a multi-center clinical trial that will evaluate the effectiveness of a new medication, DHA, in slowing the progression of AD. The study is recruiting participants with mild to moderate AD who have a caregiver available to accompany them to clinic visits.

Erin Whalen, Recruitment Coordinator for BU ADC research studies.

For more information, please call the recruitment coordinator, Erin Whalen, at 617-414-1078

ADC Happenings

Welcome

The BU ADC is pleased to welcome our new staff members: **Caleb Bliss**, data manager for the Data Core; **Mario Orozco**, clinical trial participant coordinator; **Janet Callaghan**, research nurse; and **Susan Vanderhill**, coordinator for the ADMIRE study and the ADC Education and Information Transfer Core.

We also extend a warm welcome to our new student trainees: **Moniek Damman** and **Welmoed Dekker** from the Netherlands and **Brian Panichella** from Boston College.

Congratulations

The BU ADC would like to congratulate **Drs. Carmela Abraham** and **Benjamin Wolozin** for their invited attendance of the 100th anniversary of Dr. Alois Alzheimer's lecture describing the symptoms and neuropathological examination of Auguste D, the first documented patient to suffer from a disease later named after Dr. Alzheimer. The meeting took place in November 2006 at the Psychiatric Institute in Tubingen, Germany.

BU ADC student trainee **Laura Byerly** will be joining our staff as a psychometrician for the HOPE study following her graduation from Boston University this spring.

Dr. Robert Green is the recipient of a K24 Mid-Career Investigator Award. Dr. Green will use this five-year NIH grant to discover and quantify ways of characterizing genetic risk for Alzheimer's disease and to create and evaluate real-world procedures for communicating genetic risk. A major focus of this award is to mentor junior investigators in patient-oriented research.

Dr. Kathy Horvath recently received funding from the VA Health Services Research and Development Program to conduct a clinical trial of a home safety intervention for patients with Alzheimer's disease. This study will compare the efficacy of two methods of health education on caregiver and care-recipient outcomes.

Valerie Nolen was recently appointed to the National Brain Health Initiative in partnership with the Center for Disease Control.

Goodbyes

Many thanks and best wishes to BU ADC faculty and staff who have recently taken on new positions: **Suzette Levenson**, former Data Core Director, is now Acting Associate Dean of Administration & Finance for the Boston University School of Public Health; **Debra Hanna**, former clinical research manager, is now completing her PhD in Nursing at the University of Massachusetts at Lowell; **Emily Hubbard**, former psychometrician, is now completing her Master's in Public Health at Boston University School of Public Health; **Stacy Carruth**, former study coordinator, is now serving as a Community Health Specialist at the Regional Center for Healthy Communities; **Kate Henderson**, former participant coordinator, is now volunteering in public health in Peru; and **Judy Hibschman**, former HOPE psychometrician, is enrolling in the nurse practitioner program at Columbia University.

Thanks also to our former pre-doctoral trainees, **Kevin Blankevoort** and **Karin Volkers**, and post-doctoral trainee, **Dr. Hennie Lee**, who have all returned to the Netherlands.

Save the Date

International Prevention Conference

June 9-12, 2007
Washington, DC

This conference is for clinicians, researchers, and policy advocates who want a dynamic forum to exchange knowledge about early diagnosis, treatment, and possible prevention of Alzheimer's disease.

www.alz.org/prevention conference

Memory Ride for Alzheimer's Research

July 28, 2007
Devens, MA

The 11th Annual Memory Ride, sponsored by the Alzheimer's Association, is a one-day bike ride with three different distance options: 25, 50 and 100 miles.

www.memoryride.org

Dementia Care Conference

August 26-29, 2007
Chicago, IL

This annual conference for dementia care professionals features the latest developments in Alzheimer's disease care and support.

www.alz.org/care conference

Memory Walk

September 30, 2007
Cambridge, MA

Memory Walk is the signature fundraising event of the Alzheimer's Association, bringing together family, friends, caregivers, and concerned community members – all wanting to make a difference. To participate on the Boston University Alzheimer's Disease Center Team or to sponsor our walkers, log onto our website at www.bu.edu/alzresearch for more information.

Honorary and Memorial Contributions

The Alzheimer's Disease Center welcomes honorary and memorial contributions. These gifts are an excellent way to pay tribute to a family member or friend while making a contribution to the advancement of research in the field of Alzheimer's disease.

In Memory of Antonio Carabia
Margaret Black
Albert and Marie Capone
William and Mary Murray
Luciano and Linda Pacella
Arline Schermerhorn

In Memory of June Carr
Linda Grant

In Memory of Richard C. Foley, Jr.
Kate and John Brenock-Maliszewski Family
Marsha Dean and Glenn Williamson
Irene Edmonds
Maureen Kerr
Lawrence Shea

In Memory of Doris Grossman
Leona Goren

In Memory of Kenneth Lumsden
Kristina Lumsden

In Memory of Pasquale Naccarato
Gary Cousin

In Memory of Lorraine J. Resch
Fire Apparatus Manufacturer

In Honor of Gloria Sheperd
Sharon Midura

Research Center Contact Information

If you have general questions about BU ADC research, or specific questions or comments about this newsletter, or if you would like to make a donation to support the BU ADC, please contact:

Catherine Pfau, MMHS
Administrative Manager, BU ADC
715 Albany Street, B-7800
Boston, MA 02118

Telephone: 1-888-458-BUAD
Email: buad@bu.edu

Check out our website at www.bu.edu/alzresearch

Alzheimer's Disease Center

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The Boston University Alzheimer's Disease Center (BU ADC) is primarily supported through a grant from the National Institute on Aging. The BU ADC supports cutting-edge research and provides education and clinical care to families affected by AD. Its leadership is listed below, alphabetically by Center Core.

Neil Kowall, MD, *Center Director and Administrative Core Director*

Richard Fine, PhD, *Administrative Core Associate Director*

Robert Green, MD, MPH, *Clinical Core Director and Center Associate Director*

Robert Stern, PhD, *Clinical Core Associate Director*

Christine Chaisson, MPH, *Acting Data Core Director*

Kathy Horvath, PhD, RN, *Education Core Co-Director*

Angela Jefferson, PhD, *Education Core Co-Director*

Robert Ferrante, PhD, MSc, *Murine Breeding and Molecular Genetics Core Director*

Ann McKee, MD, *Neuropathology Core Director*

The BU ADC Bulletin is published twice annually (**Dr. Angela Jefferson,** *Editor*; **Dr. Kathy Horvath,** *Co-Editor*; **Susan Vanderhill,** *Editorial Assistant*).

Clinic Information

We provide expert diagnostic evaluation and treatment services for memory-related problems. Our clinical services are available at several locations:

Alzheimer's Disease Clinical & Research Program (ADCRP)

ADCRP Clinic
Boston University
Medical Campus
Robinson Suite 7800
Boston, MA 02118
Telephone: (617) 638-7100

Boston University Neurology Associates (two locations)

Memory Assessment Clinic
Boston Medical Center
Doctor's Office Building, 7th Floor
Boston, MA 02118
Telephone: (617) 638-8456

Memory Assessment Clinic
1221 Main Street, Suite 401
Weymouth, MA 02190
Telephone: (781) 331-9944

Edith Nourse Rogers Memorial Veterans Hospital Geriatric Research, Education, & Clinical Center (GRECC, two clinics)

GRECC Dementia Management Clinic
200 Springs Road, GRECC (182B)
Bedford, MA 01730
Telephone: (781) 687-2701

GRECC Memory Diagnostic Clinic
200 Springs Road, GRECC (182B)
Bedford, MA 01730
Telephone: (781) 687-3240

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