

SPOTLIGHT ON RESEARCH

ADRC RESEARCHERS IDENTIFY BIOMARKERS FOR ALZHEIMER'S DISEASE

By Cheryl Dawes



As new treatments for Alzheimer's disease (AD) are developed, the importance of early diagnosis grows. Diagnosis early in the course of the disease increases the likelihood of success for treatments that might slow disease progression, as well as helping patients and their families make plans for future care. Although AD is the most common cause of dementia, the clinical diagnosis of probable AD remains uncertain until it is confirmed by pathological examination of brain tissue during autopsy.

ADRC researcher Dr. Jing Zhang and his colleagues have taken a major stride on the path toward early and accurate diagnosis of AD and other progressive brain diseases. Using an advanced analytical technique, they have identified proteins in the human body that may serve as "biomark-

ers" for AD, Parkinson's disease and dementia with Lewy bodies. A biomarker is a feature or condition in the body that can be objectively measured to indicate disease risk, presence, and progression.

"We're getting very close to being able to use these biomarkers for the clinical diagnosis of Alzheimer's and Parkinson's disease, and dementia with Lewy bodies," said Zhang, Associate Professor of Pathology at the UW.

Looking for biomarkers in AD is a complex, multi-step process involving ADRC researchers around the country. Pioneering work by Dr. Elaine Peskind of the UW ADRC has perfected the use of lumbar punctures in individuals with AD, a technique in which a thin needle is inserted into the lower back and a small amount of fluid is extracted. This cerebrospinal fluid (CSF) can then be analyzed to identify what chemicals are present.

Zhang and the other research-

ers conducted a multi-site study to identify specific proteins in cerebrospinal fluid from patients with neurodegenerative diseases and healthy controls. To identify and evaluate these proteins, they used a state-of-the-art technique called iTRAQ, a highly sensitive and specific method that relies on isotopic labeling of protein molecules followed by mass spectrometry analysis. The technique is a major improvement on other biomarker detection techniques, according to Zhang.

The researchers identified and measured more than 1,500 proteins in CSF samples from four groups of study volunteers—10 patients with AD, 10 patients with Parkinson's disease, 10 patients with dementia with Lewy bodies, and 10 healthy age-matched controls. After identifying the CSF proteins, Zhang and his colleagues determined which of these proteins were potential biomarkers. The researchers then compared distributions of those markers in CSF collected from patients compared to the healthy controls.

The results of this comparison enabled the researchers to determine unique panels of biomarkers that distinguished

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healthy controls from patients with neurodegenerative disease, and which distinguished between AD, Parkinson's disease and dementia with Lewy bodies. The researchers then confirmed their results with an alternative method known as Western blot analysis.

"A key to our research was that we compared three different diseases with normal controls, so we knew a particular protein response was related to a specific disease, not just a neurodegenerative disease in general," explained Zhang.

Although the study results are promising, the disease biomark-

ers Zhang and his colleagues identified must be tested in a larger group of patients before becoming part of a diagnostic tool used by clinicians. The large number of proteins that the group identified in patients with neurodegenerative diseases will likely be useful in developing methods of clinical diagnosis and monitoring disease progression.

Zhang and his colleagues are now investigating whether the biomarkers they found in CSF, which requires a lumbar puncture to obtain, are present in blood, which can be sampled in a less invasive manner.

The results of the CSF study are published in the *Journal of Alzheimer's Disease*, volume 9, August 2006. Other UW researchers who participated in the study included James Leverenz, Elaine Peskind, Cyrus Zabetian, Ali Samii, Catherine Pan, Yan Wang, Jinghua Jin, David Zhu, G. Jane Li, and Thomas Montine. The multi-site study also included researchers from Oregon Health and Science University in Portland; Baylor College of Medicine in Houston; the Fred Hutchinson Cancer Research Center in Seattle; and Applied Biosystems in Framingham, Mass. ♦

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STRANGE NEW WORLD: When Persons with Dementia Must Visit the Hospital

PART 1

By Thomas Orton

For a person with dementia, going into the hospital can be like a trip to the moon. For most older adults, a hospital stay – for tests or for surgery – is at some point inevitable. But for the dementia sufferer, time in the hospital temporarily but traumatically cuts off the familiar sources of support – friends, family, church, community. This article, and a follow-up in the next issue of *Dimensions*, will explore possible avenues for easing some of the pressure and strain on the person with dementia and everyone involved in his or her hospital care.

If the person you care for is frail or has multiple medical conditions, there is an even greater risk of an unexpected trip to the emergency room. It's a good idea to be prepared. Pack an overnight bag ahead of time with all the necessities. On a sheet of paper in large bold print, type out all personal information, such as address, contact phone numbers and e-mail addresses, date of birth, social security number, insurance information, and religious preferences. Include a list of known illnesses or conditions,

diet restrictions, food and drug allergies, medications, and normal blood pressure. Also place a copy of the individual's living will or health care advance directives in this bag. Be sure to update all of this material each time there is a change in contact information, medications or medical status.

If you do end up in the emergency room (ER), let the person you care for answer the admission questions, if possible. This will give him or her a sense of control and dignity. The sheet you typed can be used as a prompt or simply handed to the admitting clerk. Make sure a copy is included in the hospital chart. ER visits are usually long, so plan on making yourselves as comfortable as possible. Bring along non-perishable snacks for each of you and something to read. Read newspaper or magazine articles aloud to the one you care for. The reassurance of a

familiar voice will have a calming effect. Try to avoid leaving your relative alone in a waiting room, if at all possible. Even individuals who don't usually wander may forget why they are there and decide to leave, or may go looking for you and become lost.

If the hospital stay is planned ahead of time, be prepared for resistance from the one you care for, even if they have agreed to the procedure ahead of time. Instead of merely insisting, "The operation is necessary," or "You have to do this to feel better," give the person a stake in the success of the procedure, a sense that their importance and cooperation are crucial: "Your doctor and I both

need you to help us get through this difficulty." If your relative is fearful and needs reassurance, try to make sure that you or another family member will stay with them and be there when they wake up. A foot or back rub and a hug may also help to calm an anxious patient.

These days, more and more medical procedures can be handled in an outpatient setting, so be sure to ask if day surgery is



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STRANGE NEW WORLD

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a possibility. If not, find out the length of the stay and if there are any tests or X-rays that can be done beforehand to shorten the duration. If consulting physicians will be involved – an anesthesiologist or a heart surgeon, for instance – try contacting them before admission. Make sure they know that your relative has dementia, and ask what to expect before and after treatment, and what side effects or drug interactions might cause increased confusion or memory problems. Ask about recovery time and any special needs such as wound dressing. If post-operative therapy is required, try to arrange it as soon as possible.

Set up a visiting schedule with family members so that the dementia sufferer has companionship as much as possible and so that that you, as primary caregiver, will be able to take breaks.

In the hospital, every intrusion – taking blood, getting shots, and swallowing pills – creates a new opportunity for confusion, fear and agitation. A private room, if available and affordable, will reduce noise and distractions and will make the person you care for calmer. Things taken for granted at home – changing TV channels or going to the bathroom alone – be-

come suddenly more difficult and frustrating. Bring familiar objects – a favorite shawl, photographs or drawings by grandchildren – that recall the serenity of home.

As caregiver, you know this person best. You are the expert. If your mother's dinner arrives under a plastic cover, someone may need to remove the cover and point out the food and utensils. In a sense, it is up to you to "train" the hospital staff to care for this person. Non-medical employees such as custodians and X-ray technicians likely have little experience in dealing with dementia. Helpless, angry, and afraid, the person you care for might lash out, make a racial slur to the woman bringing in a meal or a snide comment about the weight of the man changing a light bulb. You might be able to head off an unpleasant exchange by quietly letting staff know about your family member's dementia. It is also important to identify and encourage sympathetic staff members. Seek out other hospital workers such as patient advocates, social workers, and chaplains, who understand hospital procedures and might offer help or suggestions to make the stay go more smoothly.

To promote awareness among the staff, some caregivers have found it helpful to post a sign on the foot of the bed stating,

for instance, "My husband has Alzheimer's disease." For someone with mild dementia, however, such a sign might be humiliating and shameful. Maintaining dignity is more important in the hospital than almost anywhere else, and you as caregiver are in the best position to ensure that that happens.

The confusion and strangeness of a hospital visit can be nerve-racking and disorienting. But there are other problems to confront. The most serious of these is delirium. Part Two of this article will discuss the hazards of delirium in the hospitalized dementia sufferer as well as considerations to be aware of when the hospital stay is over and the person you care for comes home.



Alzheimer's Association "CareFinder™" Web Tool Can Help Individuals and Families Find Best Care Options

<http://www.alz.org/carefinder/index.asp>

In addition to providing an interactive tool that recommends care options for individuals and generates questions to ask when screening care providers or facilities, CareFinder™ also provides detailed information on a variety of issues surrounding care options, including planning ahead, coordinating care, support and resources.



MEET VIKI HOYT

By Cat Olcott

Viki is the Program Coordinator for the University of Washington Alzheimer's Disease Research Center. As such, she wears many hats – she handles the recruitment line for ADRC clinical studies, helps prepare grants for submission to federal and state agencies, coordinates UW travel needs, handles food and meeting plans, budget reports, VA orders, equipment breakdowns and numerous other “go to” job functions all related to the day-to-day functioning of the ADRC.

Of her typical day she says, “There really is no schedule – I work the front desk and the phones, which means I’m open to everything and everybody. I usually have a plan, but that’s out the window five minutes after I hit my desk! It’s hectic, but I kind of like it that way.”

Of her contributions to the ADRC, probably the one she is most proud of is the ADRC Program Support Fund. This fund is a combination of individual and group donations, including in

some cases memorials from wills and estates in memory of a loved one. These donations benefit new investigators with strong backgrounds in Alzheimer's research, as well as helping purchase scientific equipment used in the Research Center. Donations to this fund help fill the gap in federal and state funding which cannot support the growing need for AD research. Under Viki's care, the Program Support fund has grown from a few donations per month to hundreds, sometimes thousands of dollars per month. “I've put a lot of time and effort into this fund. I am gratified to see that effort paying off. Every day I speak with family members who have lost a loved one to Alzheimer's. It's heartbreaking. I know the Program Support Fund is helping find a cure.”

Viki began working for the ADRC half-time in 2000, and became full-time within six months. “I was somewhat intimidated initially; all these doctors – I thought they'd have no sense of humor. I couldn't have been more off base. I work with a great group of people...funny, smart, and a little bit insane. They are so dedicated to their patients and to their work.”

Before joining the UW, Viki

dabbled in numerous professions – five years as a restaurant manager, a year cooking on a crab boat in Dutch Harbor, Alaska, work as a landscaper, and as a waitress at Duke's restaurant. Viki was a freelance journalist with the Eastside Journal newspaper; her beat was human interest and she covered stories from Bosnia to breast cancer. Writing has always been her passion. She graduated with a double BA in Communications-Journalism and Speech Communication from the UW.

Away from the office Viki spends lots of time in the large garden she started from a blackberry patch dug out by shovel. She also enjoys music (from opera to hip-hop), camping, drawing, traveling and spending time with her boyfriend.

Currently, she is in the process of an impromptu remodel, having been “homeless” since the big flood of November 6, 2006, living out of a suitcase with friends and family. “FEMA has suddenly “discovered” me; I'm their current poster child, but the last three months were hell. I'm looking forward to some alone time—that's what I really miss, that and being reunited with my large Siamese cat, Frank.” ♦

UW Alzheimer's Disease Research Center Program Support Fund

For more information please contact: Victoria Hoyt, ADRC Program Coordinator at 206-764-2749 or toll-free at 1-800-329-8387, Ext. 6-2749.

Email: victoria.hoyt@va.gov

Checks should be made out to ADRC and addressed to:

APSHCS (S-116 6E) Attn: Viki Hoyt
1660 S. Columbian Way - Seattle, WA 98108

If next of kin notification is requested, simply provide that contact information.

Current Clinical Trials

University of Washington Alzheimer's Disease Research Center

To enroll in any of the following studies, call 1-800-317-5382 or 206-764-2069. All studies open to the public.

STUDY SUBJECT	DESCRIPTION	CANDIDATE CRITERIA	TIME / PROCEDURE
Dietary Antioxidant Supplements for the Treatment of Alzheimer's Disease	Evaluates a combination of antioxidants compared to placebo to see if they are safe and cause positive changes in the levels of certain proteins in the body.	Diagnosis of probable Alzheimer's, living at home with a caregiver. Must be age 60 to 85. May be taking other Alzheimer's medications.	5 months long with 3 visits to the research center in Seattle and two phone calls.
Prazosin for the Treatment of Difficult Behaviors in Alzheimer's Disease	Evaluates usefulness of prazosin compared to placebo in treating agitation, uncooperativeness, pacing & other difficult behaviors.	Diagnosis of probable or possible Alzheimer's. Living at home with a caregiver. May be taking other medications.	10 weeks long – includes two visits to the research center and 7 phone interviews.
Genetics, Stress Hormones and Memory	Evaluates relationship among high levels of stress hormone cortisol, the type of protein (APOE) a person carries, and decline in memory.	Middle aged and older without memory problems or with mild memory problems or people with Alzheimer's. Must be living at home or in an assisted living facility.	2-8 visits to the research center over 5 years. Participants receive memory testing and have two lumbar punctures.

University of Washington and the Veteran's Administration Healthcare System

Memory Wellness Program

To enroll in any of these studies please call Seattle 206-764-2809 or Tacoma 253-583-2033

STUDY SUBJECT	DESCRIPTION	CANDIDATE CRITERIA	TIME / PROCEDURE
PACE- the Puget Sound Cognition and Exercise Study	Determine whether physical activity will improve memory and cognitive thinking abilities in older adults.	Healthy individuals age 55 years and older with and without memory problems.	Six months of either aerobic exercise or stretching exercise.
RECALL- Rosiglitazone Effects on Cognitive Abilities in Later Life	Effectiveness of rosiglitazone (an oral diabetic medication) in improving memory in older adults with mild memory impairment.	Healthy individuals age 55 years and older with mild cognitive impairment (MCI).	20 months, during which the participant will be asked to make 12 visits to the clinic.
SNIFF- Spray Nasal Insulin to Fight Forgetfulness	Looks at the beneficial effects of a nasal spray on memory for older adults with memory loss.	Healthy individuals age 55 years and older with mild cognitive impairment (MCI) or early Alzheimer's.	4 months during which the participant will be asked to make 8 visits to the clinic.
TRIM- Triglycerides and Insulin in Memory	Explores the influence of increased dietary fat on glucose and insulin metabolism, memory and biological markers associated with Alzheimer's.	Healthy individuals age 55 years and older with and without memory problems.	6 visits to the clinic in which each visit is between 2-6 weeks apart.

PARTICIPATING IN A CLINICAL TRIAL



Choosing to participate in a clinical trial is an important personal decision.

It is often helpful to talk to a physician, family members, or friends about deciding to join a trial. After identifying some trial options, the next step is to contact the study research staff and ask questions about specific trials.

A clinical trial (also clinical research) is a research study in human volunteers to answer specific health questions. Carefully conducted clinical trials are the fastest and safest way to find treatments that work in people and ways to improve health. Interventional trials determine whether experimental treatments or new ways of using known therapies are safe and effective under controlled environments. Observational trials address health issues in large groups of people or populations in natural settings.

Participants in clinical trials can play a more active role in their own health care, gain access to new research treatments before they are widely available, and help others by contributing to medical research.

Excerpted from "An Introduction of Clinical Trials." National Institutes of Health: <http://clinicaltrials.gov/ct/info/whatis#whatis>

More information is available from ADEAR (Alzheimer's Disease Education & Referral Center): <http://www.nia.nih.gov/Alzheimers/ResearchInformation/ClinicalTrials/> or by phone at 1-800-438-4380.

Alzheimer's Q & A: EARLY-STAGE RESOURCES

By Rebecca Logsdon, PhD

Question:

My father was recently diagnosed with Alzheimer's disease. Are there any resources for people who are newly diagnosed?



Answer:

One of the best local resources for education is the Alzheimer's Association Western & Central Washington State Chapter. A telephone helpline is accessible around the clock and provides information and assistance to individuals in any stage of Alzheimer's disease and to their caregivers. The Alzheimer's Association also provides early-stage memory loss services throughout Western Washington. These programs are led by trained facilitators and offer education and support to individuals who are in the early stages of Alzheimer's or dementia, and to their loved ones who care for them. The seminars provide information and education, group discussion and guest speakers on medical causes, treatment, and future planning.

To reach the Alzheimer's Association Helpline or to learn more about Early-Stage Memory Loss Services call 206-363-5500 or toll free at 1-800-848-7097.

Your father might also be interested in learning about the latest research on Alzheimer's disease. Our UW ADRC website (<http://depts.washington.edu/adrcweb/>) provides information about local research, and the Alzheimer's Disease Education and Referral website (<http://www.nia.nih.gov/Alzheimers/>) provides information about AD and national research. ♦

Alzheimer's Disease Research Center, University of Washington and VA Puget Sound Health Care System

For further information, please contact Ellen Steinbart, RN at 206-764-2112 or toll free 800-745-4511

Genetic Studies of Dementia

The Genetics Program of the Alzheimer's Disease Research Center at the University of Washington and the VA Puget Sound Health Care System is studying the role of genetics in dementia. It seeks to identify the genes responsible for various forms of dementia.

Families are being sought with two or more living affected individuals. Participation could involve an interview, examination, review of medical records and a blood sample.

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More details to come in the Spring Issue of Dimensions.

For additional information call Cat Olcott at 1-206-221-6563.

Sponsored by the University of Washington Alzheimer's Disease Research Center, Friends of Alzheimer's Research, The Western Washington Chapter of the Alzheimer's Association, The Alzheimer Society of Washington, and the UW School of Nursing's de Tornay Center for Healthy Aging. The University of Washington is committed to providing access, equal opportunity and reasonable accommodation in its services, programs, activities, education and employment for individuals with disabilities. To request disability accommodation contact the Disability Services Office at least ten days in advance at: 206.543.6450/V, 206.543.6452/TTY, 206.685.7264 (FAX), or e-mail at dso@u.washington.edu

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