

### FOCUS ON RESEARCH

## From Research Labs to Possible Treatments for Alzheimer's Disease



Research Biologist Brian Kraemer, PhD

**By Kirsten Rohde**

When people think of medical research, they often imagine scientists in lab coats peering at petri dishes through microscopes. Yet what generally makes news about Alzheimer's disease (AD) are the studies conducted with human participants, the clinical trials of promising new drug treatments. Both are important aspects of research and both can ultimately lead to the development of new treatments or even a cure for AD.

But what is going on in those labs? How does laboratory research lead to treatments for AD?

One laboratory at the University of Washington Alzheimer's Disease Research Center (UW ADRC) is looking at an organism very differ-

ent from humans: a worm known as *C. elegans*. This round worm is less than one tenth of an inch long. It is barely visible to the naked eye, and its natural habitat is often the compost pile. Yet this tiny worm has about sixty percent of the same genetic material as humans, and that's the start of the story about how laboratory research might eventually lead to new treatments for dementia.

To find out more, I met with Brian Kraemer, PhD, a UW ADRC research biologist at the VA Puget Sound Health Care System (VAPSHCS) and Research Assistant Professor at the UW. Dr. Kraemer leads a research group focusing on the most fundamental causes of neurodegeneration in AD and related disorders. His research program is funded by three grants, one of which is from the Western and Cen-

tral Washington State chapter of the Alzheimer's Association.

Dr. Kraemer first became interested in research on disorders of the nervous system when he was doing graduate work. He came to Seattle to work with Gerard Schellenberg, PhD, a geneticist affiliated with the UW-ADRC for many years. Dr. Kraemer wanted to focus his research work in the area of human neurodegenerative diseases, both because of his professional interest and for personal reasons—some members of his family have had Alzheimer's disease.

"When I came to the Schellenberg lab," he explains, "like most post-doctoral students, I focused on a number of different research areas. One of them was working to set up a model for using *C. Elegans* to study the tau pathology that causes

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# Alzheimer's Disease Research Center

University of Washington

Veterans Affairs Puget Sound Health Care System

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The Alzheimer's Disease Research Center (ADRC) is enrolling research participants in several new investigational treatment studies. **Finding treatments that actually change the disease process in the body is the focus of this new research.** Currently the only available prescriptions for the treatment of Alzheimer's disease are medications that are mostly aimed at helping with the symptoms of Alzheimer's disease such as memory loss and trouble thinking.

**These new studies are aimed at both treatment and prevention. Persons without memory loss, with mild memory loss or with Alzheimer's disease may be eligible.**

**Research participation will not cost you anything, and is open to all members of the public.**

Some research participants will receive a placebo (a treatment without active medication) for at least some portion of the research.

To participate, individuals must:

Have a diagnosis of mild to moderate Alzheimer's disease *OR*  
Have mild memory loss *OR*  
Have no memory problems

*and*

- Be age 50 or older
- Be living at home (one study will allow residents of assisted living centers to participate.)
- For people with memory loss, have a companion who can accompany the participant to all research visits

All research visits occur at the Alzheimer's Disease Research Center in Seattle.

**For more information, please call the UW Alzheimer's Disease Research Center at:**

**206 764-2069**  
**1-800 317-5382**

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neurofibrillary tangles in the brain neurons of people with AD. This research took off and became the focus of my current work.”

Research into the causes of AD and other dementias begins by looking at what is going wrong in the brain tissue of affected people. The brains of people with AD have two types of distinctive changes: the development of neurofibrillary tangles, which are twisted strands of a protein called tau that is found inside brain cells (neurons), and senile plaques, which are complex deposits of amyloid and other proteins in the brain but outside of the neurons. The research conducted in laboratories such as Dr. Kraemer’s is research that occurs at the level of DNA and the proteins within cells. This type of research works to recreate those AD-related changes to neurons seen in humans so that experiments leading to possible treatments can be conducted. Researchers do this by using simpler organisms that can be studied more quickly and in larger numbers than research with human participants.

*C. elegans* has the experimental advantage of being a very simple organism: they reproduce quickly, with a new generation about every three days, and you can see inside of them while they are still alive. Moreover, there are only 302 neurons in the adult *C. elegans*, whereas the number of neurons in humans is estimated to be as many as one hundred billion. In contrast to mice or humans, the nervous system of *C. elegans* has been completely mapped out.

Dr. Kraemer explains that “we take the human tau gene that has a dementia-causing mutation in it and put it into the worms so that the

worms ‘express’ the human tau in their neurons. In other words, we create a situation where we can see what happens if they have the same abnormal tau in their nerve cells as do humans with AD. When we do this, the neurons stop functioning normally, which in a worm shows up as problems with moving—they become slowed down and uncoordinated. When we look biochemically at the worms, we also see some other changes that are similar to what we know happens in the brain cells of humans with dementia.”

Using this model, it then becomes possible to experiment with ways to make the worms well again. One way that Dr. Kraemer and his staff approach this is by deleting genes and then searching for worms that appear to be resistant to the ill effects of the mutated tau that has been placed in them. In other words, watching under a microscope to see if the worms start moving normally. This allows the researchers to identify particular genes that when deleted from the worms (“knocked out”) allow the worms to remain unaffected by the toxic effects of the tau mutation. Dr. Kraemer and his staff have found two such genes, and one of them has a related gene in humans (mammalian SUT-2). The theory is that this gene may prevent the breaking down of abnormal proteins and may thus allow further damage to occur to the nervous system.

The next phase of Dr. Kraemer’s research is the area of study that is funded by the Alzheimer’s Association local chapter. “We’ve taken a collection of drugs that are not patented anymore, drugs that have already been tested and approved for humans for all sorts of medical conditions,” he explains, “And we’re looking to find a drug that makes the worms better. So we will system-

atically test every one of about 1,100 drugs in the worms and then, by observing them under the microscope, we will see if they get better. If so, we can narrow our search and focus on the drugs that show improvement in the worms. Our ultimate goal is to find drugs that prevent tau pathology and may lead to the development of a treatment for tau pathology (that is, neurofibrillary tangles), in AD.”

In talking with Dr. Kraemer and in having a chance to look at these little worms under a microscope, I became aware of how much time and effort goes into the search for possible treatments, even at this earliest phase of developing a model in worms and then trying to find out more about the genetics. With the support from the Alzheimer’s Association grant, Dr. Kraemer and his colleagues can now take the next step and search for possible drugs that may make a difference in worms. A drug discovery in the worms could then be applied to higher animals, and eventually to people who suffer from AD. Kraemer is appreciative of the enthusiasm and support of the Alzheimer’s Association for his research—“If this research were to pan out,” he says, “It would be fantastic.”

**Dr. Kraemer’s research program is currently funded by three grants:**

Alzheimer’s Association: “Pharmacological Inhibitors of Tau Neurotoxicity.”

VA Merit Review: “SUT-2, a Conserved Regulator of Tau Neurotoxicity.”

National Institutes on Health, ROI: “Developing Neuroprotective Strategies for Proteinopathy: A Comparative Modeling Approach.”

## Meet Taylene Watson, MSW

By Kirsten Rohde

Taylene Watson, LICSW, ACSW, is Director of Social Work at the Veterans Affairs Puget Sound Health Care System (VAPSHCS) in Seattle and a new member of the Alzheimer's Disease Research Center (ADRC) Education Core. We are honored to have Ms. Watson join us as we work to increase awareness about research, particularly in the African-American community.

It is easy to recognize Ms. Watson's commitment to the profession of social work and to working with the family caregivers of ill veterans in particular. Ms. Watson currently oversees the professional practice of about 140 social workers in the VA at Seattle and American Lake. She has worked in the VA system since 1971, addressing the social work needs of veterans in the areas of psychiatry, mental health, community residential care, medicine, surgery, primary care, and geriatric care. She also holds an appointment at the University of Washington (UW) as Clinical Associate Professor, and as part of her work there, she coordinates a training program for social work interns. In recognition of this work, the VA Social Work Department received an Outstanding Practicum Agency for the UW School of Social Work award. Among many other honors, Ms. Watson received the National VA Social Worker of the Year award in 2006.

When speaking of her years of work as a social worker, Ms. Watson describes her growing interest and concern for caregivers, "My professional passion for caregiving began when I realized how important it was to support caregivers. In 1982, I worked with veterans with PTSD

in Minneapolis, and we ran a support group for the wives and family members of these veterans. Then, in 1985, I began working in the geriatric clinic and primary care clinic at the Seattle VA; I worked with many veterans who were dealing with dementia or other illnesses. As I worked there, I realized how critical the caregivers were to maintaining the veterans' independence.



At the same time, I was the personal caregiver for my mom. I took care of her for about thirty years, and during the last three to four years she began to show severe signs of dementia."

Because of these experiences, in 1988, Ms. Watson and a colleague decided to create a caregivers conference at the VA. They put the conference together "on a shoestring" budget and had about eighty attendees, including family caregivers of veterans and medical center staff who were caregivers. This year, they will be holding the twenty-first year of the caregiver conference at the Seattle VA and the eighth year of the conference at the American Lake VA.

Ms. Watson believes that the importance of caregivers to patients is starting to catch on across the country, "I think the nation is starting to pay attention to the need to provide support and resources for caregivers," she says. "For example, there are now legislative proposals to increase the number of days of respite to which a caregiver is entitled. In my own case, I was able to provide a paid caregiver for my mom, so I could go to work. Yet I still got up early every day to give her a bath and make her breakfast before getting ready myself to go to work. It was important to me to make things OK for her. Many caregivers don't have the resources or don't know about ways to get help to do all that is needed. And being a personal caregiver just increased my knowledge about how people must cope with an illness like dementia. I'm amazed at what caregivers do and how they do it. But I know that some caregivers delay getting the help they need, and I know they even put off attending to their own medical needs while they provide care 24/7."

This year, Ms. Watson will join the ADRC team to assist us in our outreach to the African-American community. She will serve on the ADRC Minority Advisory Board, which will provide advice, guidance, and liaison services as we work to increase awareness of research opportunities. "I'm very excited that the ADRC is reaching out and that they asked me to be a part of this effort," she says. "I was lucky as a family caregiver because due to my professional experience I knew about resources and the advances in research. I think there are a lot of folks in the community who are just not aware of what is available. Culturally you just do it—you take care of your family, and you often do so without help, because it's just the right thing to do. I think

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the good thing about the new ADRC grant and the creation of this advisory board is that it will help spread the word to the minority community that there are additional sources of information and support.”

It’s easy to see that Ms. Watson will be a strong advocate for the role of social work on this outreach project. She speaks highly of the many ways that social workers can help increase awareness. She is this region’s Point of Contact for the national Veterans Caregivers Advisory Committee and has just been elected president of the Washington State Chapter of the National Association of Social Workers. She explains that “social work involvement in the community outreach project of the ADRC is critical. The social work staff at the VA has grown tremendously over the years. Social workers can now provide a wide scope of services, and we always bring the reminder that for every individual living with dementia there is a ‘family’ providing care and support, and this family may in turn need our help and support.”

We are very excited to have such an energetic advocate working with us in the ADRC. Ms. Watson will be joined on the ADRC Minority Advisory Board by Patricia Hunter (Chair), Clifford Holland, Lemanual “Lee” Jones, and Rowena Rye. We are honored by the commitment of these leaders to enable the African American community to participate fully in Alzheimer’s disease research. As we were concluding our conversation, Ms. Watson added, “I know I will retire some day, but I doubt I will ever lose the passion for helping people and their need to navigate difficult systems.”



ADRC team walkers pictured here are (l-r): Nancy Brown, Kathleen McCraw, Sarith Keo

### ADRC Team Participates in the 2009 Seattle Memory Walk

*Under the enthusiastic direction of Sarith Keo, our team captain, the Alzheimer’s Disease Research Center Memory Walk team joined 2000 other walkers at the Seattle Center on Saturday, September 12th. The weather was glorious and our team raised a total of \$2,405 for the Alzheimer’s Association. Thank you to all our family mem-*

*bers, co-workers, and friends who contributed to our team’s fundraising effort.*

*Overall over \$300,000 was raised at this wonderful annual event organized by the Western and Central Washington Chapter of the Alzheimer’s Association. If you missed it this year get ready for next fall when the chapter will again organize Memory Walks throughout the Puget Sound region. The website for the local chapter is: [www.alz.org/alzwa/](http://www.alz.org/alzwa/)*

## Would you prefer to receive *Dimensions* by email?

**If you would like to receive this newsletter by email in the future, please send your email address to: [Susan.Martin@va.gov](mailto:Susan.Martin@va.gov)**

Please put “*Dimensions* email list” in the subject line and put your name as it appears on this issue’s mailing label in

the body of the message so we can take you off the list for receiving a paper copy.

We will send future newsletters to you by email in a pdf file format. Also all issues of *Dimensions* are available at our website: [www.uwadrc.org](http://www.uwadrc.org)

# Our Common Challenge: Finding New Treatments for Alzheimer's disease

Join us for an informative and engaging evening sponsored by the **UW Alzheimer's Disease Research Center (ADRC)** and the **alzheimer's association**. You will meet ADRC researchers, **alzheimer's association** staff, as well as individuals and families who have participated in research studies. *This forum is free-of-charge.*

## When and Where

Thursday, November 19, 2009

7:00 PM – 9:00 PM

University Place Presbyterian Church

8101 27th Street West, University Place, WA 98466

**To RSVP, contact:** Linda Whiteside, **alzheimer's association**,  
800.848.7097, ext. 237



## Who should attend?

Family Caregivers, their families and friends, those with Early Memory Loss or Young-Onset, Students, Professionals, Support Group Facilitators, and the General Public



## What to expect at this research forum

Our panel will provide information about how research helps advance our common goals of prevention, treatment and support for those affected by Alzheimer's disease.



You will also hear what it is like to participate in a research study. There will be plenty of time for questions from the audience.

*Light refreshments will be served.*

At the **University of Washington ADRC** our main priority is to find the causes and treatments for Alzheimer's disease and related dementias. We believe this knowledge offers the best hope for prevention, symptom management, and a cure. Research volunteers make the difference in successful research and often find hope in the process of contributing to the effort.



At the **alzheimer's association** our vision is a world without Alzheimer's. Our mission is to eliminate Alzheimer's disease through the advancement of research; to provide and enhance care and support for all affected; and to reduce the risk of dementia through the promotion of brain health.

**alzheimer's association**

Western & Central Washington State Chapter



## IN THE NEWS

### **DHA in Alzheimer's Disease and Age-Related Cognitive Decline**

*Excerpted from the original article by Dr. Michael Rafii in the Alzheimer's Disease Cooperative Study (ADCS) newsletter, September 2009.*

During the Alzheimer's Association's July 2009 International Conference on Alzheimer's Disease (AD) in Vienna, researchers presented results from large studies of DHA (docosahexaenoic acid), an omega-3 fatty acid found in fatty fish such as salmon and mackerel. DHA is naturally found in the body in small amounts and is the most abundant omega-3 fatty acid in the brain. Previous animal studies and epidemiology studies in humans suggested that DHA might be beneficial in people with AD.

The main study was conducted by the Alzheimer's Disease Cooperative Study, a fifty-six site clinical-trial consortium supported by the National Institute on Aging. The UW ADRC participated in this study. Persons with mild to moderate Alzheimer's disease were enrolled in an eighteen-month study comparing DHA and placebo.

According to the researchers, treatment with DHA clearly increased blood levels of DHA, and it also increased the levels of DHA in study participants' cerebrospinal fluid which suggested an increase in the brain levels of DHA. However, overall, DHA treatment did not slow the rate of change on tests of mental function; although it appeared that study participants without the APOE-ε4 gene who received DHA had a slower rate of decline on some tests of mental function.

The lead researcher for this study, Joseph Quinn, MD, at Oregon Health and Science University, said, "These trial results do not support the routine use of DHA for patients with Alzheimer's."

"This study—and other recent Alzheimer's therapy trials—raise the possibility that treatments for Alzheimer's must be given very early in the disease for them to be truly effective," said William Thies, PhD, the Chief Medical and Scientific Officer at the Alzheimer's Association. "For that to happen, we need to get much better at early detection and diagnosis of Alzheimer's, in order to test therapies at earlier stages of the disease and enable earlier intervention."

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

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



[www.uwadrc.org](http://www.uwadrc.org)

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*Dimensions* is published by the University of Washington Alzheimer's Disease Research Center.

The ADRC is affiliated with the University of Washington and the Veterans Affairs Puget Sound Health Care System. The UW ADRC is funded by the National Institute on Aging and is supported by

the Friends of Alzheimer's Disease Research, the Alzheimer's Association, and members of the public.

The UW ADRC Support Fund is used to help support new junior faculty researchers with strong credentials in the field of Alzheimer's disease and also to provide direct support for ongoing re-

search projects of the ADRC. Community support of the ADRC's mission is a valued contribution to the quest to find the causes of and treatments for Alzheimer's disease and related disorders.

*For more information regarding the Alzheimer's Disease Research Center Program Support Fund, please contact Susan Martin, ADRC, Program Coordinator, at 206-764-2702, or toll-free at 1-800-329-8387, ext. 6-2702 or by email at [susan.martin@va.gov](mailto:susan.martin@va.gov).*

*Checks should be made out to ADRC and addressed to: VAPSHCS (S-116 6-East), Attn: Susan Martin, 1660 S. Columbian Way, Seattle, WA 98108.*

# DIMENSIONS

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The University of Washington Alzheimer's Disease Research Center (UW ADRC) has been funded by the National Institute on Aging since 1985 to facilitate cutting-edge research on causes and treatments of Alzheimer's disease (AD) and related dementias. In particular, the UW ADRC focuses on research that will enhance the clinical care of patients with AD and their caregivers and make treatment studies broadly available. The ADRC also provides community and professional education about AD and other forms of dementia.

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[www.uwadrc.org](http://www.uwadrc.org)

## See Inside For

**ADRC new clinical treatment trials** *see page 7*

**Upcoming event:  
Our Common Challenge:  
Finding new treatments  
for Alzheimer's disease  
November 19th in Tacoma,  
WA** *see page 6 for details*