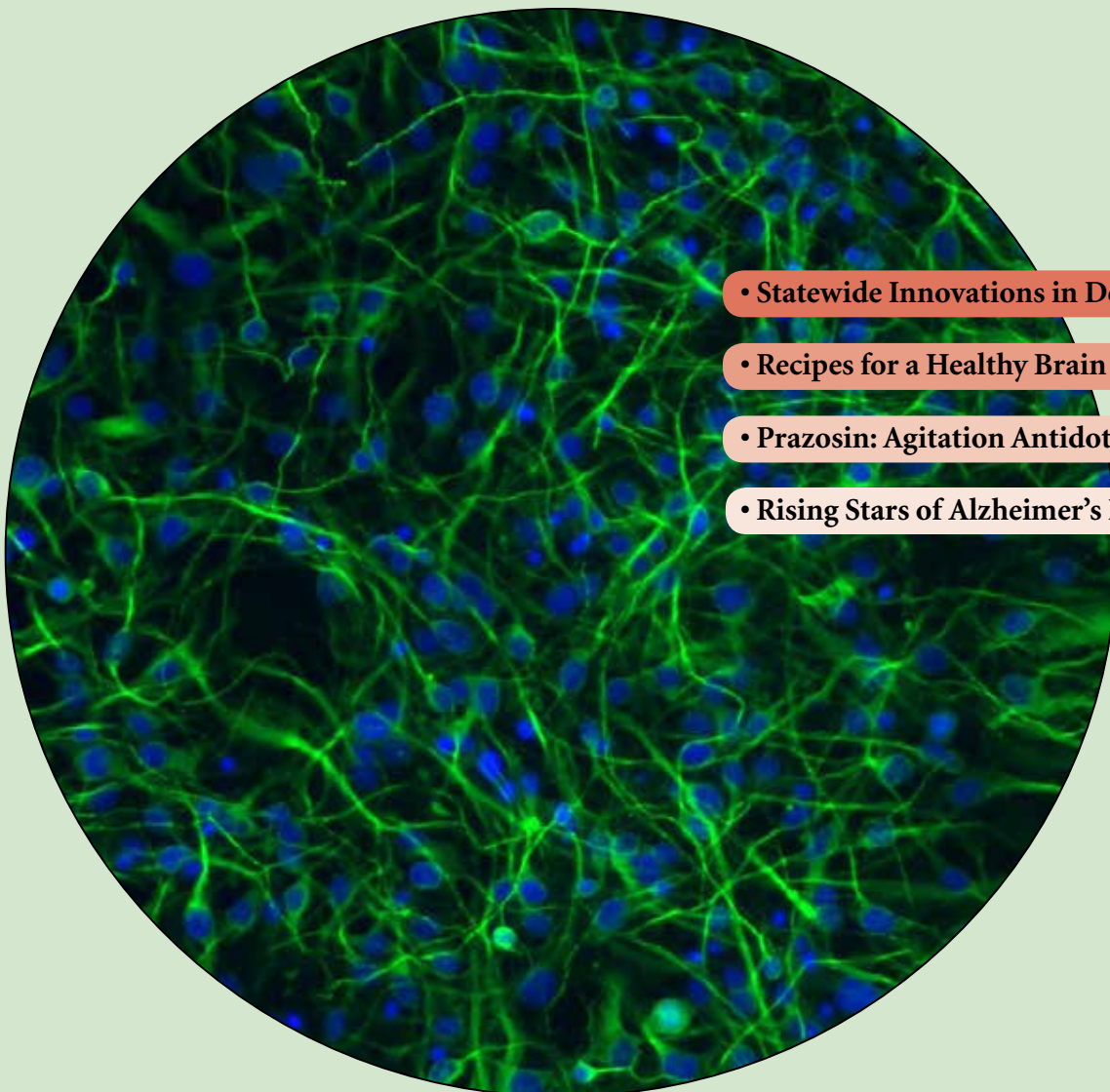


DIMENSIONS

The Newsletter of the University of Washington Alzheimer's Disease Research Center
Winter 2017

PRESTO CHANGE-O! NEURONS IN A DISH

HOW STEM CELL TECHNOLOGY WILL IMPROVE THE SEARCH FOR THERAPEUTICS



• **Statewide Innovations in Dementia Policy**

• **Recipes for a Healthy Brain**

• **Prazosin: Agitation Antidote**

• **Rising Stars of Alzheimer's Research**

WINTER 2017

Hello readers!

As we launch into a New Year, we bring you these reflections on UW ADRC happenings from 2016. We continue our focus on advancing Precision Medicine for Alzheimer's disease and related disorders that lead to dementia. As detailed in the following pages, our scientific work ranges from cultivating brain cells in a Petri dish, to measuring the air quality in neighborhoods around King County. In 2017, we are shifting our underserved outreach focus to American Indian and Alaska Native populations through collaboration with Partnerships for Native Health. We are proud to participate in efforts to foster dementia-friendly communities and to help enact a state plan to bolster services for all individuals and families affected by dementia.

Of course, none of this work could take place without your generous support. We are especially thankful for funding from the NIH as well as the Ellison Foundation. Whether you have participated in a research study, accompanied a loved one to our memory clinic, or contributed philanthropically, we are so grateful for your support of and interest in our work at UW. Each of you has helped to spread the word about the ongoing need for furthering research and improving care for Alzheimer's disease. Happy reading!



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DIMENSIONS The University of Washington Alzheimer's Disease Research Center (UW ADRC) is affiliated with the UW Medicine Memory and Brain Wellness Center (MBWC) and the Veterans Affairs Puget Sound Health Care System (VA). The UW ADRC has been funded by the National Institute on Aging since 1985 to facilitate cutting-edge research on Alzheimer's disease and other neurodegenerative conditions that cause dementia. The UW ADRC focuses on Alzheimer's disease biomarker research and advancing prevention methods and clinical treatment for dementia, particularly through precision medicine. The UW ADRC is also supported by the Friends of Alzheimer's Research, the Ellison Foundation, and members of the public.

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Featured Publications of 2016

Our ADRC researchers are often busy doing research, writing up their results, and publishing them in scientific journals. We've highlighted some papers that we think you will find interesting.

Precision Medicine

Precision Medicine: Clarity for the Complexity of Dementia // **Eric Larson, C. Dirk Keene, Paul Crane, Thomas Grabowski**

The aim of the current ADRC is a precision medicine approach to Alzheimer disease. There are three aspects of precision medicine: comprehensive risk assessment, early detection of disease processes, and molecularly tailored treatments. This paper lays out a strategy for optimal targeting and timing of efforts to prevent, stop, or slow the progression of neurodegenerative diseases.

Rapamycin in aging and disease: maximizing efficacy while minimizing side effects // **Matt Kaeberlein**

So much needs to happen before a clinical trial of a promising compound can start! Experimental geroscience has identified the compound rapamycin as a top candidate for promoting healthy aging and longevity in mammals. This paper maps the work ahead to find the optimal dosage regimen, delivery route, and targeted formulation to allow for benefits to be maximized while reducing side effects.

Seed-competent high-molecular-weight tau species accumulates in the cerebrospinal fluid of Alzheimer's disease mouse model and human patients // **Elaine Peskind, Murray Raskind, Gail Li**

In this analysis, the researchers found that one form of tau protein in the spinal fluid of Alzheimer disease patients shows a unique pattern. Researchers can now use this finding to guide the development of biomarkers for better diagnosis and to track disease progression in clinical trials.

Effects of Traumatic Brain Injury

Association of Traumatic Brain Injury With Late-Life Neurodegenerative Conditions and Neuropathologic Findings // **Paul Crane, C. Dirk Keene, Eric Larson, Laura Gibbons**

Want the good news, or the bad news? This huge, multi-center study found no link between a serious head injury and later life Alzheimer's-type dementia risk, but it did find a three-fold elevated risk for Parkinson's disease. The study linked a serious head injury before age 25 to Parkinson's disease risk at least 40 years later.

The first NINDS/NIBIB consensus meeting to define neuropathological criteria for the diagnosis of chronic traumatic encephalopathy // **C. Dirk Keene**

Chronic traumatic encephalopathy (CTE) is a disease caused by multiple, severe head injuries. The ADRC's C. Dirk Keene helped a national team to establish criteria for detecting and defining CTE in the brain, which will help to clarify how many athletes develop the condition and, thus, the true implications for sports.

Repetitive blast exposure causes specific long-term functional and structural abnormalities in mice and military Veterans // **Brian Kraemer, Elaine Peskind, David Cook**

Blasts from explosives are known to cause mild traumatic brain injury (mTBI) in combat veterans. In brain scans from veterans, the ADRC team found that the cerebellum — the brain area critical for coordinating movement and some cognitive and emotional skills — is particularly vulnerable to blasts. The findings could lead to studies into ways to prevent and treat mTBI, and related emotional difficulties. About 500,000 members of the U.S. military have been diagnosed with mTBIs.

Genetic Research

Family-based genome scan for age at onset of late-onset Alzheimer's disease in whole exome sequencing data // **Ellen Wijsman**

This study linked seven genes to Alzheimer's disease biology. ADRC researchers can now refine their understanding of how and why this disease develops in old age. These genetic discoveries also help the research community to identify biological targets for therapeutics.

Assessment of the genetic variance of late-onset Alzheimer's disease // **Paul Crane, Joey Mukherjee**

In this multi-site project investigating genetic architecture of Alzheimer's disease, about half of the risk for Alzheimer's disease in late life appears to be linked to genetics. Much of the genetic predictors have already been discovered, but there is a sizable amount still to be identified, justifying the search for further genetic hotspots.

Unusually long duration and delayed penetrance in a family with FTD and mutation in MAPT (V337M) // **Kimiko Domoto-Reilly, Tom Bird, C. Dirk Keene**

The ADRC is grateful to the families who participate in our research projects, especially those who carry rare genetic mutations that cause a neurodegenerative disease. This study reports on family members who show different ages of disease onset and symptom presentation, even though they carry the exact same mutation. The authors highlight the difficulties of genetic counseling on these issues. They hope to discover the genetic and environmental factors influencing the age of onset and disease course.

Population Research

Cranial Magnetic Resonance Imaging in Elderly American Indians: Design, Methods, and Implementation of the Cerebrovascular Disease and Its Consequences in American Indians Study // **Lonnie Nelson, Tara Madhyastha, Thomas Grabowski, Dedra Buchwald**

Little is known about Alzheimer's disease and dementia in American Indian populations. Therefore, in collaboration with Partnerships for Native Health (P4NH), the ADRC's Satellite Core is working to characterize the burden, risk factors, and manifestations of brain injury identified on MRI brain scans. In this study, the investigators recruited surviving members of a 20-year longitudinal cohort of aging American Indians from 11 American Indian communities and tribes. This research offers an unparalleled opportunity to assess Alzheimer's disease in an understudied group of rural participants. These efforts will contribute to an accurate understanding of disease in these communities, setting the stage for improved detection, treatment, and prevention for this disease.

Two novel loci, COBL and SLC10A2, for Alzheimer's disease in African Americans // **Paul Crane, Eric Larson**

Will personalized medicine be for everyone? The vast majority of genetic sequencing research has been conducted in Caucasian subjects of European descent. However, DNA varies between ethnic groups. The lack of information about the genetic variations could limit opportunities for quality genetic counseling and targeted treatment. This research study identified genetic risk factors for Alzheimer's disease in African Americans, expanding the knowledge needed to create precision medicine for a diverse population.

Presto-Change-o! Neurons in A Dish

Human-derived stem cell technology promises to accelerate the search for Alzheimer's disease therapeutics. Come travel to the edge of a scientific frontier with a writer who literally has some skin in the game.

By Genevieve Wanucha

Whenever I catch sight of the small pockmark on the inside of my left arm, I remember: In 2013, I donated a skin biopsy to research. The cells I had removed are still alive, but they're no longer skin cells. They are now brain cells. Billions of my neurons grow on Petri dishes, housed in incubators in brain research labs across the country.

First, the researchers dropped my cells into a dish of nutrient-rich broth and let them grow for a few days. Then, using a Nobel Prize-winning genetic engineering technique, they reprogrammed my skin cells into stem cells. These cells, called human induced pluripotent stem cells (iPSCs), have the ability to replicate themselves and grow into any other type of human cell.

Even its practitioners in the lab say that the cellular transformation that follows seems like "part magic." A dose of chemical growth factors instructed my stem cells to take a specific pathway of development: they sprouted branching dendrites and axons, formed synaptic connections, and sent electrical signals to their neighbors. Presto-change-o! They had differentiated into working neurons.

So what do researchers do with such a boundless supply of neurons? As the science writer here at the UW ADRC, I've learned that the application of iPSCs technology to neurons has recently become a powerful tool to study the causes of Alzheimer's disease and improve the search for effective treatments.

A New Frontier in Alzheimer's Research

Most cases of Alzheimer's disease-type dementia result from a mix of genetic, environmental and lifestyle factors. Overall, people over 65 have a 10 percent risk of developing symptoms. That level of

risk varies in subtle ways across individuals. Consider that about 20 gene variants are known to confer low levels of increased risk for Alzheimer's disease, while others endow resilience.

These variants do not cause disease on their own; rather they make it more or less likely to occur, in the context of life influences. Importantly, this variability means that every person may respond to therapies and interventions differently.

This human complexity also makes it difficult to study the mechanisms of Alzheimer's disease in model organisms. Mice and worms bred to carry rare genetic mutations have revealed a lot about the mechanisms of the rare forms of Alzheimer's disease that run in families. But because sporadic (un-inherited) Alzheimer's disease in humans lacks a very strong genetic component, researchers can't make a transgenic mouse model.

"There has been an astounding lack of research models for the most common form of Alzheimer's disease, which currently affects 5 million Americans," says Dr. Jessica Young, Assistant Professor of Pathology, UW Medicine, who has brought iPSCs into the UW ADRC. "I hope our work with iPSCs can change that situation, as the method allows us to investigate the disease directly in a person's living tissue."

In Young's lab, based at the UW Institute for Stem Cell and Regenerative Medicine (ISCRM), a storage unit contains shelves of Petri dishes full of microscopic cells, sustained at 98.6° in a pink liquid of sugar and amino acids. Her team is generating iPSCs-derived neurons from people with and without symptoms of Alzheimer's.



Dr. Jessica Young

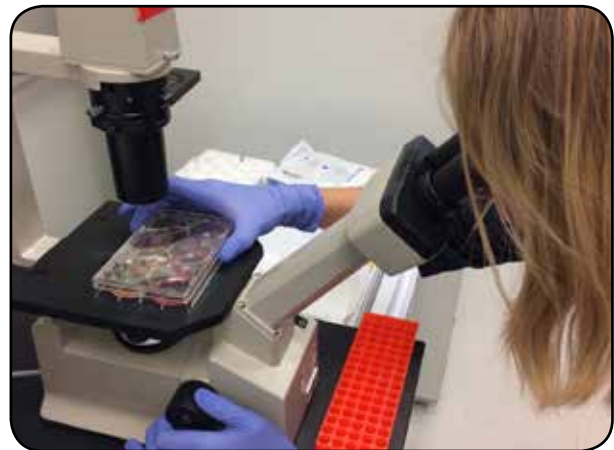
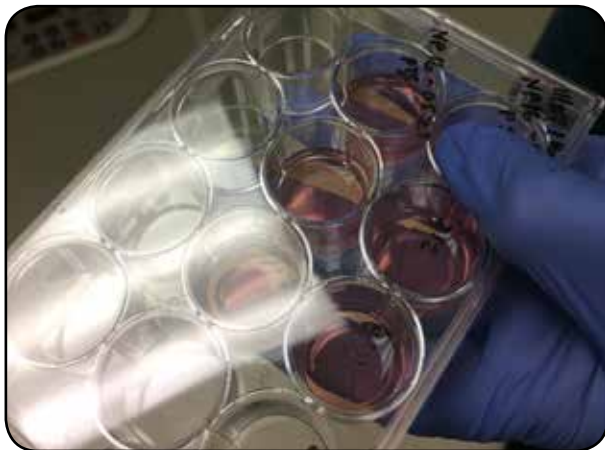
They use these cells as ‘disease-in-a-dish’ models to ask questions they can’t with a mouse. How does an individual’s unique genetic background contribute to risk? Which genotypes respond to which classes of drugs? The idea is to identify therapeutic targets and establish ways to match people to the clinical trials most relevant to their underlying condition.

In fact, Young has already demonstrated an example of how the iPSCs process can work in a precision medicine approach to Alzheimer’s disease.

How it Works

Young focuses on a gene called SORL1, an important actor in a cellular pathway that processes amyloid beta and prevents it from building up in toxic clumps in our neurons. That pathway works better in some people than others. Scientists have identified variants of SORL1 associated with increased risk of Alzheimer’s after age 65, and some that confer a protective effect. These are common variants in the U.S. population.

In previous work at the University of California San Diego, Young made neurons from the skin cells of people who carried one or more of these SORL1 variants. She treated the neurons with a compound, “brain-derived



neurotropic factor” (BDNF), that induces the activity of SORL1. This is a change that would, in theory, boost the cells’ ability to deal with amyloid beta.

She found that the neurons behaved differently depending on their SORL1 genetics. The ones with the protective variant showed a robust response to BDNF. They ended up with low levels of amyloid beta, as compared to the neurons carrying the risk variant. The cells carrying the risk variant, on the other hand, responded better to a different experimental compound.

“So, this finding sets a principle for the use of the iPSCs system to identify people who are appropriate for a clinical trial,” she said. “You can imagine that people with the SORL1 risk variant might not be right for a trial of BDNF because they wouldn’t respond to the treatment,” she says. “What’s more, the researchers might think that the trial failed, while it may have worked for a sub-group of patients.”

She and her team are now using gene-editing technology, called CRISPR, to snip out the SORL1 gene from iPSCs-derived neurons, in order to learn more about the impact of its loss. In collaboration with pharmaceutical company Biogen, they will try to target parts of this pathway for treatment.

In parallel, Young is working with the ADRC’s Dr. Suman Jayadev, Assistant Professor of Neurology, UW Medicine, to engineer methods to create iPSCs brain immune cells from patients carrying a familial gene mutation. Jayadev’s lab will find out how these cells succumb to inflammation and secrete toxic chemicals that make other brain cells sicker—and how to halt this process. **Continued on Next Page...**

8 Neuropathology's Next Top Model

To develop a truly complete laboratory model of sporadic Alzheimer's disease, researchers need to know how accurately the iPSCs neurons represent the disease process in the actual patient. There's only one way to find out. They need to analyze the cell donor's post-mortem brain tissue from autopsy, which gives definitive proof of Alzheimer's disease proteins.

Fortunately, the ADRC's Neuropathology Core, led by C. Dirk Keene, Associate Professor of Pathology, UW Medicine, offers the perfect resource in its protocol of rapid brain autopsy (one happening < 8 hours after death) for ADRC research participants.

Keene and his team have started to collect cells from each participant during brain autopsy, for the creation of iPSCs. They take samples of leptomeningeal cells, which form a type of connective tissue on the outer lining of the brain. Many of these cells are still alive at this point, so Keene and Young think that they can be differentiated into neurons.

Together, they will create a bank of iPSCs from ADRC participants. "What's amazing about this project is that we will have autopsy confirmation of Alzheimer's disease and clinical records to go along with the iPSCs neurons," says Keene. "So, cell biologists will be able to compare what they see in the living cells to what neuropathologists see in the post-mortem brain tissue." Then, they will have higher confidence in their Petri dish model.

The ADRC's bank of iPSCs will also help solve some mysteries about neurodegeneration. "We often come across cases of Alzheimer's disease that don't conform to what we expect in terms of symptoms or pattern of atrophy in the brain," says Dr. Thomas Grabowski, Professor of Neurology and Radiology, UW Medicine, and Director of the ADRC. "Now, we can make neurons out of a patient's fibroblasts after autopsy and study their physiology in living tissue. I think it's a breakthrough."

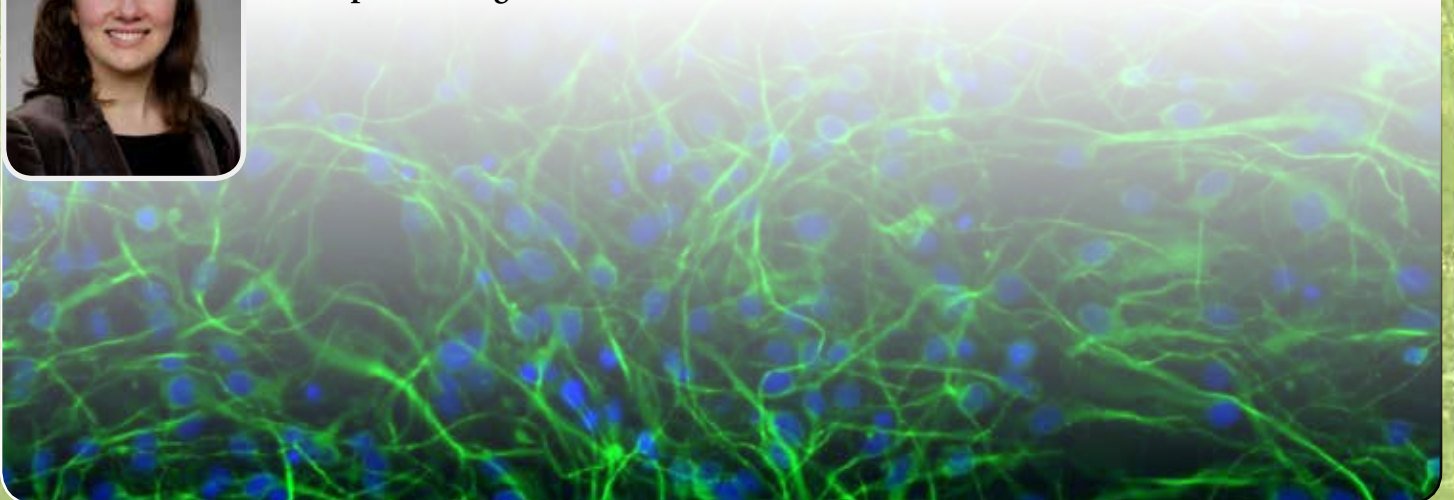
As for me, I'll always be wondering what my neurons-in-a-dish are up to. I suppose I'll have to be satisfied with just keeping a close eye on the iPSCs research unfolding down the hall. Because I—like so many of us with affected family members—have some skin in this game. •



The ADRC bank stores samples of patient stem cells frozen in liquid nitrogen.



Genevieve Wanucha, MS, is the science writer for the UW Memory and Brain Wellness Center and UW ADRC. For more news stories and features, visit www.depts.washington.edu/mbwc



Rising Stars in Alzheimer's Research

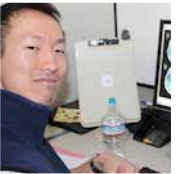
In 2016, the ADRC received funding from the National Institutes of Health for a T32 Grant program: “Neurobehavior, Neuropathology, and Risk Factors in Alzheimer’s Disease.” Our project is helping six aspiring scientists to build expertise in basic, clinical, or translational research, without having to apply for an individual position in a lab. The trainees are working in the rich and interactive research environment of the UW and the Veterans Affairs Puget Sound Health Care System. Training support is provided for three years.

“The goal of our T32 program is to train the next generation of Alzheimer’s disease researchers,” says Dr. Elaine Peskind, ADRC Clinical Core Leader, who runs the T32 program along with Dr. Brian Kraemer and Dr. David Cook, both researchers in the UW Division of Gerontology and Geriatric Medicine.

Meeet the T32 Training Grant awardees!



Sarah Waldherr, 3rd year PhD student, UW Division of Gerontology and Geriatric Medicine, UW Molecular and Cellular Biology Interdisciplinary PhD Program. Waldherr investigates the mechanisms of Alzheimer’s disease protein pathology. She aims to determine whether her findings in a genetically modified worm model translate to mammalian systems using human cell culture models and mouse models. She works in Dr. Brian Kraemer’s lab.



Phillip Hwang, 3rd year PhD student, UW Department of Epidemiology. Huang’s work focuses on sleep medication use and dementia among Veterans with post-traumatic stress disorder. He is working with Dr. Debby Tsuang at the Geriatric Research Education and Clinical Centers Home (GRECC) in the VA.



Macarena Aloï, 3rd year PhD student, UW Department of Pathology. Aloï studies the molecules that modulate inflammation in Alzheimer’s disease. She recently moved on from the T32 Grant program after being awarded an HHMI Gilliam Fellowship by the Howard Hughes Medical Institute.



Aric Logsdon, PhD, Postdoctoral Fellow, UW Department of Medicine. Logsdon studies the vascular risk factors of Alzheimer’s disease. He models cellular and physiological cerebrovascular systems to determine how blood-brain barrier perturbation may contribute to neurodegenerative disease. He works with Dr. William Banks.



Mary Nivison, PhD, Senior Fellow Trainee, UW Department of Psychiatry and Behavioral Sciences. Nivison focuses on a genetic mutation of TREM2, a receptor on microglia, which results in a very increased risk of early onset Alzheimer’s disease. In Dr. Wendy Raskind’s lab, Nivison is designing cell models to study the effects of the TREM2 mutations to ultimately try to develop therapeutic targets.



Sarah Benbow, PhD, Postdoctoral Fellow, UW Division of Gerontology and Geriatric Medicine and the VA. Benbow works in Dr. Brian Kraemer’s lab to create improved animal models to study the role of tau protein in the pathology of Alzheimer’s disease and other neurodegenerative conditions.

Recipes for a Healthy 2017

So many foods show benefits for our hearts and brains, but it's not always easy to get them into our diet on a daily basis. We've asked some of our team members to give us their favorite, quickest recipes featuring one of the key ingredients!

Go Nuts! **Dr. Angela Hanson**, geriatrician at the UW Memory and Brain Wellness Center (MBWC), recommends these little packages of unsaturated fats, antioxidants, protein, fiber, vitamins, minerals, and phytosterols. In fact, the PREDIMED study in Europe showed that regular consumption of walnuts, almonds and hazelnuts, as well as olive oil, was associated with better scores on memory tests.

To get the recommended amount of **nuts** a day (a handful), try using them on salads instead of cheese or meat, or toss them into yogurt, just like **Andrew McCormick**, social worker at the UW MBWC, does every morning with fruity flair:

Andy's Bountiful Breakfast

For 1 serving, mix together:

2 heaping tablespoons of Greek yogurt

2-3 heaping tablespoons of granola. Keep it simple with granola made from grains, seeds, and nuts.

1-2 heaping tablespoons of broken nuts, such as walnuts and almonds

Fresh or dried fruit of your choice. Suggestions: blueberries, raspberries, marionberries, blackberries, cut up apples, pears, melons, apricots, or raisins. Enjoy!



Dark and Leafy! **Collard greens** are a rich source of vitamin K. Research published in *Neurobiology of Aging* has shown that healthy people over 70 with higher vitamin K levels had better short term memory performance than those with lower levels. **Teah Hoopes**, ADRC Research Project Manager, gives her family's recipe for Collard Greens.

The Hoopes Family Collard Greens

4 servings

Prepare 1 bunch of collard greens by rinsing in cold water and chopping them.

Place the collard greens in large pot with water (just enough to cover greens) and bring to a boil. Let boil for 5 minutes and then remove from heat.

While greens are boiling, warm 1 teaspoon of olive oil on medium heat.

Add collard greens to the olive oil and add seasoning (salt, pepper, red pepper flakes) to taste.

Drizzle red wine vinegar over the collard greens just prior to serving.



Smart about Sugar! Evidence shows that a diet filled with sugar overtaxes your metabolism, setting the stage for diabetes, obesity, heart disease, and even cognitive impairment. Did you know that many prepared savory foods have added sugar? For example, bottled tomato sauces can contain as much sugar as a Pop Tart! Making tomato sauce from scratch is surprisingly easy, affordable, and so delicious that you'll never buy another jar. Every week, **Genevieve Wanucha**, science writer for the UW MBWC, cooks up a simple red sauce that celebrates the flavors of **tomatoes** and **fresh herbs**—the hallmark of this pasta topping. They deliver a rich source of heart- and brain-protective phytonutrients, flavanoids, and vitamin K.



Genevieve's Perfect Pomodoro

4 servings of sauce

In a large skillet, heat 3 tablespoons of olive oil and sauté a finely chopped shallot and clove of garlic until translucent but not brown, about 1 minute. Pour in a 28-ounce can of crushed San Marzano tomatoes and a 1/4 cup of water. Toss in 3 whole springs of fresh oregano and 3 large fresh basil leaves. Bring this sauce to a simmer and let it bubble gently for 45 minutes, stirring often to prevent the bottom from burning. Remove the wilted herbs. Add 1 teaspoon of salt and black pepper, to taste. Serve on pasta with a generous sprinkle of chopped parsley and/or basil.

Got the Blues? **Blueberries** are gaining recognition as a super food for heart and brain health. ADRC researcher **Dr. Ignacio Fernandez Mata** packs them into his morning smoothy, along with several other healthy ingredients, namely avocado.

Nacho's 'Great Start' Smoothie

1 serving

Blend: 2 cups blueberries, 1/2 cup 2% milk (or almond milk), 6 ounces Greek-style yogurt, 2 ice cubes, 1 tablespoon chia seeds, 1 ripe banana, peeled, and half of an avocado, peeled and pitted.



Always Hungry? **Avocado** toast comes recommended by **Marigrace Becker**, Program Manager of Community Education and Impact at the UW MBWC. It's one of the easiest and quickest, most filling and delicious, healthiest breakfast or lunch you can find.

Mari's Avocado Smash

With a fork, smash half of a ripe avocado onto a slice of toasted whole wheat bread. Drizzle with olive oil and sprinkle with salt and red pepper flakes, if desired. For a bigger meal, you can also add sliced hardboiled eggs, chunks of canned tuna or salmon, or red onion and baby greens.

This year, remember that what's good for the heart is good for the brain!



Collaborating for Statewide Innovation in Dementia Care Policy

By Marigrace Becker, MSW



In early 2016, the Washington State Legislature approved the WA Plan to Address Alzheimer’s Disease and Other Dementias. Dr. Kristoffer Rhoads of the UW Memory and Brain Wellness Center (Back row, 2nd from left) helped shape the plan’s development. Photo by Mikaela Louie

With a multidisciplinary team of doctors, ADRC researchers, and community education staff, the UW Memory and Brain Wellness Center (MBWC) understands the power of collaboration when it comes to promoting the well-being of people living with memory loss and their loved ones. So when the opportunity arose to play a key role in Washington State’s “Dementia Action Collaborative,” we jumped at the chance.

So what is the Dementia Action Collaborative (DAC), and how are we involved?

The WA State Plan to Address Alzheimer’s Disease and Other Dementias sets out visionary goals and recommendations on raising awareness, ensuring early and accurate diagnosis and treatment, and improving supports and services for families.

With over 100,000 Washingtonians living with dementia, and the numbers anticipated to triple by 2050, the plan can’t be more timely. Ready to take action on these recommendations, the state convened the DAC in April 2016.

The DAC is a voluntary public-private partnership that aims to guide and support the implementation of the state plan. Members are divided into three subcommittees: Public Awareness and Community Readiness, Health and Medical, and Long-Term Supports and Services. The MBWC’s expertise in the realms of clinical care, research and community are perfectly suited to support this vital work.

“Our center has a well-integrated vision for promoting the well-being of people with memory loss, and we’re the state’s primary provider of specialty diagnostic and treatment services,” says Dr. Kristoffer Rhoads, MBWC neuropsychologist. “We want to see this kind of approach filter throughout the state. So we’re glad to be involved – both for the expertise we bring, and what we can learn from others.”

Rhoads chairs the Health and Medical Subcommittee. He and his team members are taking action on three recommendations: convening an expert panel to identify evidence-based standards for diagnosis, treatment, and supportive care for people with dementia, recommending the best cognitive-

screening tools, and helping promote effective memory assessment within the Medicare Annual Wellness Visit.

Early on, Rhoads' subcommittee addressed their first goal by strategically aligning with the governor-appointed Bree Collaborative – a group focused on improving healthcare services throughout the state. Each year, this group chooses up to three health care services with high variability in treatment approach and patient outcomes, and identifies and recommends best practices. For 2017 – thanks to the advocacy of Rhoads and his team – the Bree Collaborative chose dementia.

Rhoads is excited about the progress his team has made and the impact this will have on the community. “These guidelines and tools are something primary care providers have been asking for,” says Rhoads. “Creating a standard pathway to early diagnosis is an important first step – which then enables people to get the treatment and community resources they need in a timely fashion.”

The ADRC's Dr. Suman Jayadev, UW Medicine neurogeneticist, also lends her expertise to the Health and Medical Subcommittee. She agrees with Rhoads on the value of reliable screening tools – not only as a gateway to treatment interventions that may slow changes in memory and thinking, but also a way for people to find out if they qualify for research studies. “If people can get their Alzheimer's disease identified early and accurately, they can be alerted to any good clinical trials that might be out there,” she says.

Along with medical care and research, the MBWC's experience with building dementia-friendly communities is also being put to use in the DAC. As the MBWC's program manager for community education and impact, I've had the chance to lead a DAC project team producing a fact sheet that identifies the key elements of a dementia-friendly

community.

Too often, people with memory loss and their families end up isolated because of social stigma or other barriers to inclusion. We want to make sure Washington State is a place for all people to belong – by building understanding, challenging stigma, and incorporating simple practices that people with memory loss note would help them fully participate and contribute. For example, we envision providing dementia-awareness training for bus drivers, grocery store clerks, bank tellers, and emergency responders.



In Washington, we have a head start through Momentia – a grassroots movement empowering people living with memory loss and their loved ones to stay connected and active in the community. By defining dementia-friendly communities, and by highlighting this local effort – such as the Frye Art

Museum's here:now program, the memory loss walk at Woodland Park Zoo, or the dementia-friendly volunteer program at Cherry Street Food Bank – our DAC project team hopes to inspire and equip other communities around the state to become dementia-friendly.

By the end of 2016, the DAC had completed a number of the state plan recommendations. One that has many DAC members excited is a “road map” document to help caregivers every step of the way. As Rhoads says, “the road map is going to be, and already is, a huge tangible informative tool for families.”

Collaboration is the key to these early successes. Jayadev notes, “I really enjoy that the DAC has so many facets of the community represented – people who have early Alzheimer's disease, people who are caregivers, researchers and clinicians, individuals from the state, plus other agencies like housing and senior services. And everyone is genuinely committed to working on this together!” **Continued on Next Page...**

As the medical director of the MBWC and director of the ADRC, Dr. Thomas Grabowski, Professor of Neurology, UW Medicine, has supported our involvement every step of the way. “The work of the Dementia Action Collaborative aligns perfectly with the MBWC clinic - we strive to embody the best practice in medical care, while building public understanding of Alzheimer’s disease and other dementias so our patients will be able to rely upon a community of support. We’re proud to be involved in this collaborative effort.” •



Marigrace Becker, MSW, is the Program Manager of Community Education and Impact at the UW Memory and Brain Wellness Center. You can find MBWC’s community events, educational programs, news, memory loss handbook, and more resources at the following link:
www.depts.washington.edu/mbwc/

Washington State Plan to Address Alzheimer’s Disease and Other Dementias: 7 Goals

1. Increase public awareness, engagement and education
2. Prepare communities for significant growth in the dementia population
3. Ensure well-being and safety of people living with dementia and their family caregivers
4. Ensure access to comprehensive supports for family caregivers
5. Identify dementia early and provide dementia-capable evidence-based health care
6. Ensure dementia-capable long-term services and supports are available in the setting of choice
7. Promote innovation and research related to causes of and effective interventions for dementia

Dementia-Friendly Communities for Washington State: 9 Key Elements

In a dementia-friendly community, people with memory loss...

1. Are respected as valuable members of the community.

2. Can participate confidently in their communities – their neighborhoods, stores, restaurants, banks, libraries, schools, and hospitals - knowing that the people who live and work there are dementia-aware.
3. Stay connected to their family, friends and neighbors, while having the chance to make new relationships.
4. Enjoy meaningful lives, with access to education, recreation, work or volunteer opportunities, cultural enrichment, and more.
5. Have a voice in their community and a leadership role in anything particularly impacting the lives of people with memory loss.
6. Have access to early diagnosis and post-diagnostic resources for themselves and loved ones, including medical care, education and support, financial/legal services, and advance care planning.
7. Have transportation options that help them stay involved in their community.
8. Have community housing options that provide the level of support they want, in the setting they desire.
9. Can navigate neighborhoods and public spaces because the physical environment is supportive and clear.



In 2016, we helped our community partner, the Art of Alzheimer's Marilyn Raichle, pioneer *The Artist Within* exhibit, a collection of vibrant and thought-provoking artworks by people with memory loss or dementia. The showings at Seattle City Hall and the Harborview Medical Center drew attention from the general public and even the Seattle Times, with its February 8, 2016 article *Alzheimer's art exhibit takes away fear, sows hope*.

The Artist Within exhibit is on display at on the first floor of the UW School of Social Work building, and will later travel to the Washington State Convention Center. You can find the artists' bios on the Art of Alzheimer's website: www.theartofalzheimers.net



W SCHOOL OF SOCIAL WORK
UNIVERSITY of WASHINGTON

The Artist Within

An Exhibit Presented by
THE ART of Alzheimer's

January 9 – March 31, 2017
UW School of Social Work
First Floor Gallery
4101 15th Ave NE, Seattle
8 AM–6 PM MON.–FRI.

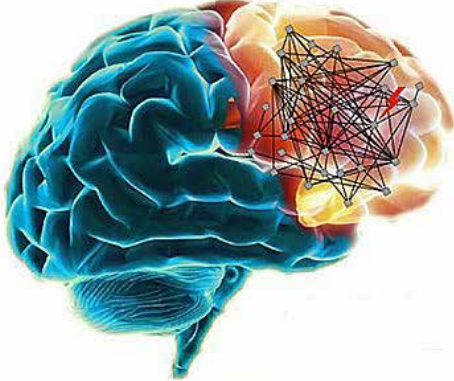
Reception: Thursday, Jan. 19, 4–6 PM



Agitation Antidote

A promising, targeted medication for disruptive behaviors is finally getting its due in a clinical trial.

As many families and caregivers know, people in the mid to later stages of dementia can be prone to agitation. Behaviors such as nighttime wandering, uncooperativeness, and aggression rank high on the list of reasons that families must place loved ones into care facilities. But there is something that can help, and may even make it possible for patients to remain at home.



At the ADRC, Dr. Elaine Peskind and Dr. Murray Raskind, both professors in the UW Department of Psychiatry and Behavioral Sciences, UW Medicine, think that the answer is prazosin, an FDA-approved drug for hypertension. As of 2013, prazosin has been used off-label in the US for many disorders, notably to relieve anxiety experienced in post-traumatic stress disorder (PTSD). In the clinic, they have observed a real benefit of this drug for disruptive agitation in patients with Alzheimer's-disease type dementia.

Now, Peskind and Raskind are co-principal investigators of PEACE-AD, a multi-center clinical trial in the Alzheimer's Disease Cooperative Study. This trial will test prazosin in 186 nursing home residents with probable or possible Alzheimer's disease. The 25 sites are located in cities across Kentucky, Texas, California, Arizona, and Washington State.

"The hope is that this study will provide evidence of the safety and effectiveness of prazosin in this patient population and establish dosage guidelines for physicians to use," says Peskind. "Because right now, there are no good treatments for disruptive agitation in dementia. What's mostly used for this population are the atypical antipsychotics, which are not that beneficial and have side effects of stroke and sedation."

Prazosin, on the other hand, carries none of those side effects in dementia patients. What's more, it's a rare example of a psychiatric drug being precisely targeted to an underlying problem in the brains of people with Alzheimer's symptoms.

For the last 35 years, Peskind and Raskind have found consistent evidence that Alzheimer's patients have excessive activity of the brain's adrenaline, a neurotransmitter called norepinephrine. On a circadian rhythm, this adrenaline hyperactivity peaks at 4pm, explaining the phenomenon of 'sun-downing,' or late afternoon irritability, in patients with dementia.

Prazosin blocks the effect of the brain's adrenaline at its source in the brain, a receptor called alpha1. As the activity quiets down, the patient, and care partner, experiences relief.

"I'm a firm believer that disruptive agitation in dementia patients represents suffering, discomfort, or distress on their part," says Peskind. "This medication could help caregivers and patients, whether they live at home, in nursing homes, or long-term care facilities."

Families dealing with a form of neurodegenerative disease associated with severe behavioral issues, such as frontotemporal degeneration (FTD), may wonder if this medication might benefit their loved ones. Peskind says that she has no reason to believe that prazosin is only effective in Alzheimer's disease-type dementia, but that research has not yet shown brain adrenaline hyperactivity in other forms of dementia.



Dr. Elaine Peskind



Dr. Murray Raskind

The good news is that families don't have to wait for the end results of the PEACE-AD clinical trial to access prazosin, as it can be used off-label. People can bring this news to their doctors. "We would be happy to take calls from peoples' doctors and give advice about how to use this medication," says Peskind. "We've done it before." •

Image Credit: Dr. Mary-Claire King, UW

Contact Information

- UW Alzheimer's Disease Research Center: 206.744.0588
- For a list of all UW ADRC Clinical Trials & Studies, please visit:
www.depts.washington.edu/mbwc/research/clinical-trials

Support the Alzheimer's Disease Research Fund

Donations help support patient- and family-centered care, research breakthroughs in Alzheimer's-type dementia and related disorders, and the training of tomorrow's physicians. And by giving — perhaps in gratitude for care, or in memory of a loved one — you can help improve the lives of your friends, your family, and others in your region.

If you would like to be our partner in enhancing health and changing lives, please contact the UW Medicine Advancement Office at 206.543.5686. To donate online, please use the following link:

www.supportuwmedicine.org/adrc



Investigating the Effects of Air Pollution on Brain Health

Air pollution in America, at the lowest it's been in four decades, is still a major public health problem. It's also a public brain health problem, linked to increased risk of cognitive decline.

Researchers from the ADRC have teamed up with the Group Health Research Institute and the UW School of Public Health to investigate the role of air pollution exposures on memory and the risk for Alzheimer's disease and other dementias.

The team of neuroscientists, environmental scientists, epidemiologists and biostatisticians are studying a cohort of aging Seattle area residents and 40 years of air pollution monitoring data from the Puget Sound Clean Air Agency. The project received more than \$3 million over five years from the National Institute of Environmental Health Sciences and the National Institute of Aging.

"While the study focuses on residents in a relatively low-pollution area, the findings will address gaps in our knowledge about the true scope of the risks of air pollution exposure to the brain, even at lower levels," says Dr. Lianne Sheppard of the UW Departments of Environmental and Occupational

Health Sciences and Biostatistics, who will co-lead the five year effort with Dr. Gail Li of the ADRC.

Ultimately, the researchers hope to provide the strong research findings needed for regulators to even consider reshaping environmental policy with the brain in mind.

"This study is particularly exciting because it adds geographical information systems (GIS) approaches to the many sources of data we are able to tap into to learn more and more about the aging brain," says Dr. Paul Crane, multiple PI of the ACT study and Professor of Medicine, UW Medicine. To improve their computer modeling of local air pollution exposure, the epidemiology team will deploy new networks of sensors to take additional measurements of ambient fine particulate matter, ozone, and nitrogen oxides in the neighborhoods of study participants.



Dr. Gail Li

A Living Learning Laboratory of Aging

The study's cohort of aging individuals comes from the Adult Changes in Thought (ACT) study, a joint project between Group Health Research Institute and the UW. The ACT Study is led by Dr. Crane and Dr. Eric Larson, clinical professor in the UW Department of Health Services and Vice President for research at Group Health.

More than 5,500 aging Group Health patients without dementia who live in King County are randomly selected to approach for enrollment in the ACT cohort. Extensive baseline information is collected, and then the health status and cognitive function of each participant is evaluated every two years. To date, more than 1,000 people have developed dementia. Researchers involved in the ACT study are investigating the environmental and genetic factors that determine the risk of developing a degenerative brain disease.

ACT—what Dr. Eric Larson, co-principal investigator and founding director of the study, calls a “living learning laboratory of aging”—provides a readymade study population, drawing on existing healthcare records to perform retrospective health research without the cost it would normally require. At the very beginning, Larson made sure that the ACT study collected information on participants' socio-economic status, places of residence and work, and neighborhood characteristics—all important data points for answering epidemiological questions about air pollution exposure.

A Matter of the Heart

The air pollution-dementia link might reside in the heart. For ten years, Sheppard has been part of the Multi-Ethnic Study of



Atherosclerosis and Air Pollution (MESA Air), the first U.S. research study to examine how long-term exposure to air pollution contributes to the development of heart disease in six U.S. cities. The long-awaited findings, recently published in *Lancet*, show that air pollution increases the accumulation

of coronary artery calcium, a subclinical marker of heart disease, even at levels near the National Ambient Air Quality Standards. Heart disease is the leading cause of death in America.

These MESA results could very well foreshadow what Sheppard and Li find out about dementia in the Puget Sound, considering the evidence that heart disease ranks high on the list of risk

“The ACT study team is so grateful for the people who participate in this study,” says Dr. Larson. “It’s a great resource for this important public health question.”

factors for dementia. In previous work in the ACT cohort, Dr. Li found that vascular risk factors for heart disease contributed to an increased risk of dementia. In this new study, she aims to figure out if reduction of cardiovascular risk factors can be a way to reduce risk of dementia.

The project also involves the study of the donated post-mortem brain tissue from ACT participants, which is rare in longitudinal epidemiologic research. This work, led by Dr. C. Dirk Keene of UW Medicine and the ADRC, aims to help identify the possible pathways, such as inflammation and oxidative damage, by which air pollution contributes to plaques and tangles or directly kills neurons.

As for the ultimate goal of improving environmental policy, Sheppard is more optimistic than impatient. She says that she chooses to study air pollution, not because it's definitely the worst pollutant, but because the existing mechanisms to tighten regulations available through the Clean Air Act, as well as the ease of monitoring air pollution, make effective research and policy change possible.

“The nice thing about air pollution exposures of all kinds is that we have control, collectively as a society, over how much pollution is acceptable,” she says. “And if we change the regulations according to scientific research, we can affect the cognitive health of everybody who breathes the air.” •

20 “They Have My Best Interests at Heart”

An Essay by Philip Culbertson



Our friend from the community tells of his journey to the diagnosis of dementia and of how his life has changed since accepting his children's help.

I'd moved back to the United States after retiring from a very gratifying career overseas and had landed a job teaching part-time at the local community college in Palm Desert, California. Late in 2011, while being driven to the college by a student, we were in a car wreck. I was severely concussed. My doctors followed the progress of my brain injury for over three years, but while they could see the physical damage to my brain, what they couldn't really tell was how much damage was concealed within those x-rays.

During those three years, two different psycho-neurologists and two different psychologists tried to make sense out of my repeated test results. Ultimately, in the fourth year, we gave up. By then it was clear that I'd lost my perspective on what was happening and what would be needed. I cooperated when my kids announced that they were moving me to Seattle in the hopes that a larger city would have more sophisticated testing equipment.

My two children tell me that I was “acting out” long before I myself can remember doing so. Certainly, I was aware that I was being extremely generous with my life savings, thinking that treating myself to new clothes (buying up to 10 shirts at a time for example), pledging funds to political and charitable organizations and taking friends to dinner often, and footing the bill, was just what people who were comfortably retired after a successful career were supposed to do. However, my children were much more frugal, having become aware that as we age, we have more and more expenses to bear.

They were right and I was foolish.

In late spring 2015, brain x-rays were showing sufficient injury that my children decided to step in and take over large parts of my life. I let them. I've heard too many stories over the past several decades to know not to argue with my kids but to hear them out. Most of the time they understood me, probably because we've been so close over 30 years. And I have always trusted that, when needed, they would have my best interests at heart — although according to their definition!

While I'm sure it was taxing for them, they persisted on presenting things this way: “Dad, here are three choices that need to be made, and we'd like you to choose the one you feel is best. Then we can all discuss together whether we agree with your choice or not.”

Their strategy has worked so far, for the most part, to everyone's benefit. In hindsight, that whole phase in which we were involved in a sort of tug-of-war was the most critical phase for me. At that point I let go of my need for control, sensing that my kids now knew better than I did about what was needed.

In early summer 2015, I flew to Seattle to tour possible places to live. We kept in mind that our search was for me—at risk of losing my mind but according to an unknown timetable. My daughter had done her homework well. I didn't have to see all the sites before I realized how well she knew me. The first place was wonderful and I wanted to move in immediately, but she insisted that I at least see the second place.

At both locations, arrangements were made for me to meet some of the residents. I found that, in both groups, each person had experienced some unique brush with death and they had grown to respect, challenge, support, and rescue one another.

And importantly, I found that there was a reliable system of professionals and carers, and that no one needed to experience alone the taxing and often frustrating things that mark the end of life. Shortly after the decision was made to move me to Seattle, both my kids took me to Harborview Medical Center, where we heard the diagnosis:

“Early Alzheimer’s—with a life expectancy of 2 - 20 years.”

The first three to four months in the residential care center were pretty rocky for all of us. I’d been single for years and certainly not used to taking orders from anyone, especially my children. I still wanted to be the parent but I was increasingly unable to make good decisions. That made me angry with them—and with myself!

The more I talked openly with others, the more I learned. Feeling ashamed is one of the great enemies of a healthy approach to Alzheimer’s and dementia. Shame can cause us to hide, stop telling the truth, avoid others, skip attending worship, not enjoy our friends, or fail to take care of our own bodies.

With my kids’ help, I accumulated a bevy of supporters, including a therapist, a hospital chaplain, the doctors at Harborview, various other professionals and specialists and a place to worship. Most importantly, I have my children and grandchildren. Together we are learning that none of us should hide in the dark out of fear, however much each of us also has individual needs to be left alone at times.



I have good days and bad days, and many days are a combination of both. I’ve always slept very well. Now I often don’t. I start into a sentence and then can’t remember what I was going to say. Sometimes I blank out on particular words, or I can’t pull up the names of friends even when they are standing near me. I have learned to write EVERYTHING down, in detail, including things that I was quite sure I’d never forget to do.

The center has taught us the importance of establishing a daily routine, possibly built around the times when we take our medications, and to prioritize our time. For example, I now have many more doctors’ appointments in my life than ever

before. No matter how intrusive I feel they are, they must be prioritized over my other commitments and activities.

In the residence where I live, I have been given a one-on-one Alzheimer’s consultant who sees me weekly. She has encouraged me to create a list of the things that I believe are making my life more manageable, most of which are supported by the medical literature. My list for her today was:

1. Play the piano, even if my hands are trembling.
2. Work crossword puzzles, the more difficult the better.
3. Go for a walk—about an hour a day.
4. Play with my grandchildren when they visit.
5. Sing weekly in a men’s barbershop chorus.
6. Maintain a part-time job—in my case as an editor of academic articles for publication.
7. Teach a course to a group of residents on Third Century Jewish literature.
8. Make sure my spiritual needs are being met on a regular basis by people whom I trust.

My journey through Alzheimer’s continues to be marked with alternating times of bravery and fear, expectation and resignation, clarity alternating with frustrating confusion, and one hell of a lot of paradox. Yet journeys like mine need to be brought into the open rather than kept in the dark, addressed rather than being ignored or minimized. By sharing our story, I believe the fear of death is challenged and ultimately even transformed. •

Philip Culbertson wrote this article for Tui Motu Magazine, where it appeared in June 2016. It is reprinted here with his permission.

Watch him share his story of memory loss with children in a local day camp as part of the MBWC’s community education workshop, ‘Our Time Has Come,’ at:

www.depts.washington.edu/mbwc/news/article/our-time-has-come

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